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Sleep and chronic rhinosinusitis: a systematic review of postoperative data

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Abstract

Introduction Patients with nasal obstruction due to chronic rhinosinusitis with nasal polyposis may present with altered sleep quality. Data on this subject in the literature remains scarce.

Objectives To evaluate changes in sleep quality and polysomnographic parameters among patients who underwent functional endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis.

Materials and Methods A systematic review was performed in three databases: PubMed, Cochrane, and Embase. The following keywords were used: chronic rhinosinusitis, nasal polyposis, sleep quality, and nasosinusal endoscopic surgery. Studies evaluating adults with nasal polyposis who underwent endoscopic nasosinusal surgery were selected. A meta-analysis was conducted to compare mean scores for polysomnographic and subjective variables from before to after the operation.

Results A systematic review and meta-analysis of three studies were performed, only one of which was randomized. The total sample consisted of 64 patients. There was a decrease in the mean AHI score and improvements in mean and minimum saturation. The mean difference in percentage of stage N3 from before to after the operation was 1.12 with a 95% CI from −3.51 to 5.75, which was non-significant. There was a mean percentage increase in REM sleep duration and a decrease in PSQI scores, which were both statistically significant ($p < 0.05$).

Conclusion There were improvements in the quality of sleep and duration of REM sleep after surgery, with no improvement in polysomnographic respiratory parameters.

Keywords
- nasosinusal endoscopic surgery
- sleep quality
- Chronic rhinosinusitis with nasal polyposis

Introduction

Nasal breathing is the physiological route of breathing, and this maintains the respiratory rhythm during sleep.[1] Airflow through the nose activates receptors that stimulate spontaneous ventilation and improve the muscle tone of the upper airways.[2] According to a study by Eriksson et al,[3] nasal obstruction is a problem reported by ~15% of the population. It is commonly related to snoring, sleep-disordered breathing, and obstructive sleep apnea (OSA).[4]

As a matter of quality of life, sleep can be severely affected among patients with nasal obstruction due to increased upper airway resistance and increased nocturnal awakenings[5]

The test is used for objectively studying sleep and the gold standard for diagnosing OSA is polysomnography. Through

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this, it is possible to quantify the apnea-hypopnea index, saturation, and even the presence of snoring.[6]

Quality-of-life questionnaires are subjective tools for assessing whether patients are suffering from sleep-related symptoms that may affect their quality of life or even whether they are at risk of developing OSA.[7]

Among the obstructive nasal causes, we find chronic rhinosinusitis (CRS), which is an inflammatory condition of the paranasal sinuses that often causes symptoms such as nasal obstruction (most commonly), facial pain, drainage of thick nasal secretion, and hyposmia for at least 12 consecutive weeks.[8] According to the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020), it has a prevalence of 5–12% of the general population and is subdivided into primary or secondary chronic rhinosinusitis, being localized or diffuse based on anatomical distribution.[9]

Chronic Rhinosinusitis with Nasal Polyposis (CRScPN) is of the diffuse primary type 2.[9] Nasal polyps are benign inflammatory lesions in the nasosinusal mucosa that usually develop bilaterally and are associated with nasal obstruction and, therefore, with a decrease in quality of life, making this disease clinically important.[10]

The treatment for CRS can be clinical, for example, through application of topical nasal corticosteroids, and/or surgical in cases of therapeutic failure, through endoscopic sinus surgery (ESS).[11]

Studies have correlated CRS with or without nasal polyposis with OSA.[9–11] There are also some studies that have assessed quality of life and sleep among individuals undergoing endoscopic sinus surgery.[12–16] However, there is a scarcity of data in the literature providing systematic analysis on changes to sleep quality and polysomnographic parameters among patients undergoing endoscopic functional surgery of the paranasal sinuses to treat chronic rhinosinusitis with nasal polyposis. This gap in the data thus forms the objective of the present study.

Materials and Methods

This study consisted of a systematic review followed by a meta-analysis. It followed the method of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[17] The study selection criteria for this review were formulated in accordance with the PICO format[18] (population, intervention, comparison, results) and types of study.

Population

Adults (aged 18 years and/or older) are diagnosed with OSA with chronic rhinosinusitis with nasal polyposis (CRSwNP).

Intervention

Functional endoscopic sinus surgery of the face (FESS).

Comparison

Improvement of polysomnographic parameters (apnea/hypopnea index (AHI), oxygen saturation, N3 and REM stages), snoring, and sleep quality.

Result

Analysis of studies in which FESS was performed on patients with nasal polyps and OSA.

Study Design

Analysis of observational and interventional studies in which ESS was performed on patients with OSA.

A systematic search was conducted in three electronic databases: PubMed, EMBASE, and Cochrane Library. This search was performed using the following Medical Subject Headings (MeSH): 'endoscopic sinus surgery' and 'sleep', along with alternative terms such as 'functional endoscopic sinus surgery' and 'sleep quality', without language restriction.

Experimental animal or in vitro studies, expert opinions, letters to the editor, systematic and literature reviews, meta-analyses, or any other descriptive studies were excluded. Abstracts were excluded if they dealt with chronic sinusitis without nasal polyposis or did not contain polysomnographic or sleep quality data.

Given the variety of definitions and classifications for chronic sinusitis with nasal polyposis, as well as the different surgical techniques used in its treatment, no specific limitation was placed on these topics. The mandatory criterion for studies to be included was that participants diagnosed with nasal polyposis who underwent endoscopic surgical treatment had been evaluated both before and after surgery, by means of polysomnography and validated sleep quality questionnaires, such as the Epworth Sleepiness Scale (ESS) [12] and the Pittsburgh Sleep Quality Index (PSQI).[13]

To assess the risk of bias in the studies, we used the Cochrane Tool.[14] In this, the following were analyzed: sequence generation, concealment of the allocation sequence, masking of participants/personnel, blinding of the evaluation of results, data on incomplete results, reporting of selective results, and other biases. ►**Figs. 1** and **2**

Two independent researchers reviewed and selected abstracts and full-text articles using the inclusion and exclusion criteria. The data thus extracted were stored in a standardized database containing the following information: authors, country, year of publication, type of study, follow-up, diagnostic method, polysomnographic data, and sleep quality questionnaire used. Any discrepancies found during the review were resolved through a new review, joint analysis, and decision-making based on the most experienced researcher.

As the results were presented on the same scale, the difference between means (DM) of the scores obtained before and after the operation was used as a summary measurement of the effect.

To calculate the overall estimate, a meta-analysis with a random-effects model was used, weighed using the inverse variance method. The variance (Tau^2) was estimated by means of the method of Dersimonian and Laird, and Higgins' inconsistency index was used to calculate heterogeneity (I^2). The mean differences from before to after the operation were compared, using a significance level of 5% and a 95% confidence interval. Forest analyses and plots were generated through the RStudio statistical software, version 1.2.1335 (Rstudio Inc, Boston, USA).

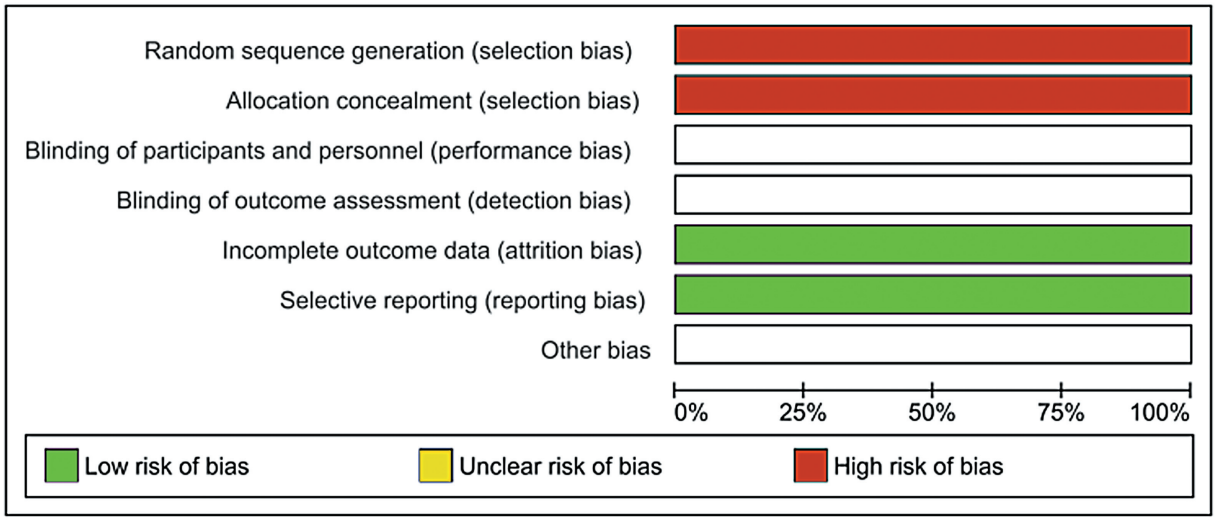

Fig. 1 Risk-of-bias graph: showing the review authors' judgments about each risk-of-bias item, presented as percentages across all the studies included.

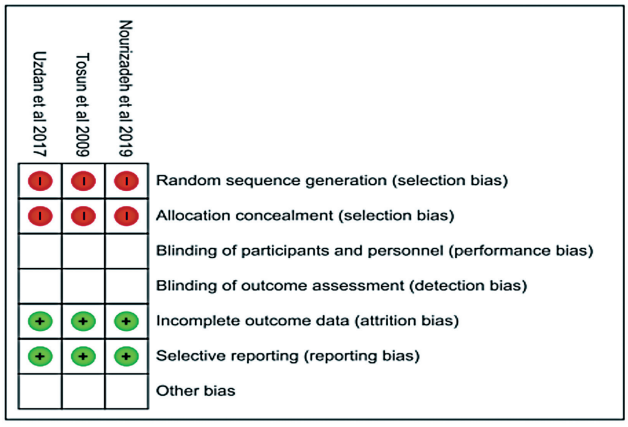

Fig. 2 Risk-of-bias summary: showing the review authors' judgments about each risk-of-bias item for each study included.

Results

From surveying the records on the research platforms, a database of around 46 studies was formed, among which eight articles remained after screening the abstracts. After the complete articles had been screened by two researchers, three studies were included in the final analysis (►**Fig. 1**).

The characteristics of these studies are summarized in ►**Table 1**. Among them, two were from Turkey and one from Iran. The sample size ranged from 15 to 27 participants (total, $n = 64$). All of them were prospective, and only one of them was randomized.[1] The ages of the participants ranged from 20 to 76 years. The postoperative follow-up period ranged from 1 to 6 months. Nasosinusal endoscopy was performed in all studies to diagnose nasal polyps, but the use of paranasal sinus tomography was only mentioned in one of them.[15]

Nasal resistance was evaluated by Nourizadeh et al[16] using acoustic rhinometry and by Uzdan et al[15] using rhinomanometry. Snoring was evaluated only in the study by Tosun et al[1] using a visual analog scale (VAS).

For studies to be included in the present review, polysomnographic data were essential, so that analyses on AHI, $SatO_2$, percentage of stage N3, and REM could be performed.

Nasosinusal endoscopic surgery can encompass polypectomy and other complementary uni or bilateral procedures, such as maxillary sinusotomy, ethmoidectomy, sphenoidectomy, frontal sinusotomy, septoplasty, and turbinectomy. No cases of revisional surgery were cited in any of the studies. Usdan et al[15] reported in their methodology that all their patients underwent the same procedure under general anesthesia, by means of the Messerklinger technique, and all underwent preoperative preparation and postoperative treatment. The other studies did not describe the technique used. ►**Fig. 3**

The selection criteria for patients with CRSwNP varied between the studies. Tosun et al[1] included cases of nasal obstruction for more than six months, with at least 50% obstruction in each nasal cavity on endoscopic examination.

Table 1 Characteristics of the studies included in the systematic review and meta-analysis

Author, year	Country	Study design	Sample size	Follow-up (months)	Sleep quality instruments
Tosun (2009)	Turkey	Prospective	27	3	ESS
Usdan (2017)	Turkey	Prospective	22	6	PSQI
Nourizadeh (2019)	Iran	Prospective	15	1	PSQI

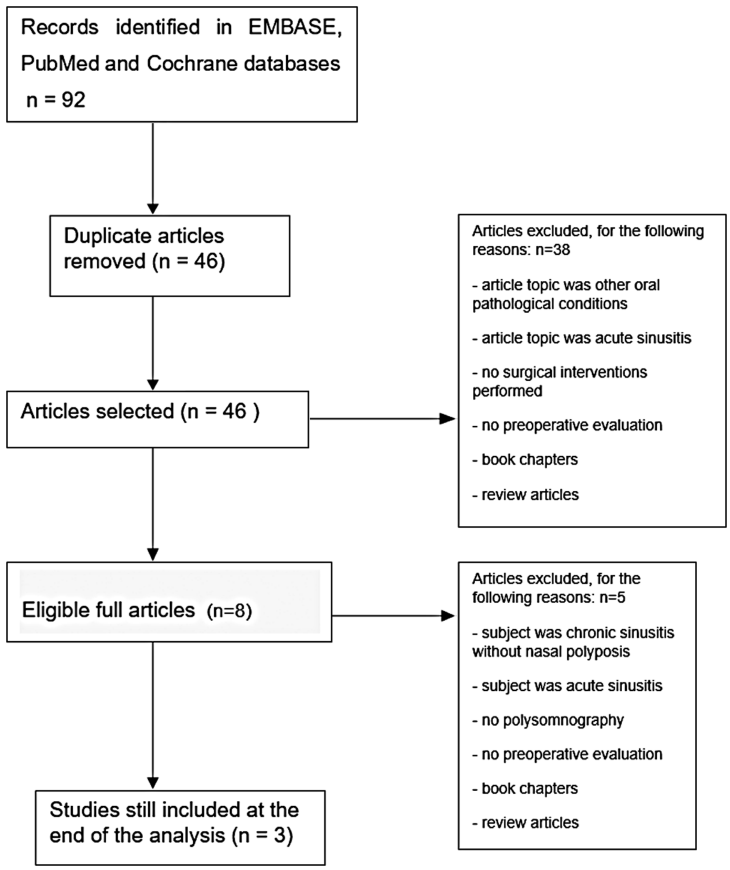

Fig. 3 PRISMA flowchart demonstrating the selection process for the articles.

Nourizadeh et al[16] selected patients with nasal obstruction, impaired sleep, and polyps in both nasal fossae (Lildholdt classification score 2–3).[19]

Uzdan et al[15] selected patients diagnosed with bilateral nasal polyps and with at least two of the following symptoms: nasal obstruction for a period not exceeding three years, anterior or posterior rhinorrhea, hyposmia or anosmia. In addition, their patients underwent nasal endoscopy and computed tomography.

Through inclusion of these three studies in a quantitative synthesis, it was possible to compare the mean scores obtained, from before to after the operation, for the following variables: apnea/hypopnea index (AHI), oximetry (minimum and average saturation during sleep), Pittsburgh sleep quality index (PSQI), percentage of stage N3 and REM sleep.

Apnea/hypopnea Index

Although there was a decrease in the mean post-intervention AHI score [DM = −1.60; 95% CI = −6.44–3.23; $I^2 = 0\%$], there was no statistical difference between the two times ($p > 0.05$) (►**Fig. 4**).

Oxyhemoglobin Saturation

Similarly, although there were increases in the average and minimum saturation levels during sleep, there was no difference between the two times for oximetry ($p > 0.05$), with an observed effect size of 1.12 [95% CI = −0.81–3.04; I^2 - 48%] for average saturation, and 1.89 [95% CI = −0.42 - 4.21; $I^2 = 0\%$] for the minimum saturation level (►**Fig. 5**).

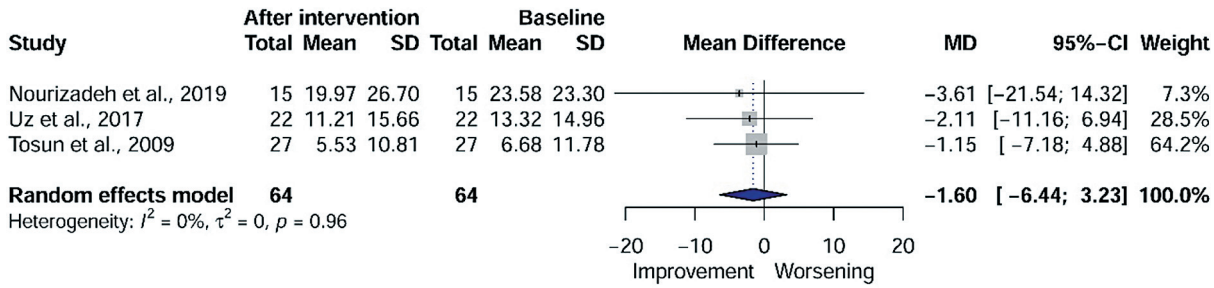

Fig. 4 Comparison of apnea/hypopnea indexes from before to after surgery among patients undergoing functional endoscopic surgery on the facial sinuses.

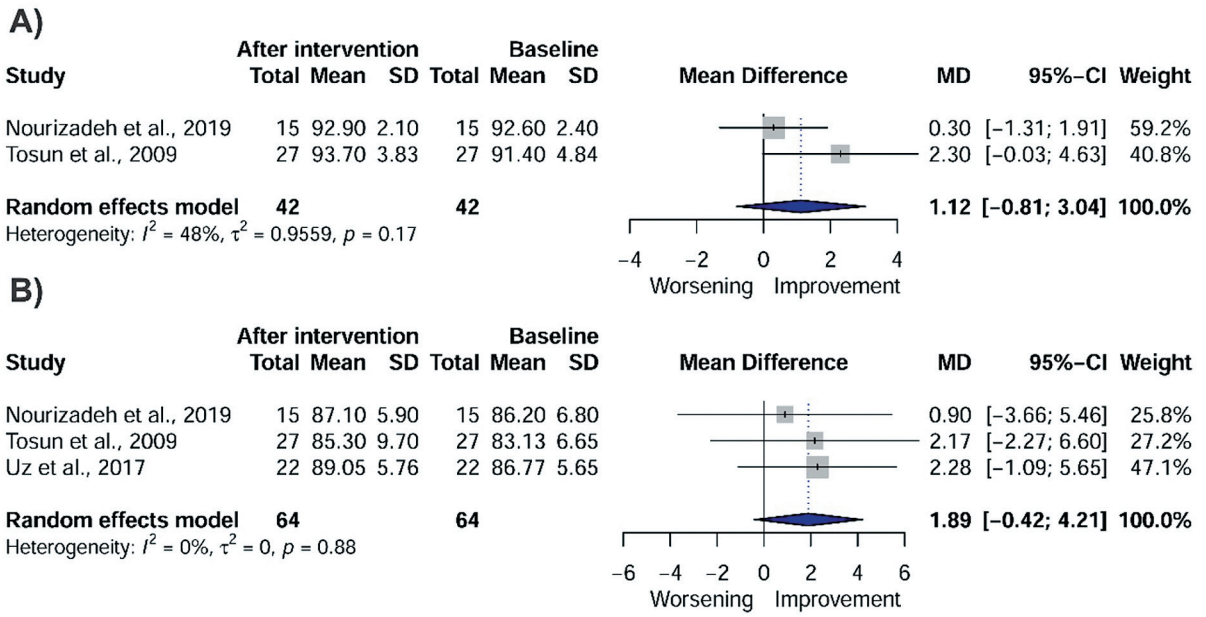

Fig. 5 Comparison of oximetry from before to after the intervention among patients undergoing functional endoscopic surgery of the facial sinuses: a) average O_2 saturation; b) minimum O_2 saturation level.

REM Sleep

There was a mean increase in the percentage duration of REM sleep, such that higher values were observed after the intervention, with an average difference of 2.28, but with confidence intervals close to the nullity line [95% CI = 0.04 - 4.51]. This difference was statistically significant ($p < 0.05$) (►**Fig. 6**).

Stage N3 Sleep

The mean difference in percentage of stage N3 from before to after the operation was 1.12, with a 95% CI between −3.51 and 5.75, thus indicating that surgery did not alter the percentage of stage 3 sleep (►**Fig. 7**).

Pittsburgh Sleep Quality Index (PSQI)

There was a decrease in PSQI scores, denoting an improvement in the quality of sleep after the intervention, with an average decrease of −2.25 [95% CI = −3.69 - −0.82; $I^2 = 0\%$], from before to after the intervention ($p < 0.05$). (►**Fig. 8**)

Discussion

In this series, there is a small number of studies included for analysis, which is due to the scarcity of studies on this topic in literature. In fact, this meta-analysis is possibly the first that relies on polysomnographic data for objective evaluation in this surgery. Some factors limited the development of this study, such as the lack of a definition of CRSwNP, which was based on different criteria in each study. For example, Nourizadeh et al[16] cited Lildholdt's classification for quantifying the presence of polyps. Tosun et al[1] used a criterion of 50% obstruction, and Usdan et al[15] considered only the presence of polyps without any other details that would quantify them. CRScPN is a broad syndrome and not yet fully understood, it has extremely complex genetic, biomolecular, and inflammatory mechanisms. Thus, the presence of polyps in the nasal cavity can be the "tip of the iceberg" of countless other pathologies, which can also interfere with the quality of sleep of affected individuals.

Several procedures may be performed during endoscopic sinus surgery, such as septoplasty, turbinectomy, polypectomy, and sinusotomy. After all, the patient who presents with a nasal

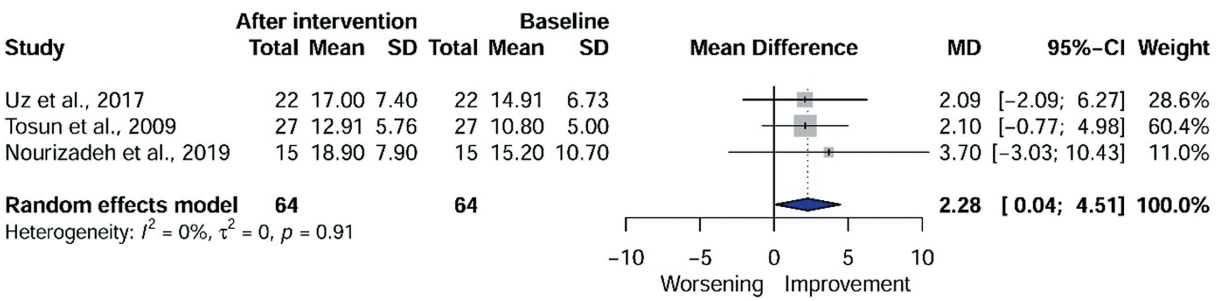

Fig. 6 Comparison of the percentage REM sleep from before to after the intervention among patients undergoing functional endoscopic surgery of the facial sinuses.

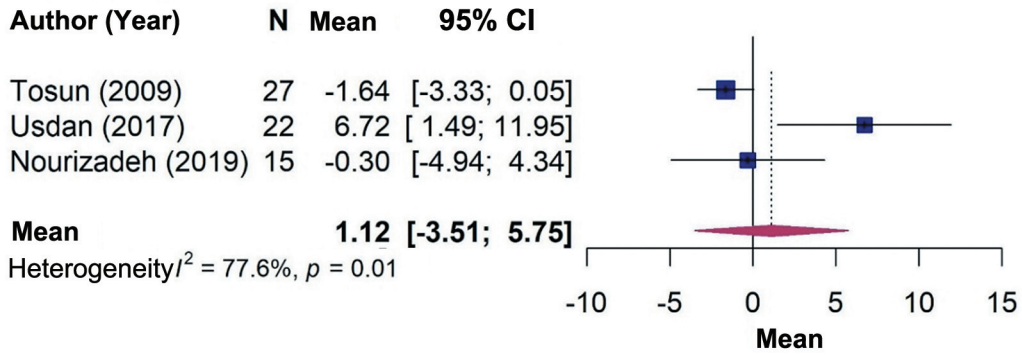

Fig. 7 Comparison of the percentage of stage N3 from before to after the intervention among patients undergoing functional endoscopic surgery of the facial sinuses.

polyp will hardly be submitted to polypectomy only if there are other anatomical alterations to be corrected simultaneously, which makes it difficult to relate the postoperative outcome only to polypectomy.[20] The absence of a randomized control group makes it difficult to distinguish the real surgical result. The results were expressed as comparisons from before to after the intervention, using the same sample. The study by Tosun et al[1] was the only one in which the sample was reported to have been randomized. We also observed that different pre- and postoperative conducts, reassessment times, and exclusion criteria for participants were adopted.

The apnea/hypopnea index (AHI), although often criticized for its limitations, remains the most used metric of OSA severity.[21]

Among these limitations, we can include the "first night effect," which is characterized by an increase in absolute sleep latency, as well as a decrease in REM sleep and a decrease in sleep efficiency. There may also be divergences during the analysis of events, possibly due to different types of monitoring (equipment, thermistors, and nasal cannulas) or even controversies in the definition of hypopneas. And, finally, the variability of sleep conditions each night is influenced by diet, level of tiredness, etc. These factors can change the comparability of research and clinical results when analyzing the AHI.[22]

The improvement in AHI after endoscopic sinus surgery remains a matter of divergence. Some studies have shown improvements in this parameter, but these were small, non-randomized clinical trials that assessed chronic rhinosinusitis in general (with and/or without nasal polyposis in the same sample).[20,23,24]

Wu et al[20] performed a meta-analysis in which there was a significant improvement in AHI.

In the meta-analysis performed by Sukato et al,[24] which analyzes the surgical outcome on sleep quality in patients with CRS (CRScPN and CRSsPN), there was a modest improvement in the AHI. In this study, this measure was considered only as polysomnographic data, and there was no statistically significant improvement after ESS, as well as two meta-analyses on the effects of nasal surgery that also indicated improvement in subjective criteria, but without significant improvement in the AHI.[25,26]

Only Nourizadeh et al[16] specified the number of patients with OSA and the outcome of AIH, but their severity classification was not disclosed.

In the literature, only limited data on the evaluation of oxyhemoglobin saturation are available. In the present study, no significant improvement in saturation after the surgical procedure was observed. We correlated this with the heterogeneity of the patients who underwent the operation. Neither was the use of the oxygen desaturation index (ODI) observed in any of the analyzed works. This index is a measure of the number of times, by a certain percentage, that saturation decreases per hour, regardless of the duration of the event.[22]

The hypothesis of Uzdan et al[15] was that sleep disorders among patients with CRSwNP might be more related to pathophysiological mediators of the disease than to nasal obstruction itself.

Many studies fail to analyze polysomnographic data when comparing treatments due to difficult access to laboratories, high cost, and patients' objections to performing tests. For

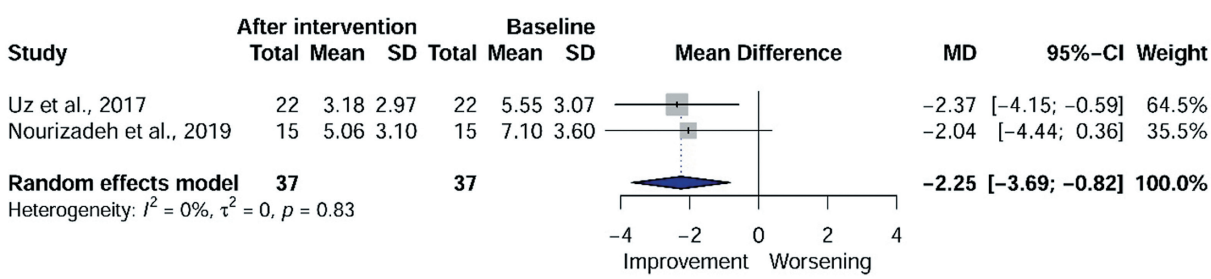

Fig. 8 Comparison of scores from the PSQI questionnaire from before to after the intervention among patients undergoing functional endoscopic surgery of the facial sinuses.

the evaluation of respiratory data, the use of home monitoring could be an alternative to this problem.[27,28]

Regarding sleep architecture, the parameters analyzed were N3 and REM stages because they are more related to sleep quality. There are few studies on the subject, possibly due to the previously mentioned difficulty in passing the exam. There was no statistically significant difference in relation to stage N3, in agreement with the other results.

Rapid eye movement (REM) sleep occurs during around 20–25% of total sleep time among adults, and this form of sleep is important for learning and memory. It is a restorative stage that can be impaired by nasal obstruction.[29] Significant improvement was found in our analysis, although this did not occur in other studies.

Snoring is a common complaint among patients with nasal obstruction and is also related to satisfaction with the quality of sleep after surgery. It can be diagnosed through polysomnography, but it is difficult to analyze because it is an annoyance that is often of an individualized nature and also involves important extra-nasal factors.[30,31] In our sample, snoring was evaluated using a visual analog scale (i.e., a subjective criterion) in a single study,[1] and it was not possible to include it in the meta-analysis. There are some apps on smartphones that enable monitoring of snoring at home, thus making it easier to analyze. However, the number of validated studies on the practical use of this app remains limited.[32]

For future research, the evaluation of the rate of arousals (arousals), the percentage of stage N3, and REM can be considered better metrics in the polysomnographic analysis of sleep quality and are more objective than snoring.[33,34]

OSA is a heterogeneous disease, and understanding its underlying reasons is critical for deciding on therapeutic approaches. The main pathophysiological causes include a compromised or collapsible upper airway, ineffectiveness of the pharyngeal dilator muscles, low arousal threshold, and hypersensitivity of respiratory control.[5]

Thus, certain subgroups would be more likely to benefit from nasal surgery, such as non-obese, positional apnea, and mild apnea patients. The identification of this phenotype in candidates for surgery could generate more consistent results.[35]

The subjective sleep assessment was performed using the Epworth Sleepiness Scale (ESS) and the Pittsburgh Sleep Quality Index (PSQI). In relation to ESS, the correlation with AHI is still uncertain.[36] It was not possible to analyze this parameter statistically because we had only one study.[1] The PSQI is a self-report instrument for evaluating several aspects of sleep, such as quality, delay, duration, efficiency, use of medication, etc. The result regarding the improvement of this parameter agreed with the literature.

CRSwNP is a recurrent chronic disease and, despite the existence of surgical treatment for it, knowledge of its biomolecular mechanism has shown promise in the search for more effective treatments and for improvement of patients' quality of life.[11]

Studies of markers for type 2 disease, nasal nitric oxide dosage, and anatomopathology of the removed polypoid lesions are some of the resources to be used for this.[9]

Interleukin (IL) 1-b (β) and tumor necrosis factor α (TNF-a) have a negative impact on sleep quality. IL-13 inhibits spontaneous sleep and non-REM sleep in patients with nasal polyps and has been linked to the etiology of polyposis. Moreover, levels of type-1 vascular adhesion molecules are altered in patients with sleep apnea, and these molecules are also related to recurrent polyposis.[15] Thus, patients with CRSwNP present impaired deep sleep, and those who have sleep disorders and nasal polyps are more prone to recurrence, thereby perpetuating this cycle.[15]

Use of immunobiological agents, especially those that inhibit the Th-2 inflammatory response, has been increasingly studied in relation to the treatment of CRSwNP over recent years and may form a strategy for breaking this cycle. These are biological drugs produced from living organisms that target specific molecular pathways that are involved in the pathogenesis of inflammatory diseases such as asthma.[37]

In summary, our meta-analysis provides a study on the effect of endoscopic sinus surgery relating to CRSwNP on sleep quality. Our results showed that there was a statistically significant effect, according to two validated sleep instruments (ESS and PSQI), regarding increasing the percentage of REM sleep. A mild improvement in AHI was found. In this way, nasal surgery could contribute to reducing the severity of OSA as well as the symptoms of drowsiness. We suggest that further studies be performed with standardization in the participant group from diagnosis (for example, through tomographic and endoscopic classifications), in the type of procedure performed, in the longest follow-up period, and in the analysis of polysomnographic parameters such as stage N3, REM, and index of awakenings.

Conclusion

Endoscopic nasosinusal surgery improves sleep quality and REM sleep duration, but there is no improvement in polysomnographic respiratory parameters.

Ethical Statement

This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of Interest

The authors declare that there were no conflicts of interest in conducting this study.

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