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ANA MARIA FARIA FERREIRA DE OLIVEIRA

AVALIAÇÃO DO SONO EM PACIENTES COM RINOSSINUSITE CRÔNICA COM POLIPOSE NASAL ANTES E APÓS CIRURGIA ENDOSCÓPICA NASOSSINUSAL: REVISÃO SISTEMÁTICA E META-ANÁLISE

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Dissertação apresentada à Faculdade de Ciências Médicas da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título de Mestra em Ciências, na área de Fisiopatologia Cirúrgica.

ORIENTADOR: PROFESSOR DOUTOR ALMIRO JOSÉ MACHADO JÚNIOR
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Dedico este trabalho, primeiramente, a Deus, que conduz minha vida e me dá forças para cumprir meus propósitos, dedico aos meus Pais(José e Sandra), que tanto se empenharam para que eu pudesse estudar e seguir em busca do conhecimento e, também, ao meu marido Giovanni, meu grande parceiro de vida, que sempre me apoia em todos os momentos.

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Resumo

Introdução: Pacientes com obstrução nasal por rinossinusite crônica com polipose nasal podem apresentar alteração na qualidade do sono. A literatura ainda possui poucos dados sobre o assunto.

Objetivos: avaliar as alterações na qualidade do sono e parâmetros polissonográficos em pacientes submetidos à cirurgia endoscópica funcional nasossinusal para rinossinusite crônica com polipose nasal.

Métodos: Foram selecionados estudos avaliando adultos com polipose nasal submetidos à cirurgia nasossinusal endoscópica. Foi realizada uma revisão sistemática nas seguintes bases de dados: Pubmed, Cochrane e Embase, com as seguintes palavras-chave: rinossinusite crônica, polipose nasal, qualidade do sono, cirurgia endoscópica nasossinusal. A metanálise comparou a média dos escores obtidos entre os momentos pré e pós-operatório para variáveis polissonográficas e subjetivas.

Resultados: Foram selecionados cinco artigos, incluindo três estudos, apenas um randomizado. A amostra total foi composta por 64 pacientes. Houve diminuição do escore médio do IAH, melhora da saturação média e mínima. A diferença média entre pós e pré para STAGE N3% foi de 1,12 com IC de 95% entre -3,51 e 5,75 sem significância. Houve aumento médio no percentual de duração do sono REM e diminuição nos escores do PSQI, ambos com significância estatística ($p < 0,05$).

Conclusão: Houve melhora na qualidade do sono e na duração do sono REM após a cirurgia, sem melhora nos parâmetros respiratórios polissonográficos.

Palavras chave: cirurgia endoscópica naso-sinusal; qualidade do sono; rinossinusite crônica com polipose nasal.

Abstract

Introduction: Patients with nasal obstruction due to chronic rhinosinusitis with nasal polyposis may present 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.

Methods: A systematic review was carried out in three databases: PubMed, Cochrane and Embase. The following key words 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: Five articles were selected, comprising three studies among which only one 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 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.

SUMÁRIO

1. Introdução

A Apneia Obstrutiva do Sono (AOS) é um distúrbio do sono crônico caracterizado por episódios de obstrução parcial ou completa das vias aéreas superiores, resultando em dessaturação de oxigênio, fragmentação do sono e sonolência diurna. Uma série de efeitos negativos para a saúde tem sido atribuídos à casos não tratados, incluindo o aumento de doenças cardiovasculares, alterações neurocognitivas e aumento das taxas de mortalidade.[1] Além disso, a AOS demonstrou ser um fator de risco independente para a morbidade cardiovascular, incluindo hipertensão, doença coronariana, insuficiência cardíaca congestiva, arritmias, hipertensão pulmonar, acidente vascular cerebral, morte súbita, resistência à insulina e, também, a doença do refluxo gastroesofágico.[2]

Considerada um problema de saúde pública, tem prevalência de 32,8% na população adulta do estado de São Paulo.[3]Acomete, principalmente, indivíduos com obstrução de via aérea superior e homens obesos, com idade entre 40 e 60 anos.[4]

Os critérios diagnósticos baseiam-se em sinais e sintomas clínicos que podem ser identificados em consulta através de anamnese direcionada ao sono e comorbidades, exame físico atento às alterações anatômicas comuns à patologia como também os exames polissonográficos e monitoramentos portáteis domiciliares.[5]

Os sintomas comumente relatados pelos pacientes que sofrem de distúrbios obstrutivos do sono incluem cefaleia matinal, diminuição da libido, sonolência excessiva diurna, fadiga, ronco alto, irritabilidade, despertares noturnos frequentes, noctúria, diminuição da concentração e perda da memória.[6] O ronco está presente entre 85% e 96% dos pacientes, sendo sua correlação muitas vezes utilizada com triagem para pacientes apneicos.[7]

O exame utilizado para o estudo do sono e padrão-ouro para o diagnóstico a AOS é a polissonografia. Por meio dela é possível quantificar o índice de apnéia-hipopnéia, saturação e mesmo a presença de roncos.[8]

Alterações na musculatura orofaríngea, baixo limiar de excitação respiratória, fraca resposta do muscular (genioglosso) à pressão faríngea negativa e hipersensibilidade do controle respiratório durante o sono são fatores envolvidos na patogênese da AOS.[9]

Alterações anatômicas podem ser encontradas no hipodesenvolvimento maxilo-mandibular, palato, língua e cavidades nasais. Em se tratando de qualidade de

vida, o sono pode ser severamente afetado em pacientes com obstrução nasal devido ao aumento da resistência das vias aéreas superiores.[10]

Dentre as causas nasais encontramos a rinossinusite crônica (RSC) que é uma condição inflamatória dos seios paranasais que frequentemente causa sintomas como obstrução nasal (mais comum), dor facial, drenagem de secreção nasal espessa e hiposmia por pelo menos 12 semanas consecutivas.[11] A prevalência estimada na população geral é de 5-12%.[12] A RSC tradicionalmente é dividida em com e sem polipose nasal, porém trata-se de uma doença heterogênea complexa com diferentes fenótipos e endótipos. Outros fenótipos encontrados são: rinossinusite fúngica, rinossinusite infecciosa, doença respiratória exacerbada por aspirina, fibrose cística, pediátrica e por outras doenças sitêmicas.[13]

A Rinossinusite Crônica Sem Polipose Nasal (RSCsPN) é atribuída à obstrução mecânica do complexo ostiomeatal, enquanto a (RSCcPN) foi considerada uma doença difusa da mucosa de base eosinofílica. Alguns pesquisadores levantam a hipótese de que ambas não sejam doenças distintas, mas a presença de pólipos seja o resultado de uma inflamação mais prolongada e grave.[14]

Os pólipos nasais são lesões inflamatórios benignas na mucosa nasossinusal que geralmente se desenvolvem bilateralmente e estão associados a obstrução nasal e, como consequência, a diminuição da qualidade de vida, tornando esta doença clinicamente importante.[15]

O tratamento da RSC pode ser clínico, por exemplo, através da aplicação de corticoides nasais tópicos e/ou cirúrgico, em casos de falha terapêutica, por meio da *Funtional Endoscopy Sinus Surgery (FESS)*. Alguns pacientes submetidos a esta cirurgia relacionam a redução prolongada dos sintomas nasais a uma melhora da qualidade de vida.[16]

Pacientes com obstrução nasal devido a Rinossinusite Crônica com Polipose Nasal apresentam piora na qualidade do sono e a cirurgia nasal melhoraria este parâmetro e reduziria o risco de Apneia Obstrutiva do Sono.[17]

Existem diversos estudos relacionando a RSC com e sem polipose nasal a AOS. Há, também, trabalhos que avaliam qualidade de vida e sono dos indivíduos submetidos a *FESS*. Entretanto, há escassez de dados da literatura que analisem sistematicamente as alterações na qualidade do sono e nos parâmetros polissonográficos de pacientes submetidos a cirurgia funcional endoscópica dos seios

paranasais para rinossinusite crônica com polipose nasal, sendo este o objetivo desta pesquisa.

2. Objetivos

2.1- Objetivo geral

O objetivo do presente estudo foi avaliar alterações na qualidade do sono e nos parâmetros polissonográficos de pacientes submetidos a cirurgia endoscópica funcional dos seios paranasais para rinossinusite crônica com polipose nasal.

2.2- Objetivos específicos:

2.2.1- Avaliar o índice de apneia e hipopneia pré e pós cirurgia endoscópica nasal

2.2.2- Avaliar índice de dessaturação pré e pós cirurgia endoscópica nasal

2.2.3- Avaliar o ronco pré e pós cirurgia endoscópica nasal

2.2.4- Avaliar por meios de questionários parâmetros subjetivos do sono pré e pós cirurgia endoscópica nasal

3. Método

3.1 Metodologia:

Este estudo tratou-se de uma revisão sistemática seguida de meta-análise as quais seguiram o método Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[18] que se utiliza de alguns itens para coleta e análise de dados, tais como:

- Critérios de Inclusão: os critérios foram formulados de acordo com a população, intervenção, comparação, resultados e tipos de estudo (tabela 1).

  - População: Adultos (idade igual e/ou superior a 18 anos), diagnosticados com rinossinusite crônica com polipose nasal (RCcPN) submetidos a polissonografia antes e após cirurgia.
  - Intervenção: realização de cirurgia endoscópica funcional dos seios da face *(FESS)*
  - Comparação: melhora de parâmetros polissonográficos, ronco e qualidade do sono.
  - Resultado: análise de estudos em que foi realizada uma *FESS* em pacientes com pólipos nasais e AOS.

- Desenho do estudo: análise de estudos observacionais e intervencionais em que foi realizada uma *FESS* em paciente portador de AOS.

- Estratégia de pesquisa: foi realizada a busca sistemática, no período de Fevereiro à Maio de 2021, nas seguintes bases de dados eletrônicos: PubMed, EMBASE, Biblioteca Cochrane com início após a aprovação do projeto. A pesquisa foi realizada usando Medical Subject Headings (MeSH) 'apneia obstrutiva do sono', 'sinusite' 'ronco', 'polissononografia' e 'adulto' e termos alternativos 'AOS', 'RCcPN', *'FESS'*, sem restrição de idioma. Foram desenvolvidas estratégias de pesquisas específicas aos bancos de dados.

- Seleção de estudos:

- Critérios de inclusão: estudos observacionais e intervencionais em que foi realizada a *FESS* em pacientes submetidos a polissonografia antes e após cirurgia. Não houve restrições quanto ao idioma ou tempo de publicação.

- Critérios de exclusão: foram excluídos estudos experimentais em animais ou in vitro, opiniões de especialistas, cartas ao editor, revisões sistemáticas e da literatura, meta-análises ou quaisquer outros estudos descritivos.

Resultados

Artigo (submetido)

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 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.

Methods: A systematic review was carried out in three databases: PubMed, Lilacs and Cochrane. The following key words 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 carried out, 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 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: endoscopic sinus 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 approximately 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 used for objectively studying sleep and the gold standard for diagnosing OSA is polysomnography. Through 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,

as a consequence, 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]

Several studies have correlated CRS with or without nasal polyposis, with OSA. There are also some studies that have assessed quality of life and sleep among individuals undergoing endoscopic sinus surgery. 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 meta-analysis. It followed the method of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[12] The study selection criteria for this review were formulated in accordance with the PICO format[13] (population, intervention, comparison, outcome) and types of study.

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

Intervention: Functional endoscopic sinus surgery of the face *(FESS)*.

Comparison: polysomnographic parameters (apnea/hypopnea index (AHI), oxygen saturation, N3 and REM stages), snoring and sleep quality before and after sugery.

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

Study design: A systematic review and meta-analysis.

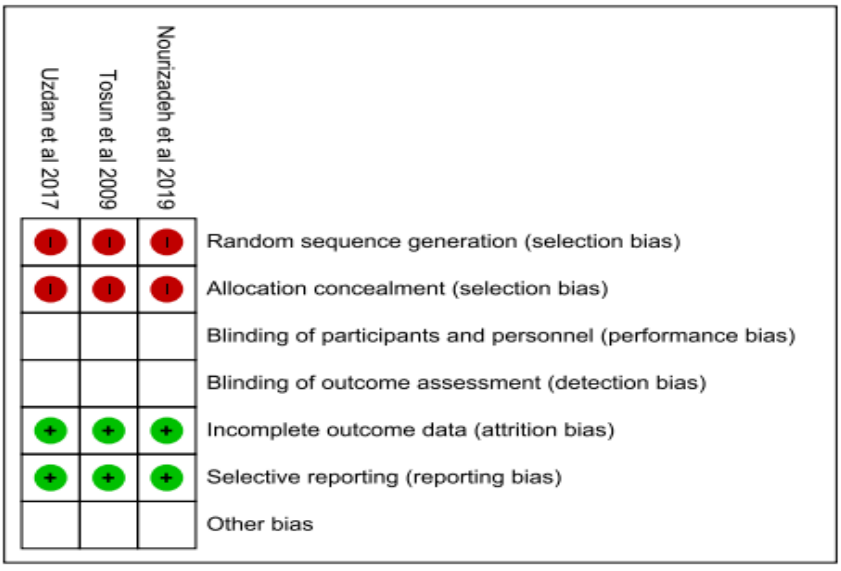
A systematic search was conducted in three electronic databases: PubMed, EMBASE, Lilacs and Cochrane Library. This search was carried out using the following Medical Subject Headings (MeSH): 'endoscopic sinus surgery' and 'sleep', along with alternative terms such as 'functional endoscopic sinus surgery' 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)[14] and the Pittsburgh sleep quality index (PSQI).[15]

To assess the risk of bias in the studies, we used the Cochrane Tool.[16] 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.

Figure 1- Risk-of-bias summary: showing the review authors' judgments about each risk-of-bias item for each study included.



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, from before to 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, weighted 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).

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 (Figure 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 for in order to diagnose nasal polyps, but use of paranasal sinus tomography was only mentioned in one of them.[17]

Nasal resistance was evaluated by Nourizadeh et al[18] using acoustic rhinometry and by Uzdan et al[17] 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[17] reported in their methodology that all their patients underwent the same procedure under general anesthesia, by means of the Messerklinger technique, and also all underwent preoperative preparation and postoperative treatment. The other studies did not describe the technique used.

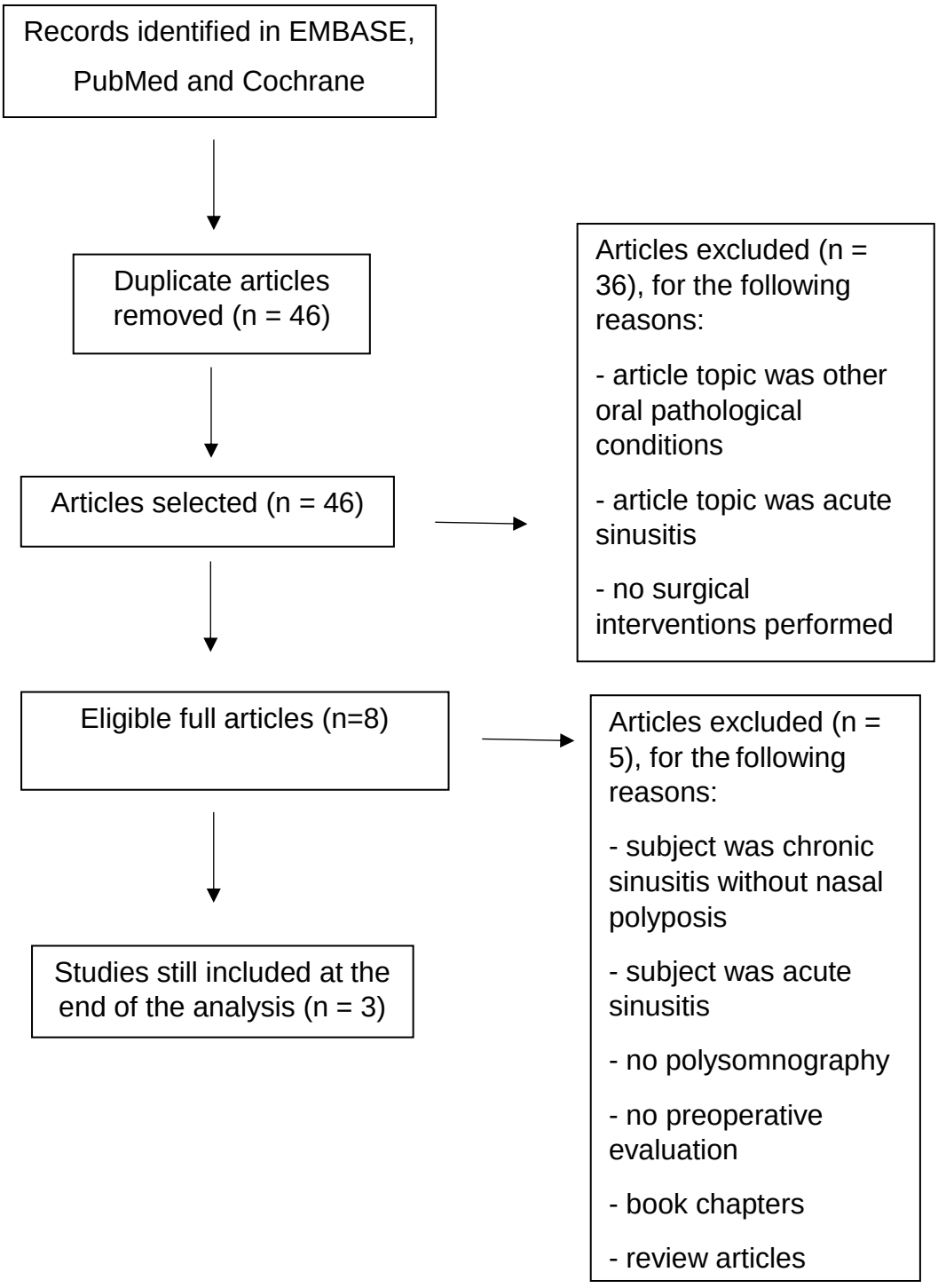


Figure 1. PRISMA flowchart demonstrating the selection process for the articles.

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

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. Nourizadeh et al[18] selected patients with nasal obstruction, impaired sleep and polyps in both nasal fossae (Lildholdt classification score 2-3).[19]

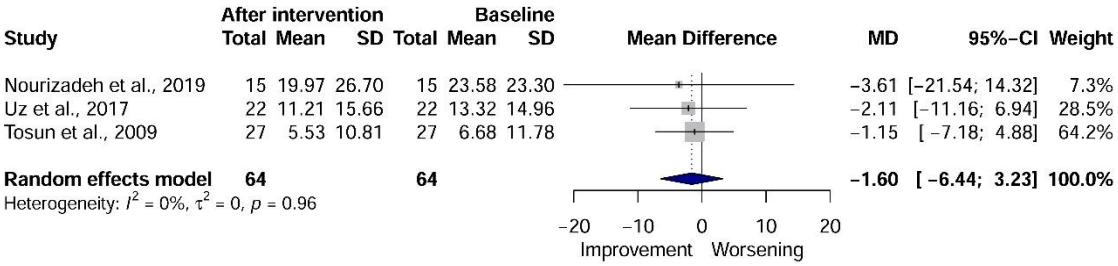
Uzdan et al[17] selected patients diagnosed with bilateral nasal polyps and with at least two of the following symptoms: nasal obstruction for a period not exceeding three years, anterior or posterior rhinorrhea, hyposmia or anosmia. In addition, their patients underwent nasal endoscopy and computed 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 ($p > 0.05$) (Figure 2).

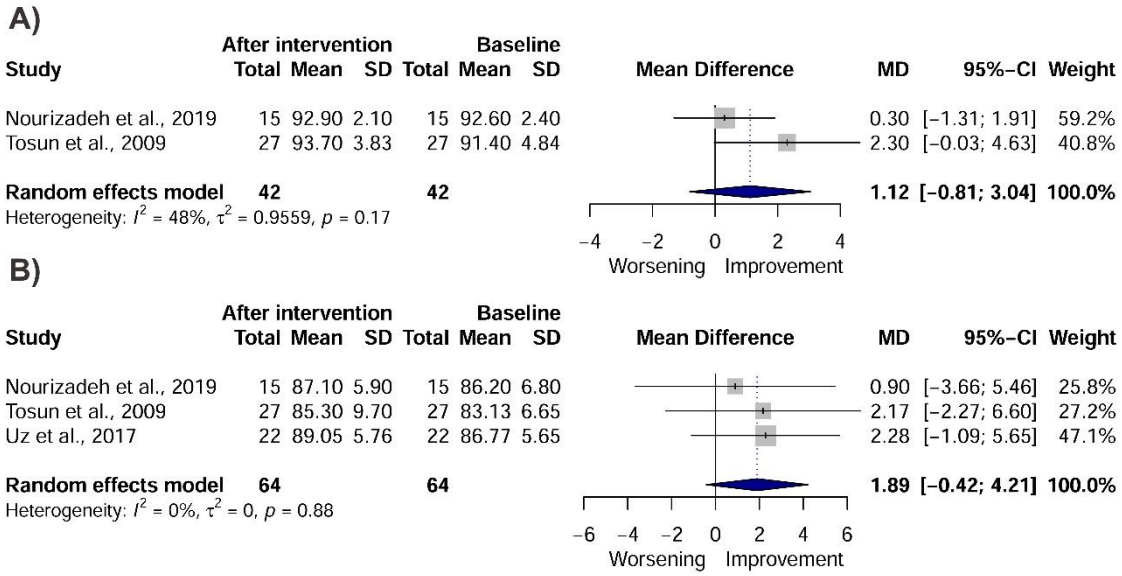
Figure 2 - Comparison of apnea/hypopnea indexes from before to after surgery among patients undergoing endoscopic sinus surgery.



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 (Figure 3).

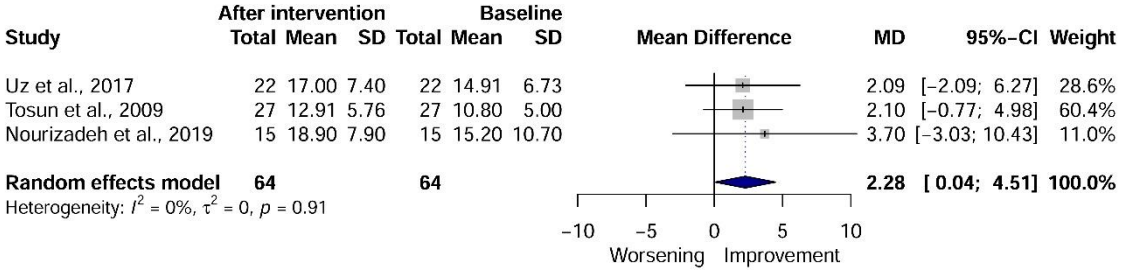
Figure 3 – Comparison of oximetry from before to after the intervention among patients undergoing endoscopic sinus surgery: a) average O_2 saturation; b) minimum O_2 saturation level.



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 ($p < 0.05$) (Figure 4).

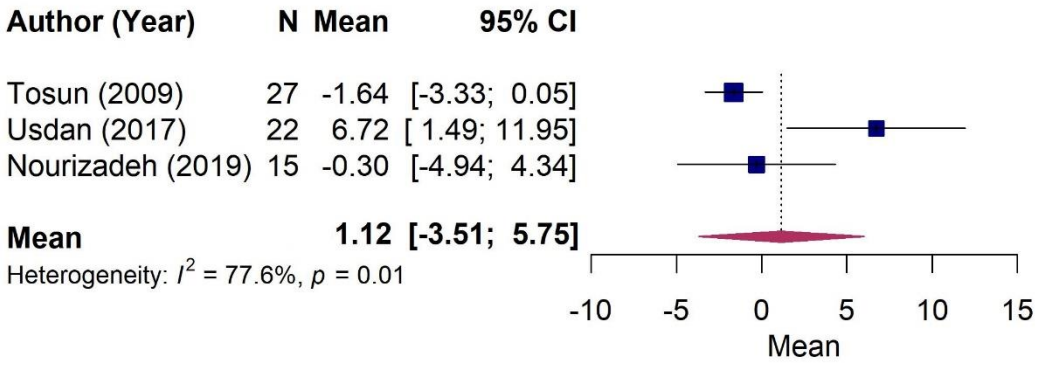
Figure 4 – Comparison of the percentage REM sleep from before to after the intervention among patients undergoing endoscopic sinus surgery.



Stage N3

The mean difference in percentage of stage N3 from before to after the operation was 1.12, with 95% CI between -3.51 and 5.75, thus indicating that surgery did not alter the percentage of stage 3 sleep (Figure 5).

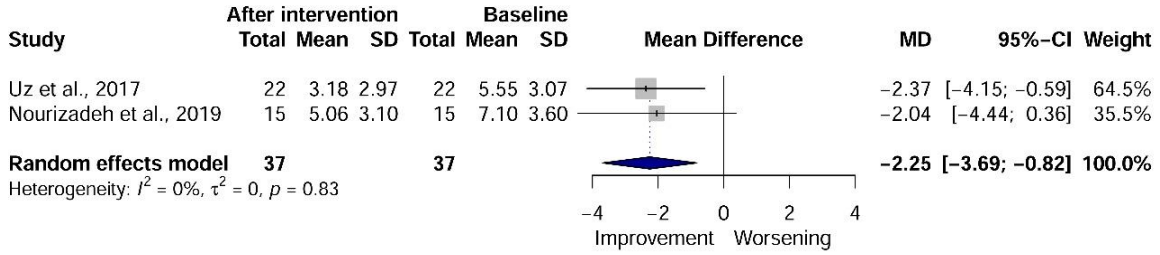
Figure 5 – Comparison of the percentage of stage N3 from before to after the intervention among patients undergoing endoscopic sinus surgery. Inside the figure: Author (year); Mean; 95% CI; Heterogeneity.



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 ($p < 0.05$).(Figure 6)

Figure 6 - Comparison of scores from the PSQI questionnaire from before to after the intervention among patients undergoing endoscopic sinus surgery.



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 the literature. In fact, this meta-analysis is possibly the first that relies on polysomnographic data for objective evaluation in this particular type of surgery. Some factors limited the development of this study, such as the lack of definition of CRSwNP, which was based on different criteria in each study. For example, Nourizadeh et al[18] cited Lildholdt's classification for quantifying the presence of polyps. Tosun et al[1] used a criterion of 50% obstruction and Usdan et al[17] 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 nasal 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 commonly 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 for 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, 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[18] 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 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[17] 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' objection to performing tests. For 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 accessing 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 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 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: 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 improvement of this parameter was in agreement 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.[37]

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

Interleukin (IL) 1-b (beta) and tumor necrosis factor alpha (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.[17] 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.[17]

Use of immunobiological agents, especially those that inhibit the Th-2 inflammatory response, has been increasingly studied in relation to 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.[38]

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), with regard to increasing the percentage of REM sleep. 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 carried out 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 sinus surgery may improve sleep quality and REM sleep duration, but there is no improvement in polysomnographic respiratory parameters.

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Acknowledgement

This study formed a master's dissertation in the field of surgical sciences, within the discipline of otorhinolaryngology at UNICAMP, Brazil.

Conflict of Interest

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

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Conclusão

Por fim, constatamos que ainda há escassez de estudos que contemplem dados polissonográficos na avaliação do sono após cirurgia endoscópica nasossinusal.

Nesta análise, houve melhora da qualidade do sono e duração de sono REM, porém não houve melhora nos parâmetros respiratórios polissonográficos.

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Anexo 1 – Dispensa de Comitê de Ética

UNICAMP

CEPUNICAMP

PRP pró-reitoria de pesquisa unicamp

Cidade Universitária "Zeferino Vaz", 30 de junho de 2021.

SIGAD: Of. CEP nº 93/2021

Prof. Dr. Almiro José Machado Junior
Pesquisador Responsável

REF.: DISPENSA DE APRESENTAÇÃO DE PROJETO DE PESQUISA PARA AVALIAÇÃO DO SISTEMA CEP-CONEP.

Prezado Senhor,

Informamos que a pesquisa intitulada "**Apneia Obstrutiva do Sono em pacientes com Rinossinusite Crônica com Polipose Nasal: revisão sistemática e meta-análise**", para fins de dissertação de mestrado do Programa de Pós-Graduação em Ciência da Cirurgia, da Faculdade de Ciências Médicas, cuja aluna pesquisadora é Ana Maria Faria Ferreira de Oliveira, destina-se a avaliar alterações na qualidade do sono e nos parâmetros polissonográficos de pacientes submetidos a cirurgia funcional endoscópica dos seios paranasais para rinossinusite crônica com polipose nasal.

Deste modo, baseados no projeto anexado ao documento, o estudo não necessita tramitar pelo Comitê de Ética em Pesquisas envolvendo Seres Humanos, tendo em vista que será realizada uma revisão sistemática da literatura e meta-análise.

Ressaltamos que se houver qualquer alteração no escopo do projeto, na qual envolva seres humanos, o CEP/Unicamp deve ser informado para fins de deliberação sobre essas mudanças.

Atenciosamente,

Dra. Renata Maria dos Santos Celeghini
COORDENADORA DO COMITÊ DE ÉTICA EM PESQUISA
UNICAMP

Documento assinado. Verificar autenticidade em sigad.unicamp.br/verifica
Informar código 1E286DF6 A3A24170 A018163C 0286505F

Anexo 2- Registro no PROSPERO

De: CRD-REGISTER
Enviado:sexta-feira, 5 de fevereiro de 2021 03:02
Para: ANAMARIA.OTORRINO@HOTMAIL.COM
Assunto: PROSPERO Registration message [229327]

Dear Ms OLIVEIRA,

We apologise for the delay in dealing with your registration, an ever-increasing number of applications has led to a backlog and substantial delays for some users.

PROSPERO is currently prioritising submissions related to COVID-19. To enable us to focus on these submissions, and to avoid additional delay, during the pandemic we will automatically publish submissions that have been waiting more than 30 days for registration.

This applies to your systematic review "Obstructive sleep apnea in patients with chronic rhinosinusitis with nasal polyposis: systematic review and meta-analysis" which was published on our website on Feb 04, 2021.

The records will be published exactly as submitted, without review by the PROSPERO team, so the public record will indicate:

"To enable PROSPERO to focus on COVID-19 registrations during the 2020 pandemic, this registration record was automatically published exactly as submitted. The PROSPERO team has not checked eligibility"

Review owners have always been responsible for the quality and content of PROSPERO records, and high-quality well-written records will continue to speak for themselves.

Your registration number is: CRD42021229327

You are free to update the record at any time, all submitted changes will be displayed as the latest version with previous versions available to public view. Please also give brief details of the key changes in the Revision notes facility and remember to update your record when your review is published. You can log in to PROSPERO and access your records at https://www.crd.york.ac.uk/PROSPERO

Best wishes for the successful completion of your review.

Yours sincerely,

PROSPERO Administrator
Centre for Reviews and Dissemination
University of York
York YO10 5DD
t: +44 (0) 1904 321049
e: CRD-register@york.ac.uk
www.york.ac.uk/inst/crd

PROSPERO is funded by the National Institute for Health Research and produced by CRD, which

is an academic department of the University of York.

Email disclaimer: https://www.york.ac.uk/docs/disclaimer/email.htm

Other non-commercial resources that may be of interest
SRDR-Plus is a systematic review data management and archival tool that is available free of charge http://srdrplus.ahrq.gov.

Congresso da Fundação Otorrinolaringologia
26 a 28.08.2021 | São Paulo - SP

CERTIFICADO

Certificamos que **Ana Maria Faria Ferreira de Oliveira** participou do **"20º Congresso da Fundação Otorrinolaringologia"** realizado em São Paulo - SP, como **apresentador do trabalho científico, "Sleep assessment in chronic rhinosinusitis patients with nasal polyposis before and after nasosinusal endoscopic surgery: systematic review and meta-analysis"**, com o autor principal: **Ana Maria Faria Ferreira de Oliveira** e **tendo como Coautores: Fabio Tadeu Moura Lorenzetti, Luiz Gabriel Signorelli, Edilson Zancanella, Almiro José Machado Júnior,** no dia **26/08/2021**

Carga Horária: 10 Minutos

Ricardo Ferreira Bento
Professor Titular da Disciplina de Otorrinolaringologia da FMUSP

FO Fundação Otorrinolaringologia Desde 1995

Richard Louis Voegels
Presidente do 20º Congresso da Forl
Presidente da Fundação Otorrinolaringologia

CFO-20/2021d

Anexo 4- Submissão Revista

IO International Archives of Otorhinolaryngology <onbehalfof@manuscriptcentr
11/04/2023 12:08

Para: anamaria.otorrino@gmail.com Cc:anamaria.otorrino@gmail.com; drfabiootorrino@yahoo.co...

11-Apr-2023

Dear Mrs. de Oliveira,

Your manuscript entitled "Sleep and chronic rhinosinusitis: a systematic review of postoperative data " has been successfully submitted online and is presently being given full consideration for publication in International Archives of Otorhinolaryngology.

Your manuscript ID is: IAORL-2023-04-1531-SR

Please mention the above manuscript ID in all future correspondence or when calling the Editorial Office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at https://mc.manuscriptcentral.com/iaorl and edit your user information as appropriate.

You can also view the status of your manuscript at any time by checking your Author Center after logging in to https://mc.manuscriptcentral.com/iaorl.

Thank you for submitting your manuscript to International Archives of Otorhinolaryngology.

Sincerely,

Adilson Montefusco
Editorial Office
International Archives of Otorhinolaryngology
iaorl@iaorl.org