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The Confluence of Chronic Rhinosinusitis and Obstructive Sleep Apnea: A Comprehensive Review of Pathophysiology, Epidemiology, and Therapeutic Interventions

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The Confluence of Chronic Rhinosinusitis and Obstructive Sleep Apnea: A Comprehensive Review of Pathophysiology, Epidemiology, and Therapeutic Interventions

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Abstract

Background: Chronic rhinosinusitis (CRS) and obstructive sleep apnea (OSA) frequently coexist, sharing inflammatory and anatomical pathways consistent with the "United Airway" This review examines the synergistic dysfunction linking these conditions. **Methods:** We conducted a comprehensive review synthesizing literature on the epidemiology, pathophysiology—including cytokine cascades and microbiome dysbiosis—and therapeutic outcomes of surgical and medical interventions for comorbid CRS and OSA. **Results:** Large-scale datasets confirm CRS as an independent risk factor for OSA. Pathophysiologically, the disorders are linked by mechanical obstruction, systemic cytokine spillover (IL-6, TNF-a), and nasopharyngeal microbiome dysbiosis (e.g., *S. aureus* biofilms). Therapeutically, Endoscopic Sinus Surgery (ESS) significantly improves subjective sleep quality (SNOT-22) and reduces CPAP pressure requirements, although it yields only trivial reductions in the Apnea-Hypopnea Index (AHI). Biologics like Dupilumab demonstrate rapid efficacy in improving sleep domains for CRS with nasal polyps. **Conclusion:** CRS and OSA are inextricably linked via mechanical and inflammatory mechanisms. A holistic "United Airway" management approach—optimizing nasal patency to facilitate CPAP adherence and reduce systemic inflammatory burden—is critical for improving patient outcomes.

Keywords: obstructive sleep apnea; rhinosinusitis; snoring

1. Introduction

The concept of the "United Airway" has traditionally linked allergic rhinitis and asthma, yet a similar, perhaps more mechanically complex relationship exists between chronic rhinosinusitis (CRS) and obstructive sleep apnea (OSA). As otorhinolaryngologists, the compartmentalization of the airway into "nasal" and "pharyngeal" segments often obscures the physiologic continuity that dictates respiratory health. CRS is defined by persistent mucosal inflammation of the nose and paranasal sinuses lasting greater than 12 weeks, manifesting as nasal obstruction, rhinorrhea, facial pain, and

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hyposmia [1]. OSA is characterized by repetitive collapse of the upper airway during sleep, leading to intermittent hypoxia, sleep fragmentation, and systemic sympathetic activation [2].

Historically, the association between nasal obstruction and sleep-disordered breathing was viewed primarily through a mechanical lens: a blocked nose necessitates mouth breathing, which destabilizes the airway. However, contemporary research has unveiled a far more intricate interplay involving systemic inflammatory cascades, neurological reflex arcs, and microbial ecology. Evidence from the World Trade Center (WTC) health registry indicates that CRS symptoms are an independent risk factor for OSA, even after controlling for obesity and demographic variables, suggesting that sinonasal inflammation acts as a distinct driver of sleep apnea pathogenesis [3].

This review aims to provide an up-to-date reference for the clinician-scientist, integrating data from population-based studies, molecular biology, and surgical outcomes research. By understanding the nuanced mechanisms—such as the role of Staphylococcus aureus biofilms in perpetuating inflammation or the impact of IL-6 on neural regulation—we can better tailor interventions that address both the sinonasal and sleep-related components of these debilitating conditions.

2. Literature Research Strategy

To examine the synergistic dysfunction between Chronic Rhinosinusitis (CRS) and Obstructive Sleep Apnea (OSA), a systematic search of electronic databases was conducted, including PubMed/MEDLINE, Scopus, and Google Scholar. The search aimed to synthesize literature on epidemiology, pathophysiology—specifically involving cytokine cascades and microbiome dysbiosis—and therapeutic outcomes.

2.1. Search Criteria and Keywords

The search strategy employed Boolean operators to combine key terms. Primary search strings included:

- ("chronic rhinosinusitis" OR "sinusitis") AND ("obstructive sleep apnea" OR "OSA" OR "sleep-disordered breathing").
- "nasal obstruction" AND "CPAP adherence".
- "endoscopic sinus surgery" AND "sleep quality" AND "AHI".
- "biologics" OR "dupilumab" AND "sinonasal polyposis" AND "sleep".

2.2. Inclusion and Exclusion Criteria

Articles were selected based on their relevance to the "United Airway" concept. Inclusion criteria focused on:

- Large-scale epidemiological datasets and population-based studies (e.g., TriNetX database and World Trade Center health registry).
- Clinical trials and meta-analyses evaluating surgical (ESS) and medical (Intranasal Steroids (INCS), xylitol, biologics) interventions.
- Molecular and neurophysiological studies exploring cytokine spillover (IL-6, TNF-alpha) and the nasopharyngeal reflex.
- Metagenomic research regarding the "oralization" of the nasal microbiome and bacterial biofilms.

2.3. Data Extraction and Synthesis

The review period spanned from the earliest relevant records through January 2025, prioritizing peer-reviewed articles published in the last decade to ensure the inclusion of contemporary therapeutic advancements such as Hypoglossal Nerve Stimulation (HGNS) and monoclonal antibodies. Subjective outcomes were analyzed through validated tools such as the SNOT-22, PSQI, and STOP-Bang questionnaire.

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3. Epidemiology and the Burden of Comorbidity

3.1. Prevalence and Risk Analysis

The co-occurrence of CRS and OSA is not merely coincidental but represents a significant epidemiological intersection. Analysis of the TriNetX US Collaborative Network database, which encompasses over 1.8 million CRS patients and 480,000 OSA patients, identified a substantial cohort of nearly 94,000 individuals suffering from both conditions [4]. This large-scale data reveals that patients with comorbid CRS and OSA (CRS-OSA) exhibit a unique and more severe clinical phenotype compared to those with either condition in isolation.

Specifically, the CRS-OSA cohort demonstrates significantly higher rates of systemic comorbidities, including hypertension, diabetes mellitus, and obesity [4]. The odds of requiring endoscopic sinus surgery (ESS) are nearly two-fold higher in patients with comorbid OSA (OR: 1.91) compared to CRS-only patients, indicating that the presence of sleep apnea may be a marker for recalcitrant sinonasal disease [4] Furthermore, longitudinal studies in Taiwan have shown that a diagnosis of OSA is associated with a hazard ratio of 3.18 for the subsequent development of CRS, suggesting a bidirectional causality where OSA-induced systemic inflammation predisposes the nasal mucosa to chronic infection.[5]

3.2. Specific Populations and Environmental Triggers

The relationship between environmental exposure, CRS, and OSA provides further insight into the inflammatory basis of these diseases. In the WTC responder cohort, individuals exposed to caustic dust and fumes exhibited an OSA prevalence of approximately 75%, vastly higher than the general population [3,6]. In this group, the severity of CRS symptoms—specifically nasal obstruction and rhinorrhea—served as a potent predictor for the presence of OSA . This data supports the hypothesis that environmental insults initiate a chronic inflammatory response in the upper airway that propagates downstream, compromising pharyngeal patency.

3.3. Diagnostic Overlap and Symptom Masking

A critical challenge in clinical practice is the significant overlap in symptomatology. Fatigue, non-restorative sleep, and cognitive dulling are hallmarks of both OSA and CRS. In a study utilizing the Sino-Nasal Outcome Test-22 (SNOT-22), sleep dysfunction was identified as one of the most severe domain impairments in CRS patients.[7] Moreover, the Korea National Health and Nutrition Examination Survey (KNHANES) found that among the cardinal symptoms of CRS, nasal obstruction and olfactory dysfunction were most strongly associated with high-risk scores on the STOP-Bang questionnaire, [1a screening tool questionnaire that assesses eight clinical criteria (snoring, tiredness, observed apnea, high blood pressure, BMI, age, neck, and gender) to determine the risk of obstructive sleep apnea. This symptom masking can lead to delayed diagnosis; a patient complaining of "fatigue" may be treated solely for sinusitis while an underlying moderate-to-severe OSA remains unaddressed, or conversely, an OSA patient may struggle with CPAP intolerance due to undiagnosed polyposis.

4. Pathophysiological Mechanisms

The mechanisms linking CRS to OSA are multifactorial, involving a complex interplay of anatomical mechanics, inflammatory signaling, neurological reflexes, and microbiological shifts.

4.1. Anatomical and Mechanical Interactions

The most established link between nasal pathology and OSA is the Starling resistor model, which posits that the upper airway behaves as a collapsible tube. An increase in upstream resistance (nasal obstruction) necessitates the generation of greater negative intraluminal pressure during

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inspiration to maintain airflow. If this negative pressure exceeds the critical closing pressure (Pcrit) of the pharynx, collapse occurs [8].

The Role of Mouth Breathing and Nasal Obstruction

Chronic nasal obstruction forces a switch to oral breathing, a physiological adaptation with deleterious consequences for airway stability.

- **Mandibular Biomechanics:** Opening the mouth rotates the mandible inferiorly and posteriorly, shortening the length of the pharyngeal dilator muscles and narrowing the retroglossal dimensions [7].
- **Bypassing Nasal Physiology:** The nose functions to filter, humidify, and warm inspired air. It is also the primary site of nitric oxide (NO) production. NO is a potent vasodilator that enhances oxygen uptake in the lungs. Mouth breathing bypasses these protective mechanisms, potentially reducing blood oxygen saturation even in the absence of frank apnea [9].
- **Airway Resistance Variability:** While awake nasal resistance is often measured via rhinomanometry, studies have shown that "awake" resistance does not always correlate linearly with the Apnea Hypopnea Index (AHI) severity [3]. This suggests that dynamic changes in nasal resistance during recumbency—driven by venous pooling in the turbinates and the loss of sympathetic tone during sleep—may be more clinically relevant than static daytime measurements [3].

4.2. The Inflammatory Cascade

Current literature increasingly frames OSA as a systemic inflammatory disorder, sharing common pathways with CRS. This "Two-Hit" hypothesis suggests that localized nasal inflammation (Hit 1) primes the airway for collapse, while the resultant intermittent hypoxia (Hit 2) generates systemic inflammation that further aggravates mucosal disease[1].

4.2.1. Cytokine Spillover

The intermittent hypoxia characteristic of OSA activates the nuclear factor kappa-B (NF-kappa-B) pathway, leading to the upregulation of pro-inflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-alpha), Interleukin-6 (IL-6), and Interleukin-8 (IL-8) [2,10]. These cytokines are not confined to the serum; they are detectable in the nasal lavage of OSA patients, correlating with disease severity [11].

In patients with CRS with nasal polyps (CRSwNP), comorbid OSA exacerbates the inflammatory profile. Research indicates that moderate-to-severe OSA is associated with a broad upregulation of Type 1 (IL-6, CXCL-1), Type 2 (IL-4, IL-13), and Type 3 (IL-17A) immune markers within the polyp tissue itself [11]. This suggests that OSA contributes to a "pan-inflammatory" state, potentially making the CRS more refractory to standard medical therapy.

4.2.2. Oxidative Stress and Mucosal Injury

Reperfusion injury following apneic events generates reactive oxygen species (ROS). Biomarkers of oxidative stress, such as lipid peroxidation products and 8-hydroxy-2-deoxyguanosine, are elevated in OSA patients [12]. This systemic oxidative stress may impair the epithelial barrier function of the nasal mucosa, increasing susceptibility to bacterial colonization and perpetuating the cycle of chronic sinusitis..

4.3. Neurophysiology: The Nasopharyngeal Reflex

The neural regulation of upper airway patency is critical and often compromised in the CRS-OSA dyad. The "nasopharyngeal reflex" (or negative pressure reflex) describes the activation of pharyngeal dilator muscles, primarily the genioglossus, in response to negative pressure in the upper airway.

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4.3.1. Afferent Blockade

The nasal mucosa is rich in trigeminal afferents that detect airflow and pressure. Chronic inflammation, edema, or polyposis may dampen the sensitivity of these receptors, reducing the afferent input required to trigger the compensatory contraction of the genioglossus muscle [13]. This "de-afferentation" leaves the pharyngeal airway vulnerable to collapse during the negative pressure swings of inspiration.

4.3.2. State-Dependent Muscle Activity

Contradictory data exists regarding genioglossus activity. During wakefulness, OSA patients often exhibit increased genioglossus activity compared to controls, a neuromuscular compensation for anatomical narrowing [14]. However, this compensation is lost at sleep onset. Studies utilizing local anesthesia of the nasal mucosa have demonstrated a reduction in pharyngeal muscle tone, confirming the existence of a reflex arc connecting the nose to the pharynx [15]. In CRS patients, chronic mucosal disease may essentially mimic this anesthetized state, impairing the reflex mechanism that protects airway patency [13]. Furthermore, studies involving tracheostomized patients show that bypassing the upper airway reduces genioglossus activation, reinforcing the necessity of local airflow stimuli for maintaining muscle tone [16].

4.4. Microbiome Dysbiosis and the "Oralization" of the Airway

Emerging metagenomic evidence points to the sinonasal microbiome as a key mediator in the CRS-OSA relationship. Dysbiosis—an imbalance in the microbial community—is a hallmark of both conditions.

4.4.1. Microbial Shifts and Prevotella Enrichment

16S rRNA gene sequencing has revealed that the nasal microbiome of patients with severe OSA differs significantly from healthy controls. There is a distinct "oralization" of the nasal flora, characterized by an enrichment of anaerobic oral commensals such as Streptococcus, Prevotella, Veillonella, and Fusobacterium [17]. Prevotella abundance, in particular, has been correlated with OSA severity and inflammatory markers [18]. This migration of oral bacteria likely results from the altered aerodynamics of mouth breathing and potential retrograde aspiration during apneic events.

4.4.2. Bacterial Biofilms, CRS and OSAS

Recent evidence supports the hypothesis that bacterial biofilms play a pivotal role in the pathophysiology of chronic upper airway inflammatory diseases, particularly CRS and adenotonsillitis. As highlighted by Tamashiro et al [19], the sessile nature of biofilms within the sinonasal and adenoidal mucosa confers significant resistance to antimicrobial therapy and host immune clearance. This persistence acts as a chronic inflammatory reservoir, driving mucosal edema and lymphoid hypertrophy—critical anatomic factors in airway narrowing. Consequently, biofilm-mediated chronic inflammation may be a key underlying mechanism exacerbating upper airway resistance and contributing to the severity of OSA, suggesting that targeting biofilm eradication could improve outcomes in sleep-disordered breathing management.

5. Clinical Interactions and Therapeutic Implications

The coexistence of CRS and OSA creates unique clinical challenges, particularly regarding the tolerance of positive airway pressure therapy and the selection of surgical interventions.

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5.1. Impact on CPAP Adherence, Safety and Efficacy

CPAP remains the gold standard treatment for OSA, yet long-term adherence rates are suboptimal, often hovering around 50%.[20] Nasal pathology is a primary determinant of CPAP success.

- **Pressure Intolerance:** High nasal resistance necessitates higher CPAP pressures to effectively stent the airway. These higher pressures can lead to mask leaks, aerophagia, and patient discomfort, driving non-compliance [21,22].
- **CPAP-Induced Rhinitis:** Paradoxically, CPAP therapy itself can induce nasal symptoms. The delivery of high-flow, dry air can cause mucosal desiccation, release of inflammatory mediators, and vasodilation, leading to iatrogenic congestion. Studies have shown that CPAP use is associated with neutrophil infiltration and elevated cytokines in nasal lavage fluid [23]. Heated humidification is the standard intervention to mitigate these effects, shown to decrease nasal resistance and reduce mucosal inflammation [10].
- **Air Leak Complications:** In rare cases, particularly in patients with prior lacrimal surgery or wide sinusotomies, CPAP pressure can cause air regurgitation into the eye via the nasolacrimal duct [24]. Furthermore, recent cadaveric studies indicate that approximately 32% of delivered CPAP pressure is transmitted to the sphenoid sinus after surgery [25]. While generally safe, this pressure transmission warrants caution in the immediate post-operative period following skull base procedures to prevent pneumocephalus.

5.2. Antibiotic Stewardship

The diagnostic confusion between CRS and OSA often leads to the inappropriate use of antibiotics. Patients with undiagnosed OSA presenting with "sinus headache" and fatigue are frequently prescribed repeated courses of antibiotics. Data from the TriNetX database confirms that CRS-OSA patients utilize significantly more antibiotics and oral steroids than CRS-only patients [4]. However, successful treatment of the OSA component—whether through surgery or CPAP—has been shown to reduce the frequency of antibiotic prescriptions, highlighting the importance of treating the underlying sleep disorder to prevent antimicrobial resistance [4].

5.3. Quality of Life Synergies

Independent of hypoxic burden, CRS exerts a profound negative impact on sleep quality. The Pittsburgh Sleep Quality Index (PSQI) and SNOT-22 sleep domains consistently show impairment in CRS cohorts. This sleep disruption is likely driven by a combination of physical obstruction and cytokine-mediated "sickness behavior" (fatigue, malaise) [6]. Consequently, therapies directed at CRS often yield substantial improvements in subjective sleep quality due to an improvement in sleep fragmentation, even if they do not resolve the physiological obstruction of OSA.

6. Medical Management Strategies

The management of the comorbid CRS-OSA patient requires a hierarchical, multimodal approach that optimizes the upper airway to facilitate sleep therapies.

6.1. Topical Therapies and Irrigations

- **Intranasal corticosteroids (INCS) and saline irrigations** are foundational. INCS reduce mucosal edema and have been shown to improve sleep quality and reduce daytime dysfunction, even in OSA patients without frank CRS [26].
- **Xylitol Irrigation:** A significant advancement in topical therapy is the use of xylitol. Unlike simple saline, xylitol lowers the salt concentration of the airway surface liquid, enhancing innate antimicrobial defenses. Meta-analyses indicate that xylitol nasal irrigation significantly improves SNOT-22 scores and sinonasal well-being in post-surgical patients compared to saline

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alone [27]. Mechanistically, xylitol exhibits anti-adhesive properties against S. aureus and Pseudomonas aeruginosa, potentially disrupting the biofilm reservoirs that perpetuate inflammation [28].

6.2. Biologic Therapies

The advent of monoclonal antibodies targeting Type 2 inflammation has revolutionized the management of recalcitrant CRSwNP, with profound implications for sleep.

- **Dupilumab (anti-IL-4/13R\alpha):** Recent real-world studies and clinical trials demonstrate that Dupilumab induces rapid and significant improvement in sleep quality parameters (SNOT-22 sleep domain, Epworth Sleepiness Scale, PSQI) [29]. Notably, this improvement often occurs within the first month of therapy, preceding maximal polyp regression. This suggests that Dupilumab may improve sleep via central mechanisms or systemic cytokine modulation, independent of purely anatomical changes. Animal studies have shown that IL-4 and IL-13, when administered directly into the brain, inhibit NREM (and sometimes REM) sleep, demonstrating clear central effects. In humans, the data are indirect (plasma levels and genetics), but consistent with a modulatory role of these cytokines on sleep architecture and quality. [30,31].
- **Mepolizumab (anti-IL-5) and Omalizumab (anti-IgE):** The SYNAPSE and MUSCA trials have confirmed that Mepolizumab and Omalizumab significantly improve sleep and fatigue scores in patients with severe CRSwP and comorbid asthma [32,33]. These agents reduce the eosinophilic burden that contributes to mucosal thickening and and inflammation.

The economic analysis of these drugs suggests that Dupilumab may offer a favorable cost-per-responder profile in specific healthcare settings, making it a viable option for patients with severe, sleep-disrupting CRSwNP [34].

7. Surgical Interventions: Outcomes and Mechanisms

The role of surgery in the CRS-OSA patient is nuanced. While Endoscopic Sinus Surgery (ESS) is not a standalone cure for moderate-to-severe OSA, it plays a critical adjunctive role in the therapeutic algorithm.

7.1. Endoscopic Sinus Surgery (ESS)

The primary goal of ESS in the context of OSA is to reduce nasal resistance, clear inflammatory load, and facilitate CPAP use.

7.1.1. Impact on AHI vs. Sleep Quality

Meta-analyses consistently demonstrate a dichotomy in surgical outcomes. While ESS and isolated nasal surgery lead to statistically significant improvements in subjective sleep quality (ESS scores, PSQI, SNOT-22), they typically result in only trivial or non-significant reductions in the Apnea-Hypopnea Index (AHI) [35–39]. AHI reductions are generally less than 5 events per hour, which is rarely curative for patients with established OSA [40].

However, the improvement in specific sleep symptoms is robust. Post-operative analysis of SNOT-22 domains reveals significant reductions in "difficulty falling asleep" (58% of patients reporting improvement), "waking up tired" (66% improvement), and "fatigue" [40].

Currently, there is some consensus that the AHI should not be the sole metric used to measure the outcomes of OSA treatment. Other parameters, such as the oxygen desaturation index (ODI), Hypoxic Burden, and % nightime oxygen saturation below 90% (t90), have emerged as more robust measurement tools because they provide a better correlation with the consequences of untreated OSA. Similarly, the subjective improvement of daytime OSA symptoms is also considered a measure of success for both surgery and medical treatment [41–44].

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7.1.2. Facilitation of CPAP Therapy

A critical, often overlooked benefit of ESS is its impact on CPAP parameters. By reducing nasal resistance, ESS allows for a reduction in the therapeutic pressure required to maintain airway patency. Systematic reviews indicate a mean reduction in CPAP pressure of approximately 2-3 cm H2O following nasal surgery [22]. This pressure reduction can be pivotal in converting a non-compliant patient into a compliant user, as lower pressures are associated with greater comfort and fewer mask-related side effects [45].

7.1.3. Extent of Surgery: Full-House and Draf III

The extent of surgery correlates with inflammatory control. "Full-house" ESS (complete opening of all sinus cavities) is often required for diffuse CRS. For recalcitrant frontal sinus disease, the Endoscopic Modified Lothrop Procedure (Draf III) provides maximal drainage. While technically demanding, Draf III has been shown to offer superior improvements in SNOT-22 scores and QoL compared to less aggressive techniques in revision cases [46]. Although direct data linking Draf III to AHI reduction is sparse, the maximal reduction in inflammatory surface area and improvement in airflow dynamics supports its utility in the complex CRS-OSA patient [47,48].

7.2. Hypoglossal Nerve Stimulation (HGNS)

For OSA patients who are intolerant of CPAP, Hypoglossal Nerve Stimulation (HGNS) offers an implantable alternative. A key question has been whether nasal pathology compromises the efficacy of HGNS, which relies on an open nasal airway for optimal ventilation. A retrospective analysis of HGNS outcomes revealed that patients with nasal pathology including CRS (deviated septum, turbinate hypertrophy, polyps) achieved AHI reductions and ESS score improvements comparable to those with normal nasal anatomy [49]. This finding is reassuring, suggesting that HGNS remains a viable option even in patients with imperfect nasal airways, potentially because the therapy actively recruits pharyngeal dilators, bypassing the reliance on the Starling resistor mechanics that govern passive airflow.

Table 1. Comparative Efficacy of Interventions on Sleep Parameters in CRS-OSA.

Intervention	**Target Mechanism**	**Impact on AHI**	**Subjective Sleep Quality (SNOT-22/PSQI)**	**CPAP Impact**
Standard ESS	Reduce nasal resistance; Clear inflammation	Minimal/Trivial (<5 events/hr) [35]	Significant Improvement [40]	Reduces therapeutic pressure (2-3 cmH2O); Improves adherence [22]
Dupilumab	Block IL-4/IL-13 (Type 2 inflammation)	Not primary outcome	Rapid, significant improvement [29]	Not available
Mepolizumab	Block IL-5 (Eosinophil maturation)	Not primary outcome	Significant improvement	Not available

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				in sleep/fatigue domains [33]	
Xylitol Irrigation	Reduce S. aureus adhesion; Osmotic gradient		Unknown	Significant improvement in sinonasal well-being [27,28]	Not available
Hypoglossal Nerve Stimulation	Pharyngeal dilator recruitment		Significant Reduction (Therapeutic)	Significant Improvement [49]	Alternative to CPAP; Efficacy maintained despite nasal pathology [49]

8. Discussion: Synthesizing the United Airway Model

The evidence reviewed herein strongly supports a transition from viewing CRS and OSA as distinct comorbidities to recognizing them as intertwined manifestations of a "United Airway" dysfunction. The data supports a synergistic, "Two-Hit" pathophysiological model.

8.1. The "Two-Hit" Synergistic Model

1. Hit 1 (Anatomical/Mechanical): CRS induces structural nasal obstruction. This forces obligate mouth breathing, which alters mandibular geometry and bypasses the physiological benefits of nasal NO, thereby increasing the work of breathing and destabilizing the pharyngeal airway [7].
2. Hit 2 (Inflammatory/Neural): The resultant OSA induces intermittent hypoxia, generating a systemic inflammatory response (IL-6, TNF-alpha) and oxidative stress. This systemic inflammation spills over into the nasal mucosa, exacerbating CRS severity. Concurrently, the chronic inflammation of CRS dampens the afferent signaling of the nasopharyngeal reflex, impairing the neuromuscular compensation (genioglossus activation) that would otherwise protect the airway [3].

8.2. Discrepancies in "Resistance"

A crucial insight derived from the WTC and general population studies is the disconnect between "awake" nasal resistance and sleep pathology. The finding that subjective sensation of obstruction predicts sleep dysfunction better than rhinomanometry suggests that we may be measuring the wrong parameter, or measuring it at the wrong time. "Sleep" nasal resistance, which increases due to recumbency and venous congestion, likely plays a more pivotal role than the static resistance measured in a clinic [3] Furthermore, the sensation of obstruction may trigger central nervous system responses—anxiety or hyperarousal—that fragment sleep independent of hypoxic events [3].

8.3. Therapeutic Hierarchy and Decision Making

For the clinician managing the CRS-OSA patient, the data supports a specific hierarchical approach:

- Screening is Mandatory: Given the high prevalence of comorbidity, all CRS patients should be screened for OSA using validated tools (STOP-Bang), and all CPAP-intolerant patients should undergo nasal endoscopy or CT scan screening looking for CRS signs.

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- Integrate the use of the NOSE (Nasal Obstruction Symptom Evaluation) scale into the screening for OSA in all patients with CRS. Patients with sleep-related symptoms and elevated subjective scores (such as SNOT-22 > 40 or NOSE > 50) should undergo further evaluation, including nasofibroscopy, to identify structural or inflammatory factors causing sleep disturbances and CPAP intolerance.
- Medical Optimization First: Aggressive medical management with topical steroids and high-volume irrigations (specifically xylitol) should be the first line to reduce inflammatory burden [28].
- The Role of Biologics: In patients with severe CRSwNP and significant sleep disruption, biologics like Dupilumab offer a unique dual benefit, rapidly improving sleep quality through mechanisms that may extend beyond simple polyp shrinkage [29].
- Surgical Counseling: Patients considering ESS must be counseled appropriately. The goal of nasal surgery in the context of OSA is not to cure the apnea (normalize AHI) but to improve sleep quality and fragmentation, reduce snoring, and, crucially, facilitate the use of CPAP or oral appliances by lowering resistance [22].

9. Future Directions

While our understanding of the CRS-OSA interface has deepened, several frontiers remain unexplored. The role of the microbiome offers enticing possibilities; if "oralization" of the nasal cavity drives inflammation, could probiotic interventions or targeted antimicrobial therapies (beyond broad-spectrum antibiotics) restore homeostasis and improve sleep? The correlation between Prevotella abundance and OSA severity suggests a microbial biomarker that warrants further investigation [18].

Additionally, the neurophysiology of the nasopharyngeal reflex requires further mapping. If we can identify the specific molecular mechanisms by which inflammation dampens trigeminal afferent sensitivity, we may be able to develop neuro-modulatory therapies that restore airway reflexes without the need for mechanical stents or invasive surgery.

10. Conclusions

Chronic rhinosinusitis and obstructive sleep apnea are inextricably linked through a complex web of anatomical, inflammatory, and neurological pathways. The presence of one condition frequently exacerbates the other, leading to a cycle of inflammation, obstruction, and systemic morbidity. This review underscores the necessity of a holistic "United Airway" approach. By integrating aggressive medical management, targeted biologic therapies, and judicious surgical intervention aimed at restoring nasal function and facilitating sleep therapies, the otorhinolaryngologist can significantly alleviate the heavy burden of disease carried by these patients. The future of care lies in breaking the cycle of inflammation and restoring the physiological harmony between the nose and the pharynx.

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References

1. Cha, H.; Kim, D.; Lee, H.W.; Lee, Y.; Baek, B.J.; Lee, J.Y.; Choi, J.H. Relationship between chronic rhinosinusitis and risk of obstructive sleep apnea. *Sci. Rep.* 2024, *14*, 21379.
2. Kheirandish-Gozal, L.; Gozal, D. Obstructive sleep apnea and inflammation: proof of concept based on two illustrative cytokines. *Int. J. Mol. Sci.* 2019, *20*, 459.

 doi:10.20944/preprints202512.0769.v2

3. Ayappa, I.; Laumbach, R.; Black, K.; Weintraub, M.; Agarwala, P.; Twumasi, A.; Udasin, I.; Harrison, D.; Chitkara, N.; Rapoport, D.M.; et al. Nasal resistance and inflammation: mechanisms for obstructive sleep apnea from chronic rhinosinusitis. *J. Clin. Sleep Med.* 2024, *20*, 1627–1636.
4. Garvey, E.; Duffy, A.; Tekumalla, S.; Naimi, B.; Kahn, C.; Yang, A.; Wang, J.; Lee, J.; Gray, S.; Chowdhury, N.I.; et al. Obstructive sleep apnea and chronic rhinosinusitis: understanding the impact of OSA on CRS disease burden. *Otolaryngol. Head Neck Surg.* 2024, *171*, 1879–1886.
5. Kao, L.T.; Hung, S.H.; Lin, H.C.; Liu, C.K.; Huang, H.M.; Wu, C.S. Obstructive sleep apnea and the subsequent risk of chronic rhinosinusitis: a population-based study. *Sci. Rep.* 2016, *6*, 20786.
6. Bagchi, N.; Sanders, H.; Chen, Y.; Black, K.; Twumasi, A.; Udasin, I.; Harrison, D.; Chitkara, N.; Rapoport, D.M.; Ayappa, I.; et al. 0474 The effects of chronic rhinosinusitis and obstructive sleep apnea on sleep quality. *Sleep* 2018, *41*, A179. doi:10.1093/sleep/zsy061.473.
7. Chirakalwasan, N.; Ruxrungtham, K. The linkage of allergic rhinitis and obstructive sleep apnea. *Asian Pac. J. Allergy Immunol.* 2014, *32*, 276.
8. Georgalas, C. The role of the nose in snoring and obstructive sleep apnoea: an update. *Eur. Arch. Oto-Rhino-Laryngol.* 2011, *268*, 1365–1373.
9. Friedman, M.; Tanyeri, H.; Lim, J.W.; Landsberg, R.; Vaidyanathan, K.; Caldarelli, D. Effect of improved nasal breathing on obstructive sleep apnea. *Otolaryngol. Head Neck Surg.* 2000, *122*, 71–74.
10. Koutsourelakis, I.; Vagiakis, E.; Perraki, E.; Karatza, M.; Magkou, C.; Kopaka, M.; Zakynthinos, S. Nasal inflammation in sleep apnoea patients using CPAP and effect of heated humidification. *Eur. Respir. J.* 2011, *37*, 587–594.
11. Kim, D.K.; Lee, B.C.; Park, K.J.; Son, G.M. Effect of obstructive sleep apnea on immunity in cases of chronic rhinosinusitis with nasal polyps. *Clin. Exp. Otorhinolaryngol.* 2021, *14*, 390–398.
12. Maniaci, A.; Iannella, G.; Cocuzza, S.; Vicini, C.; Magliulo, G.; Ferlito, S.; Cammaroto, G.; Meccariello, G.; De Vito, A.; Nicolai, A.; et al. Oxidative stress and inflammation biomarker expression in obstructive sleep apnea patients. *J. Clin. Med.* 2021, *10*, 277.
13. Shusterman, D. Trigeminal function in sino-nasal health and disease. *Biomedicines* 2023, *11*, 1778.
14. Eckert, D.J.; McEvoy, R.D.; George, K.E.; Thomson, K.J.; Catcheside, P.G. Genioglossus reflex inhibition to upper-airway negative-pressure stimuli during wakefulness and sleep in healthy males. *J. Physiol.* 2007, *581*, 1193–1205.
15. Doherty, L.; Nolan, P.; McNicholas, W. Effects of topical anesthesia on upper airway resistance during wake–sleep transitions. *J. Appl. Physiol.* 2005, *99*, 549–555.
16. Malhotra, A.; Fogel, R.B.; Edwards, J.K.; Shea, S.A.; White, D.P. Local mechanisms drive genioglossus activation in obstructive sleep apnea. *Am. J. Respir. Crit. Care Med.* 2000, *161*, 1746–1749.
17. Wu, B.G.; Sulaiman, I.; Wang, J.; Shen, N.; Clemente, J.C.; Li, Y.; Laumbach, R.J.; Lu, S.E.; Kanwal, R.; Thomas, B.C.; et al. Severe obstructive sleep apnea is associated with alterations in the nasal microbiome and an increase in inflammation. *Am. J. Respir. Crit. Care Med.* 2019, *199**, 99–109.
18. Guo, Y.; Sun, S.; Wang, Y.; Chen, S.; Kou, Z.; Yuan, P.; Han, W.; Yu, X. Microbial dysbiosis in obstructive sleep apnea: a systematic review and meta-analysis. *Front. Microbiol.* 2025, *16*, 1572637.
19. Tamashiro, E.; Antunes, M.B.; Palmer, J.N.; Cohen, N.A.; Anselmo-Lima, W.T. Implications of bacterial biofilms in chronic rhinosinusitis. *Braz. J. Infect. Dis.* 2009, *13*, 232–235.
20. Nsair, A.; Hupin, D.; Chomette, S.; Barthélémy, J.C.; Roche, F. Factors influencing adherence to auto-CPAP: an observational monocentric study comparing patients with and without cardiovascular diseases. *Front. Neurol.* 2019, *10*, 801.
21. Milinovic, K.; Pavlinac Dodig, I.; Lusic Kalcina, L.; Pecotic, R.; Ivkovic, N.; Valic, M.; Dogas, Z. Adherence to CPAP therapy in obstructive sleep apnea: A prospective study on quality of life and determinants of use. *Eur. J. Investig. Health Psychol. Educ.* 2024, *14*, 2463–2475.
22. Camacho, M.; Riaz, M.; Capasso, R.; Ruoff, C.M.; Guilleminault, C.; Kushida, C.A.; Certal, V. The effect of nasal surgery on continuous positive airway pressure device use and therapeutic treatment pressures: a systematic review and meta-analysis. *Sleep* 2015, *38*, 279–286.

 doi:10.20944/preprints202512.0769.v2

23. Yang, Q.; Li, H.; Wu, W.; Huang, X.; Tu, B.; Ma, Y.; Deng, H.; Li, M.; He, H.; Li, C.; et al. Effect of continuous positive airway pressure on allergic rhinitis in patients with obstructive sleep apnea–hypopnea syndrome. *Ther. Clin. Risk Manag.* 2018, *14*, 1507–1513.
24. Wrede, J.E.; Parsons, E.C.; Watson, N.F. A novel treatment for nasolacrimal air regurgitation into the eye with CPAP: the total face mask. *J. Clin. Sleep Med.* 2018, *14*, 1415–1417.
25. D'Souza, G.E.; Duffy, A.; Mandloi, S.; Garvey, E.; Naimi, B.; Hannikainen, P.; Tekumalla, S.; Wang, J.; Lee, J.; Gray, S.; et al. CPAP-induced sphenoid sinus pressures after endoscopic sinus surgery. *Int. Forum Allergy Rhinol.* 2024, *15*, 68.
26. Ali, M.M.; Ellison, M.; Iweala, O.I.; Spector, A.R. A sleep clinician's guide to runny noses: evaluation and management of chronic rhinosinusitis to improve sleep apnea care in adults. *J. Clin. Sleep Med.* 2023, *19*, 1545–1552.
27. Kang, Y.J.; Stybayeva, G.; Hwang, S.H. Role of xylitol nasal irrigation in the management of chronic sinusitis: A systematic review and meta-analysis. *Clin. Otolaryngol.* 2025.
28. Jiang, R.S.; Chiang, Y.F.; Liang, K.L. Efficacy and safety of xylitol nasal irrigation after functional endoscopic sinus surgery: a randomized controlled study. *Biomedicines* 2024, *12*, 1377.
29. Ferri, S.; Montagna, C.; Casini, M.; Malvezzi, L.; Pirola, F.; Russo, E.; Paoletti, G.; Canonica, G.W.; Heffler, E. Sleep quality burden in chronic rhinosinusitis with nasal polyps and its modulation by dupilumab. *Ann. Allergy Asthma Immunol.* 2024, *132*, 69–75.Krueger, J. (2008).
30. Krueger, J. The role of cytokines in sleep regulation. *Curr. Pharm. Des.* 2008, *14*, 3408–3416.
31. Riva, G.; Garetto, M.; Borgione, M.; Piazza, F.; Prizio, C.; Dellea, D.; De Benedetto, L.; Pecorari, G. Dupilumab improves sleep quality in chronic rhinosinusitis with nasal polyps. *Am. J. Otolaryngol.* 2024, *45*, 104310.
32. Meltzer, E.O.; Mullol, J.; Ko, J.; Saenz, R.; Steinke, J.W.; Millette, L.A.; Gevaert, P. Omalizumab improves sleep and health status for patients with chronic rhinosinusitis with nasal polyps: An analysis of randomized clinical trials. *Int. Forum Allergy Rhinol.* 2024, *14*, 1163–1172.
33. Mullol, J.; Fokkens, W.J.; Smith, S.G.; Keeley, T.; Zhang, L.; Howarth, P.; Jones, N.; Mayer, B.; Bachert, C. The impact of mepolizumab on sleep impairment in CRSwNP: post hoc analyses of SYNAPSE and MUSCA. *Rhinology* 2024, *62*, 669–680.
34. La Mantia, I.; Ottaviano, G.; Ragusa, M.; Trimarchi, M.; Foglia, E.; Schettini, F.; Cocuzza, S.; Cantone, E. Multidimensional impact of dupilumab on chronic rhinosinusitis with nasal polyps. *J. Pers. Med.* 2024, *14*, 45.
35. Wang, M.; Liu, S.Y.C.; Zhou, B.; Li, Y.; Cui, S.; Huang, Q. Effect of nasal and sinus surgery in patients with and without obstructive sleep apnea. *Acta Oto-Laryngol.* 2019, *139*, 467–472.
36. Tosun, F.; Kemikli, K.; Yetkin, S.; Ozgen, F.; Durmaz, A.; Gerek, M. Impact of endoscopic sinus surgery on sleep quality in patients with chronic nasal obstruction due to nasal polyposis. *J. Craniofac. Surg.* 2009, *20*, 446–449.
37. Sukato, D.C.; Abramowitz, J.M.; Boruk, M.; Goldstein, N.A.; Rosenfeld, R.M. Endoscopic sinus surgery improves sleep quality in chronic rhinosinusitis: a systematic review and meta-analysis. *Otolaryngol. Head Neck Surg.* 2018, *158*, 249–256.
38. Jiang, R.S.; Liang, K.L. The influence of functional endoscopic sinus surgery on sleep related outcomes in patients with chronic rhinosinusitis. *Int. J. Otolaryngol.* 2019, *2019*, 7951045.
39. El Rassi, E.; Mace, J.C.; Steele, T.O.; Alt, J.A.; Smith, T.L. Improvements in sleep-related symptoms after endoscopic sinus surgery in patients with chronic rhinosinusitis. *Int. Forum Allergy Rhinol.* 2016, *6*, 414–422.
40. Correa, E.J.; Conti, D.M.; Moreno-Luna, R.; Sánchez-Gómez, S.; Reina, C.O.C. Role of nasal surgery in adult obstructive sleep apnea: a systematic review. *Sleep Sci.* 2024, *17*, e310–e321.
41. Tam, S.; Woodson, B.; Rotenberg, B. Outcome measurements in obstructive sleep apnea: Beyond the apnea-hypopnea index. *Laryngoscope* 2014, *124*, 2420–2424.
42. Malhotra, A.; Ayappa, I.; Ayas, N.; Collop, N.; Kirsch, D.; McArdle, N.; Mehra, R.; Pack, A.; Punjabi, N.; White, D.; et al. Metrics of sleep apnea severity: Beyond the AHI. *Sleep* 2021, *44*, zsab030.
43. Qayyum, N.; Cole, A.; Khayat, R.; Grosberg, A. Improving the cardiovascular outcomes of obstructive sleep apnea: Towards more precise hypoxia-based models of disease severity. *Curr. Sleep Med. Rep.* 2025, *11*, 315.

 doi:10.20944/preprints202512.0769.v2

44. Pang, K.; Olszewska, E.; Vicini, C.; Pang, C.; Rotenberg, B. Sleep goal index (SGI) – New outcome measures, beyond apnea hypopnea index. *Med. Res. Arch.* 2025, *13*, 6601.
45. Najafi, A.; Naeimabadi, N.; Sadeghniiat-Haghighi, K.; Salmani-Nodoushan, M.; Rahimi-Golkhandan, A. Continuous positive airway pressure adherence in patients with obstructive sleep apnea syndrome. *Sleep Med.* 2019, *64*, 58–61.
46. Georgalas, C.; Detsis, M.; Geramas, I.; Terzakis, D.; Liodakis, A. Quality of life outcomes in frontal sinus surgery. J. Clin. Med. 2020, *9*, 2145.
47. Elshamy, I.; Askar, M.; Khalifa, M.; Tomoum, M.; Hamad, M. Clinical evaluation of primary endoscopic frontal sinus surgery grade 6 (Draf III) in patients with moderate to severe eosinophilic chronic rhinosinusitis with polyps: a randomized study. *Egypt. J. Otolaryngol.* 2024, *40*, 215.
48. Leventi, A.; Chatzinakis, V.; Papargyriou, G.; Georgalas, C. Enhancing frontal sinus surgery: Assessing the long-term impact of free grafts and flaps in Draf III procedures. *J. Pers. Med.* 2024, *14*, 396.
49. Adibi, I.; Nayak, A.; Saeedi, A.; Yu, K.; Bentan, M.; Nord, R.S. Impact of nasal pathology on efficacy of hypoglossal nerve stimulation for obstructive sleep apnea. *Laryngoscope* 2025.