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Sleep disruption in chronic rhinosinusitis

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Abstract

Introduction—Chronic rhinosinusitis (CRS) is a common disease of the upper airways and paranasal sinuses with a marked decline in quality of life (QOL). CRS patients suffer from sleep disruption at a significantly higher proportion (60 to 75%) than in the general population (8–18%). Sleep disruption in CRS causes decreased QOL and is linked to poor functional outcomes such as impaired cognitive function and depression.

Areas covered—A systematic PubMed/Medline search was done to assess the results of studies that have investigated sleep and sleep disturbances in CRS.

Expert commentary—These studies reported sleep disruption in most CRS patients. The main risk factors for sleep disruption in CRS include allergic rhinitis, smoking, and high SNOT-22 total scores. The literature is inconsistent with regard to the prevalence of sleep-related disordered breathing (e.g. obstructive sleep apnea) in CRS patients. Although nasal obstruction is linked to sleep disruption, the extent of sleep disruption in CRS seems to expand beyond that expected from physical blockage of the upper airways alone. Despite the high prevalence of sleep disruption in CRS, and its detrimental effects on QOL, the literature contains a paucity of studies that have investigated the mechanisms underlying this major problem in CRS.

Keywords

Chronic rhinosinusitis (CRS); infection; respiratory; sleep; sleep disruption

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Declaration of interest

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1. Introduction

Chronic rhinosinusitis (CRS) is a disease of the upper airways that is both common (affecting more than 10 million Americans) [1] and serious (it is associated with more than 60 limited productivity days throughout the year for each patient [2]). CRS results in a significant decline in quality of life (QOL) [3]. Consequently, CRS is associated with a high financial burden on society – an estimated 60 billion US dollars per year [4]. Patients with CRS often report deficiencies in their general state of health and QOL [5,6] that are as severe as for chronic diseases such as end-stage renal disease [7] and severe asthma [8]. While it has been assumed that these QOL deficits relate to their sinonasal symptoms, these patients commonly also complain of fatigue, lack of a good night's sleep, difficulty in concentrating, and impaired memory and productivity. These symptoms are directly or indirectly linked to sleep deprivation and can also affect QOL. Studies investigating sleep and sleep quality in CRS have shown that 60–75% of individuals with CRS complain of poor sleep [9–12], which is considerably higher than the proportion of such complaints in the general population (8–18%) [13]. Sleep disruption in CRS causes a significant decline in QOL [9] and is linked to poor functional outcomes such as impaired cognitive function [14] and depression [9,14]. These outcomes undoubtedly contribute to the reported poor QOL [15] in CRS. Sleep disturbance is also a common complaint among patients with other inflammatory diseases of the upper airways such as allergic rhinitis (AR) [16,17], which is indicative of a link of sleep disturbance to inflammation and/or blockage of the upper airways. In a larger context, numerous other chronic diseases with an inflammatory mechanism are associated with sleep disruption. Among others, these conditions include gastrointestinal inflammatory diseases such as inflammatory bowel disease [18] and autoimmune rheumatoid diseases like rheumatoid arthritis [19]. The high prevalence of sleep disruption in these inflammatory conditions points to the possible role of systemic inflammatory mediators such as cytokines as contributors to sleep disruption in CRS.

Few studies have investigated sleep and conditions related to disturbed sleep in CRS. This review article aims to provide a summary of these findings by discussing the results of studies on sleep and sleep quality in CRS. A systematic PubMed/Medline search with keywords of CRS and sleep was done. The selected articles were reviewed carefully and relevant results of these studies are summarized.

2. Extent and prevalence of sleep disruption in CRS

Previous studies investigating sleep disturbance and sleep quality in CRS have used varied questionnaires. The results of these studies are summarized in Table 1. One of the commonly used sleep quality measures is the Pittsburgh sleep quality index (PSQI), an 18-item, self-reported measure of sleep quality during a 4-week time period. Sleep quality is scored in a range of 0–21 based on these questions, and a score of 5 or more is indicative of poor sleep quality [20]. Alt et al. found a mean PSQI score of 9.4 in a multicenter series of 268 CRS patients. In that study, 75% of patients reported PSQI score above 5 [9]. Similar PSQI scores were observed in a cohort of CRS patients from Utah (mean ± SD; 9.85 ± 4.74) [11] and in a two-center cohort from Singapore and Ontario (10.9 ± 2.8) [21]. A recent study from Taiwan evaluated a series of CRS patients with the Epworth Sleepiness Scale (EpSS) and found that

38.1% of this cohort had EpSS scores above 10, indicative of daytime sleepiness [10]. Interestingly, the same study found objective evidence for clinically significant nighttime apnea (apnea–hypopnea index [AHI] scores above 5) in 64.1% of CRS patients.

Bengtsson et al. used the Basic Nordic Sleep Questionnaire for subjective evaluation of sleep in a large population-based study [12]. In this study, participants with symptoms of CRS had significantly higher odds of five major sleep-related symptoms compared with those without CRS symptoms; difficulty inducing sleep (odds ratio [OR] [95% confidence interval (CI)] 3.98 [2.9–5.4]), snoring (OR 3.13, CI 2.2–4.4), difficulty maintaining sleep (OR 3.44, CI 2.6–4.6), early morning awakening (OR 4.71, CI 3.5–6.4), and excessive daytime sleepiness (OR 4.56, CI 3.4–6.2) [12]. A study in France evaluated sleep disturbances and QOL in a group of patients with CRS with nasal polyps (CRSwNP) in comparison with controls who denied rhinitis symptoms, using a questionnaire capturing four domains related to sleep: (1) difficulties in falling asleep, (2) difficulties in falling asleep after nocturnal awakening, (3) involuntarily inadequate sleep time, and (4) inefficient sleep. They found that a significantly higher proportion of CRSwNP patients suffered from all of the above symptoms. In comparison with controls, the OR (95%CI) of sleep disturbance in CRSwNP cases was 2.25 (1.54–3.29), which remained significant after adjusting for comorbid AR and asthma [22]. These results show that sleep disruption is a significant and common problem in the vast majority of CRS patients and involves multiple elements of sleep, including falling asleep, remaining asleep during the night, difficulty waking up in the morning, and daytime fatigue.

3. Risk factors for sleep disruption in CRS

We found three studies that examined the association of different demographic and disease-related factors with poor sleep in order to identify potential risk factors for development of sleep disruption in CRS. Alt et al. found that poor sleep quality is significantly associated with tobacco use [9]. Tobacco use is a known risk factor for sleep disruption in the general population as well [23,24].

A large prospective study of 572 adult patients with CRS found that the severity of multiple CRS-related symptoms was significantly correlated with sleep impairment. These symptoms included nasal obstruction, anterior nasal drainage, facial pain/pressure, headache, and cough [25]. Similarly, Jiang et al. reported finding a strong association between nasal blockage and daytime sleepiness [10]. They also found a significant correlation between daytime sleepiness and SNOT-22 scores [10]. SNOT-22 is a validated standard test that consists of 22 questions covering 5 main domains: (1) nasal, (2) extra nasal, (3) ear/facial symptoms, (4) psychological, and (5) sleep dysfunction [26]. The positive correlations between SNOT-22 scores and daytime sleepiness or sleep dysfunction are partly explained by the fact that five of the questions in the SNOT-22 are designed to capture sleep dysfunction. However, based on the fact that nasal symptoms in CRS are also positively correlated with sleep dysfunction [25], part of the correlation between SNOT-22 and sleep could be explained by the nasal symptoms captured by this test. From these findings, it is fair to conclude that CRS patients with higher SNOT-22 scores should be screened for sleep dysfunction more carefully.

Ando et al. showed an association between polyp scores and sleep disruption in CRS [25]. In contrast, in other studies, objective CRS severity scores, including CT scan scores (Lund Mackay score [LMK]) and endoscopy grading, were not associated with increased risk of poor sleep quality [9] or increased daytime sleepiness [10]. Furthermore, in CRS, neither CT scans nor endoscopic scores were associated with sleep apnea [10]. The lack of association between LMK or endoscopic scores and sleep dysfunction, especially in the context of significant association of sleep with symptoms scores, is controversial and requires further investigation.

Ando et al. had found that AR in CRS was a predictor of an increased risk of sleep impairment [25], which was found to be associated with sleep disturbances in CRS in other studies as well [12]. In a population-based study, among individuals with rhinitis symptoms, those with reported environmental allergies were 1.8 times more likely to have moderate-to-severe sleep-disordered breathing [27]. Of note, AR patients, especially those with moderate-to-severe disease, are at risk for significant sleep disturbance [28]. Therefore, it is particularly important to screen for sleep disturbances in CRS patients with allergic sensitization.

4. Importance and relevance of sleep disruption in CRS

We have summarized the results of studies that attempted to test the association of sleep disruption with QOL and other health outcomes in CRS in Table 2.

4.1. Sleep disruption and QOL in CRS

Sleep disruption in CRS is shown to cause a significant decrease in QOL. In one study, patients with poor sleep quality (PSQI > 5) had significantly worse QOL scores measured by the Rhinosinusitis Disability Index (RSDI) and worse symptom/outcome scores measured by SNOT-22 [9]. Both of these scores correlated significantly and positively with total sleep quality scores as well as with sleep quality-related variables including sleep latency, sleep duration, sleep efficiency, need for sleep medicine, and daytime dysfunction [9]. DeConde et al. investigated factors associated with choosing surgical treatment for CRS by comparing SNOT-22 items between 72 patients electing continued medical management versus 291 patients who elected functional endoscopic sinus surgery (FESS). Patients who chose surgery had significantly higher rates of sleep disruption in spite of having similar sinus and nasal-specific symptoms than the medical group [30]. The results of this study suggest a significant effect of sleep related symptoms on patients' well-being and subsequently their choice of treatment [30].

4.2. Sleep disruption and mental health

CRS patients are at higher risk for depression compared with healthy controls. A case-control study evaluated depression in CRS patients in comparison with healthy controls using the Beck Depression Inventory II (BDI) and found that BDI scores were significantly higher in patients with CRS even when controlling for comorbid conditions including asthma and AR [31]. Sleep disruption often clusters with fatigue, pain, and depression in the context of other illnesses such as malignancies [32] and autoimmune diseases like

rheumatoid arthritis [33]. In rheumatoid arthritis, sleep deprivation can result in increased fatigue, depression, and pain [33]. In a report by Alt et al., poor sleep in CRS was associated with a history of depression ($p = 0.020$) [9]. A second study by the same group evaluated the link between depression, pain, and sleep disruption in CRS by standard questionnaires evaluating these conditions and found a significant positive correlation between sleep quality, measured by PSQI, and all pain measures ($p < 0.05$). In this study, positive correlations were found between pain measures and total PSQI score or the 3 PSQI subdomains that measure sleep latency, sleep quality, and daytime dysfunction (all p values < 0.05). Interestingly, the link between sleep dysfunction and pain was limited to CRS patients who were at risk for depression, indicative of the clustering of these major symptoms in CRS [29].

4.3. Sleep disruption and cognitive function

Another important problem commonly observed in CRS patients is lack of concentration or decreased productivity, suggestive of cognitive impairment. Two studies assessed cognitive function of CRS patients using a subjective questionnaire called Cognitive Failures Questionnaire (CFQ) which measures three domains of cognitive function. In a study by Soler et al. [14], CRS patients scored significantly worse on the CFQ than did healthy controls (mean ± SD of 38.3 ± 16.5 vs. 30.9 ± 12.5 in CRS vs. controls, respectively; $p = 0.009$). Interestingly, the CFQ scores correlated significantly with sleep quality measured by PSQI; $r = 0.557$, $p < 0.001$. This study also tested the cognitive function of CRS patients by an objective method using a battery of tests from the Automated Neuropsychological Assessment Metrics computerized platform. They found a significant reduction in one domain of cognitive function, simple reaction time, in CRS patients compared with healthy controls [14]. Tarasidis et al. [15] found a similar mean CFQ score of 40.53 ± 18.14 in 70 CRS patients and a significant but weak correlation between cognitive function and pain scores in these cases. In that study, there were no healthy control subjects for comparison.

Sleep disturbance is linked to cognitive dysfunction [34]. However, the exact mechanism through which poor sleep promotes cognitive dysfunction impairment remains to be studied. Potentially, sleep disruption can result in fatigue and lack of attention, contributing to cognitive dysfunction in CRS patients. However, it is also possible that in CRS, both sleep disruption and cognitive impairment stem from a common cause, like inflammation. Increased pro-inflammatory cytokines can cause both sleep disturbance [35,36] and cognitive decline [37]. The chronic inflammatory state and increased cytokines in patients with CRS [38] could be responsible for the link between poor cognitive dysfunction and sleep disturbance in these patients.

5. Mechanism of sleep disruption in CRS

The mechanisms underlying sleep disruption and poor sleep quality in CRS are unknown. It is generally assumed that any condition resulting in inflamed and enlarged nasal turbinates, such as AR or CRS, will result in nasal air passage obstruction and sleep disruption [39]. It has been previously shown that complete nasal obstruction can increase apneic episodes and transient hypoxia [40,41] in healthy individuals, supporting the notion that nasal obstruction

causes sleep disruption. It should also be noted that other CRS-related factors such as facial pain and headache can affect falling asleep and result in nighttime awakening as well. These symptoms were shown to be associated with sleep disruption in CRS [25]. However, we could not find any mechanistic study evaluating the underlying mechanism of sleep disruption in CRS, beyond a small study showing an association between expression of messenger ribonucleic acid (mRNA) for a few inflammatory cytokines in sinus tissue and sleep disturbance in CRS patients [42]. This study suggests that inflammation is the underlying mechanism of sleep disturbance in CRS patients. This notion is supported by other studies that showed an association between inflammatory diseases like IBD [18] or rheumatoid arthritis [15] and poor sleep.

5.1. Nasal blockage and sleep disruption

In a large population-based study focused on understanding the link between nasal blockage and sleep-disordered breathing, participants with symptoms of rhinitis were significantly more likely to report chronic excessive daytime sleepiness and chronic non-restorative sleep than those who rarely had rhinitis symptoms [27]. In a large multicenter study of patients with AR, nasal obstruction was significantly associated with poorer sleep quality [28]. It is noteworthy that subjective nasal blockage was correlated with objective nasal airflow measured by acoustic rhinometry ($r = 0.45$, $p < 0.01$) [43]. Therefore, reported nasal blockage could potentially be a reliable marker of decreased nasal airflow. Nasal airflow was correlated with respiratory distress index ($r = 0.67$, $p = 0.03$) at night [43], supporting its link to disordered breathing during sleep. A study on chronobiology of patients with AR showed that nasal airflow has a circadian rhythm – nasal blockage increases during the night and peaks at 6 AM [44]. Furthermore, two studies have shown that positional variation can affect nasal patency, which is lowest in the supine position [45,46]. These two factors can further compromise nasal air passage during nighttime sleep.

Another line of evidence linking nasal blockage to sleep disruption is the improvement of sleep-related symptoms in patients with obstructive sleep apnea (OSA) following nasal surgeries aimed to improve the nasal air passages. One study showed that correction of deviated nasal septum reduces snoring and sleepiness (measured by Snoring Outcomes Survey and EpSS, respectively) and increases disease-specific QOL in adult patients with OSA and deviated nasal septum [47]. Another study investigated 25 OSA patients who had nasal obstruction due to hypertrophied turbinates or septal deviation causing nasal airway compromise as well as narrowing of retroglossal or retropalatal airways, consistent with their diagnosis of OSA [48]. These patients were evaluated before and after nasal surgery, septoplasty, or turbinate reduction. In 14 of 25 cases, the nasal airflow increased significantly and these were called responders in the study. AHI, respiratory disturbance index (RDI), and subjective sleep-related symptoms improved significantly in responder patients. The AHI and RDI changes after surgery were minimal in 11 nonresponders [48]. Although this evidence indicates that improving nasal passages decreases apnea at night, these results might only be applicable to OSA patients and thus would be relevant to only subset of CRS patients with OSA.

Few studies have shown a significant association between nasal blockage and sleep disruption in CRS [10,25]. In contrast, a recent study on 28 CRS patients who completed the Nasal Obstruction Symptom Evaluation and the PSQI failed to show a correlation between any of the 4 questions about nasal obstruction and sleep quality [49]. The negative result of the latter study might be due to its small sample size, resulting in a beta-error, or the relatively high CRS severity of this series of patients – all had refractory CRS with mean SNOT-22 scores of 58.6 [49]. It is possible that in severe CRS, factors other than obstruction play a more dominant role in sleep disruption. In such cases, the chronic inflammation and changes in systemic mediators of inflammation such as cytokines may play a role in the observed sleep disruption. Along these lines, Alt et al. found a positive correlation between increased IL-4 and TGF-β mRNA expression in sinus tissue and sleep dysfunction (one domain of sleep disruption measured by PSQI). In addition, a link was observed between increased IL-13 and poor sleep quality [42]. However, it is not known how local tissue expression of cytokines can result in sleep disruption and larger studies evaluating sleep and its association with systemic inflammatory mediators in CRS are needed to investigate this hypothesis.

6. Effect of sinus surgery on sleep in CRS

Few studies have investigated the effect of FESS on sleep quality in CRS patients. These studies are summarized in Table 3. El Rassi et al. reported significant improvements for all sleep-related questions measured by SNOT-22 in a large study of 334 CRS patients who underwent FESS and were followed up postoperatively for an average of 14.5 months. These symptoms included ‘difficulty in falling asleep,’ ‘waking up at night,’ ‘lack of a good night’s sleep,’ ‘waking up tired,’ and ‘fatigue’ [50]. Similarly, DeConde et al. reported a significant improvement in sleep-related questions of SNOT-22 in the follow-up visits after surgical intervention compared to baseline sleep dysfunction scores in a multicenter cohort of CRS patients undergoing surgery (mean ± SD change of −5.7 ± 7.0) [30]. They compared the relative change for sleep dysfunction questions between this surgical cohort with a cohort of CRS cases from the same institute who did not undergo FESS and were managed medically. The medical cohort had a significant improvement in sleep as well, but the surgical cohort had a significantly greater change in sleep compared with the medical cohort (−5.7 ± 7.0 vs. −1.5 ± 6.7; $p < 0.001$) [30]. It is noteworthy that baseline scores for the sleep questions were significantly higher in the surgical cohort (13.7 ± 6.8) than in the medical cohort (10.5 ± 6.2), while the reported follow-up sleep dysfunction scores were similar in the two cohorts: 8.0 ± 6.9 in the surgical cohort and 9.0 ± 7.6 in the medical cohort. This higher severity of baseline sleep disturbance in the surgical cohort could be the reason for a greater change in that group [30]. Alt et al. [11] evaluated the sleep quality of 301 CRS cases undergoing FESS at four academic tertiary care centers using the PSQI before and after surgery. The preoperational global PSQI score was 9.4 ± 4.6, which improved by 2.2 points after surgery [11]. FESS seemed to decrease the sleep disruption in both CRSsNP and CRSwNP patients. A two-center study from Canada and Singapore used the EpSS and the PSQI to evaluate a series of CRSsNP patients prior to and 6 months after sinus surgery [21]. Both the EpSS and the PSQI showed significantly improved scores in these individuals. The EpSS scores decreased from 14.7 ± 3.1 to 9.1 ±1.1, $p < 0.01$ and the global PSQI decreased

from 10.9 ± 2.8 to 5.3 ± 2.2, $p < 0.01$. Of note, this study had eliminated CRSwNP cases and those with septal deviation in order to analyze the impact of the sinus surgery on sleep irrespective of improvements in nasal air passages. The study showed that although nasal obstruction scores did not change following the surgical intervention, sleep symptoms improved significantly [21]. Similarly, in a study on 27 CRSwNP cases, FESS and polypectomy scores showed a significant improvement in mean daytime sleepiness scores along with decreased nasal resistance following surgery. In this cohort the EpSS score decreased from 9.44 ± 4.07 to 4.14 ± 3.15, $p < 0.01$ [51].

These findings show that sleep-related symptoms of CRS patients improve after surgical management of CRS. However, this improvement is not completely explained by a decrease in nasal blockage after surgery (at least not in CRSsNP) and is potentially due to removal of extensive inflammatory tissue and/or improvement of other symptoms of CRS, such as facial pain/pressure, that can affect sleep.

7. OSA in CRS

OSA is a common sleep disorder characterized by complete or partial collapse of posterior pharynx structures, resulting in noisy breathing, brief periods of awakening during sleep, and repetitive episodes of hypoxia [52]. OSA has been associated with CRS in a few studies. In a study done in Taiwan, up to 64.7% of patients with CRS showed evidence of sleep-related breathing disorders with apnea suggestive of OSA [10]. In contrast, in a report from the United States, physician-diagnosed OSA was found in only 15% of CRS cases [53]. In another study on a series of CRSwNP patients, patients had mean AHI scores of 6.85, indicative of minimal apnea, despite high PSQI scores before surgery, indicating that apnea is not the sole cause of sleep disruption in CRS [51].

On the other hand, OSA patients were shown to have a higher risk of CRS. A study investigating the risk of CRS in OSA patients found that the adjusted hazard ratio of subsequent CRS for patients with OSA compared to controls was 3.18 (95% CI: 2.27–4.45), which was similar in both genders [54].

The underlying mechanism of this association is still unknown. Furthermore, a lack of large CRS studies with objective methods of sleep evaluation makes it difficult to distinguish between sleep disruptions due to other causes versus those due to OSA. One potential factor explaining the increased risk of OSA in CRS could be the similar demographics of these two conditions: they both have a similar age distribution, increased risk in male gender, and link to high BMI. Indeed, obesity is one of the main risk factors for OSA, which is also linked to CRS [55].

It was previously thought that colonization of continuous positive airway pressure (CPAP) machine with bacteria might be a risk factor for development of rhinosinusitis in OSA patients. However, a recent study showed no association between sinusitis symptoms measured by the chronic sinusitis survey and the presence of bacterial colonization in CPAP machines [56].

7.1. Effect of FESS on sleep apnea in CRS patients with comorbid OSA

Two studies evaluated whether surgical management of CRS can improve sleep and QOL of CRS patients with comorbid OSA. In the first study, 405 CRS patients were enrolled, out of which 60 (15%) had OSA. Among these, 285 CRS patients provided preoperative and postoperative survey responses, with a mean ± SD of 13.7 ± 5.3 months of follow-up. Using disease-specific QOL measures (RSDI and SNOT-22), CRS patients with and without comorbid OSA improved significantly. However, participants without OSA had significantly greater improvements on PSQI global (−1.9 ± 4.0 vs. −0.5 ± 3.7; $p = 0.03$), sleep quality (−0.4 ± 0.8 vs. −0.03 ± 0.7; $p = 0.02$), and sleep disturbance (−0.4 ± 0.7 vs. −0.1 ± 0.7; $p = 0.03$) scores. These findings indicate that in patients with CRS and OSA, sleep is affected by both conditions and sleep disturbances cannot be treated solely by addressing the CRS. Further strategies targeting OSA are needed to improve the sleep and the QOL of these patients [53].

The second study enrolled 56 patients with OSA and CRS who underwent combined septoplasty with bilateral submucosal inferior turbinate reduction and concurrent ESS. In these patients, the preoperative and postoperative polysomnography reports were compared. The main variables compared included AHI, mean and minimum oxygen saturation, sleep efficiency, and sleep staging. The AHI scores significantly decreased from 33.5 ± 22.0 to 29.4 ± 20.8 after combined nasal and sinus surgery, $p = 0.009$. In this study, patients were grouped, based on their AHI, as mild, moderate, or severe OSA. AHI scores improved in patients with moderate OSA (from 22.3 ± 4.8 to 20.7 ± 8.2, $p = 0.023$) and severe OSA (from 52.3 ± 21.4 to 43.6 ± 23.9, $p = 0.034$), while patients with mild OSA did not show significant changes in AHI [57]. Of note, despite statistically significant changes of the AHI, surgery did not completely improve the AHI, which was still well above the cutoff of 5 for normal sleep, reinforcing the idea that in CRS patients with comorbid OSA, sleep apnea needs to be treated with effective therapeutic measures targeting OSA. Similarly, in a series of CRSwNP patients undergoing FESS who did not carry the diagnosis of OSA, there was no significant difference between preoperative and postoperative mean values of AHI; 6.85 versus 5.53 before and after FESS, respectively, $p = 0.55$ [51].

It is noteworthy that a few other studies evaluated the effect of nasal surgery aiming to decrease nasal obstruction in OSA patients with symptoms of nasal congestion but not having CRS. The majority of these studies showed a benefit in reducing snoring and daytime sleepiness [58–61]. However, except for one study [58], these studies failed to show a significant improvement in RDI or AHI after nasal surgery [58,59,61] which is in agreement with studies in CRS.

8. Expert commentary

Sleep disruption is a common complaint of CRS patients; it affects their mental and physical health and results in impaired QOL. The literature is inconsistent with regard to the prevalence of disordered breathing, e.g. sleep apnea, in CRS, which might be due to variations in methods or in populations studied. Although nasal obstruction is linked to sleep disruption, the extent of sleep disruption in CRS seems to be greater than expected based on physical blockage of the airways. It is possible that inflammation from the nose and sinuses

contributes greatly to sleep disturbance; however, this hypothesis has not been adequately evaluated. Finally, there is paucity of studies that have investigated the mechanisms of this major problem in CRS.

9. Five-year view

This review highlighted the urgent unmet need of mechanistic studies to elucidate the mechanism of poor sleep in CRS patients. The potential factors that could affect sleep and need to be investigated include inflammation with focus on inflammatory pathways that can directly or indirectly cause sleep disruption. Finding the underlying mechanisms of sleep disruption is the first step in order to identify new therapeutic targets to design effective interventions to prevent and treat this common and clinically important comorbidity of CRS. Furthermore, future studies are needed to clarify the inconsistency in the current literature with regard to the prevalence of sleep-related disordered breathing (e.g. OSA) in CRS patients.

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Key issues

- Studies investigating sleep and sleep quality in CRS have shown that 60–75% of individuals with CRS complain of poor sleep.
- Sleep disruption in CRS patients involves multiple elements of sleep, including falling asleep, remaining asleep during the night, difficulty waking up in the morning, and daytime fatigue.
- Sleep disruption in CRS causes a significant decline in QOL and is linked to poor functional outcomes such as impaired cognitive function and depression in CRS.
- The mechanisms underlying sleep disruption and poor sleep quality in CRS are unknown. Possibly contributing factors to sleep disruption in CRS include nasal obstruction, facial pain and chronic inflammation.
- Obstructive sleep apnea has been associated with CRS in a few studies. However, the literature is inconsistent with regard to the prevalence of OSA in CRS.

Table 1

Results of studies measuring sleep quality in CRS.

Name and year of publication	Sample type	Study participants	Method or questionnaires used to asses sleep	Results
Serrano E et al. [22] 2005	Case control	212 CRS with nasal polyposis (CRSwNP)	A questionnaire capturing 4 domains related to sleep	Compared with healthy controls, OR (95%CI) of sleep disturbance in CRSwNP cases was 2.25 (1.54–3.29)
		502 controls		
Alt et al. [9] 2013	Cross sectional	268 CRS patients	PSQI	75% of patients reported PSQI scores above 5, indicative of poor sleep
				Mean PSQI score was 9.4
Alt et al. [11] 2014	Cohort	301 CRS patients	PSQI	72% of patients had PSQI scores above 5, indicative of poor sleep
				Mean ± standard deviation PSQI score was 9.4 (4.6)
Rotenberg et al. [21] 2015	Cohort	53 CRS without nasal polyposis (CRSsNP)	EpSS	Mean ± standard deviation EpSS was 14.7 ± 3.1; cutoff is 10
			PSQI	Mean ± standard deviation PSQI score was 10.9 ± 2.8; cutoff is 5
Jiang et al. [10] 2016	Cross sectional	139 CRS patients	EpSS	38.1% of this cohort had EpSS scores above 10, indicative of sleep disruption
			Polysomnography	64.1% of CRS patients had clinically significant nighttime apnea (apnea-hypopnea index scores above 5)
Bengtsson et al. [12] 2016	Population-based cohort	26,647 subjects, 2249 (8.4%) had CRS	Basic Nordic Sleep Questionnaire	CRS patients had significantly higher odds of all five major sleep-related symptoms measured by the questionnaire

CRS: chronic rhinosinusitis; OR: odds ratio; CRSwNP: CRS with nasal polyps; PSQI: Pittsburgh Sleep Quality Index; EpSS: Epworth Sleepiness Scale.

Table 2

Studies evaluating the association of sleep disruption with quality of life(QOL) and other related health outcomes in CRS.

Name and year of publication	Study participants	Questionnaire used to asses sleep	Questionnaires used to asses QOL or other outcomes	Results
Alt et al. [9] 2013	268 CRS patients	PSQI	RSDI; measuring *QOL* in CRS	Patients with poor sleep quality (PSQI < 5) had significantly worse QOL scores on both the RSDI ($p < 0.001$) and the SNOT-22 ($p < 0.001$)
			SNOT-22: measuring *QOL* in CRS	
				Poor sleep was associated with a history of depression
Soleretal. [14] 2015	50 CRS patients	PSQI	- CFQ: measuring *cognitive function*	CRS patients had significantly worse CFQ and FSS scored compared with controls; total CFQ scores (38.3 ± 16.5 vs. 30.9 ± 12.5; $p = 0.009$) and the FSS (4.2 ± 1.6 vs. 3.0 ± 1.5; $p = 0.001$)
	50 controls		FSS: measuring *fatigue*	Significant correlation between CFQ and sleep quality measured by PSQI; $r = 0.557$, $p < 0.001$
Tarasidis et al. [15] 2015	70 CRS patients	-	CFQ: measuring *cognitive function*	Significant correlation between cognitive dysfunction and pain; Spearmen $R = 0.321$, $p < 0.01$
			SF-MPQ and BPI-SF; measuring *pain*	Significant correlation between disease-specific QOL scores and cognitive function scores measured by the SNOT-22 ($R = 0.395$, $p < 0.01$) and the RSDI ($R = 0.528$, $p < 0.01$)
			RSDI and SNOT-22 measuring *QOL*	
Cox et al. [29] 2016	68 CRS patients	PSQI	SF-MPQ: measuring *pain*	Significant positive correlations between total PSQI scores and all pain measures ($R = 0.38–0.61$, $p \leq 0.05$)
			BPI-SF: measuring *pain*	Significant positive correlations between total PSQI scores and PHQ-2 scores ($R = 0.46$, $p < 0.05$). The relationship between pain and sleep dysfunction scores was only seen in patients with depression
			PHQ-2: screening for *depression*	

PSQI: Pittsburgh Sleep Quality Index; RSDI: Rhinosinusitis Disability Index; CFQ: Cognitive Failures Questionnaire; FSS: Fatigue Severity Scale; SF-MPQ: Short-Form McGill Pain Questionnaire; PHQ: Patient Health Questionnaire; BPI-SF: Brief Pain Inventory Short Form.

Table 3

Studies evaluating the effect of surgical treatment of CRS on sleep.

Name and year of publication	Study participants	Treatment modality used for CRS	Follow-up	Method or questionnaires uses to asses sleep	Results
Tosun et al. [51] 2009	27 CRSwNP	FESS	3 months	EpSS	EpSS score decreased from 9.44 ± 4.07 to 4.14 ± 3.15, $p < 0.01$
				Polysomnography	No significant difference between preoperative (6.85) and postoperative (5.53) mean values of apnea-hypopnea index
DeConde et al. [30] 2014	291 CRS patients	FESS	>6 months	5 sleep-related questions in SNOT-22 questionnaire	Significant improvements for all sleep-related questions; mean ± SD change of −5.7 ± 7.0
Alt et al. [11] 2014	301 CRS patients	FESS	Average of 13.1 months	PSQI	Significant improvement in PSQI; mean decrease of 2.2 points in global PSQI scores
Rotenberg et al. [21] 2015	53 CRSsNP	FESS	6 months	EpSS	EpSS decreased from 14.7 ± 3.1 to 9.1 ± 1.1, $p < 0.01$
				PSQI	PSQI decreased from 10.9 ± 2.8 to 5.3 ± 2.2, $p < 0.01$
El Rassi et al. [50] 2016	334 CRS patients	FESS	Average of 14.5 months	5 sleep-related questions in SNOT-22 questionnaire	SNOT-22 sleep domain scores improved from 13.7 ± 6.8 to 7.7 ± 6.6, $p < 0.001$

EpSS: Epworth Sleepiness Scale; SNOT: Sinonasal Outcome Test; FESS: Functional Endoscopic Sinus Surgery.

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