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PhD THESIS

THE CPAP THERAPY ADHERENCE RELATED TO THE EMOTIONAL AND COGNITIVE PROFILE OF THE PATIENT WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

– A B S T R A C T –

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INTRODUCTION

Sleep is an essential and natural state that significantly impacts our health and well-being. It helps consolidate memories, regulate emotions and physical recovery, and improve cognitive function. However, sleep disruption and a lack of adequate sleep are becoming increasingly prevalent in modern society.

Sleep medicine is a complex and multidisciplinary medical specialty that includes over 80 pathological entities and focuses on diagnosing and treating sleep disorders and disturbances. Obstructive sleep apnea syndrome (OSAS) represents the most prevalent and clinically important sleep-related breathing disorder, manifested by repetitive episodes of partial or total airflow obstruction in the upper airway during sleep, resulting in intermittent hypoxia, sleep fragmentation and a reduced oxygen supply to vital organs. Untreated, it leads to excessive daytime sleepiness and increases the risk of chronic disease, mental disorder, cognitive impairment and decline, risk of car accidents, and inefficiency at work.

Continuous positive airway pressure (CPAP) therapy is the most efficient and used treatment for obstructive sleep apnea. It improves various aspects of an individual's health, including daytime alertness, cardiovascular health, mental health conditions such as depression and anxiety, performance, concentration, and memory consolidation. However, some patients may not accept or tolerate it as a treatment option. In such cases, poor adherence to therapy can adversely affect patients' ability to experience the full range of potential benefits.

The increasing prevalence of obstructive sleep apnea in medical practice globally can be attributed to several factors, including improved diagnostic capabilities, heightened patient awareness, lifestyle changes, and the proliferation of risk factors such as obesity. As awareness grows, so does the understanding of OSA's significant impact on depression, anxiety, and cognitive function.

The quantity and quality of sleep have decreased in developing countries while obesity rates continue to rise. These worldwide problems have led to an increased risk of chronic diseases or the worsening of existing ones due to obstructive sleep apnea. Emotional and cognitive well-being is crucial to every individual's quality of life. Therefore, the impact of adherence to CPAP therapy on the emotional and cognitive profile of sleep apnea patients is an important topic to be studied because depression, anxiety, and cognitive decline are commonly associated with sleep apnea syndrome, and CPAP therapy has been shown to have significant benefits in managing these issues.

The first section of this thesis provides an overview of obstructive sleep apnea syndrome, encompassing its definition, epidemiology, risk factors, pathophysiology, complication, diagnosis, and treatment. The evaluation of the association between OSA,

depressive and anxiety symptoms, and cognitive impairment with underlying mechanisms and the role of CPAP therapy in improving these conditions.

The research component of this thesis consists of three sections. The first study investigates the effect of CPAP therapy on depression and anxiety symptoms in moderate to severe OSA patients. The second study evaluates the impact of CPAP therapy on global cognition over one year of follow-up on patients with moderate to severe OSA. The patients were selected from the Clinical Hospital for Infectious Diseases and Pulmonology, Timisoara, from January 2020 to January 2022. Lastly, a comprehensive literature review is conducted to present an overview of self-reported scales for identifying depression and anxiety symptoms in OSA adult patients.

GENERAL PART

Obstructive Sleep Apnea Syndrome is a sleep disorder characterized by decreased airflow during sleep, leading to symptoms like diurnal sleepiness, unrefreshing sleep, fatigue, or snoring. It is associated with comorbidities such as cardiometabolic, mood disorder, or cognitive impairment. The severity of OSA is quantified by the Apnea Hypopnea Index (AHI), which measures the number of respiratory events of apnea and hypopnea types occurring in one hour of sleep.

The risk factors related to OSA are represented by obesity, age, sex, skeletal and soft tissue abnormalities, endocrine pathology, chronic smoking, and alcohol consumption. Untreated, OSA contributes to cardiovascular diseases like hypertension and stroke, arrhythmias like atrial fibrillation, coronary artery disease, heart failure, metabolic syndrome and diabetes, erectile dysfunction, depressive and anxiety symptoms, and cognitive impairment. Moreover, obstructive sleep apnea syndrome affects tumorigenesis and development, with nocturnal hypoxemia being associated with all-cancer incidence in OSA patients.

The diagnosis of OSA involves a rigorous interview about symptoms, sleep history that describes bedtime and wake time, sleep duration, sleep hygiene, working conditions (shift work, drivers), medical history, and clinical examination. If the clinical assessment indicates obstructive sleep apnea (diurnal and nocturnal symptoms, obesity, comorbidities), overnight testing like polysomnography (PSG), cardiorespiratory polygraphy (PG), and pulse oximetry are required.

Treatment options include surgery, such as nasal and bariatric surgery, and non-surgical treatments, such as positional therapy, mandibular advancement devices, and

continuous positive airway pressure (CPAP). Sleep hygiene, weight loss, dietary changes, and quitting smoking can help manage OSA.

According to the American Academy of Sleep Medicine, CPAP remains the first-line therapy in OSA, but satisfactory adherence is necessary for beneficial effects. Adherence to CPAP therapy is defined as using a device for more than four hours per night of sleep, 70% of the time reported to a month. Therefore, healthcare providers, sleep doctors, and insurance companies all work towards ensuring compliance. It is essential to note that the more the patient adheres to CPAP treatment and increases its usage, the more symptoms improve. However, compliance is influenced by OSA severity, societal and cultural variables, economic conditions, and comorbidities requiring specialized care.

Obstructive sleep apnea is characterized by atypical respiratory occurrences, heart rate fluctuations, and sleep interruptions, often leading to excessive daytime sleepiness and neuropsychological symptoms such as irritability, trouble concentrating, depression, and anxiety. The relationship between depression, anxiety, and obstructive sleep apnea is complex and multifactorial. OSA patients experience intermittent interruptions in breathing and frequent arousals, leading to poor-quality sleep, which can cause mood disruptions, an imbalance in cortisol levels, and impairments in cognitive processes. Anxiety also leads to irregular cortisol levels, which may lead to anxiety-related diseases. Sleep deprivation and intermittent hypoxemia are associated with alterations in immune function and inflammation, leading to elevated levels of pro-inflammatory cytokines.

Anxiety disorders are linked to elevated CRP levels in the bloodstream, which are associated with both anxiety and obstructive sleep apnea. Structural and functional abnormalities in the brains of patients associated with OSA and depression have been found. The serotoninergic system plays a crucial role in regulating mood, the sleep-wakefulness cycle, and the modulation of upper airway muscle tone during sleep.

Patients diagnosed with OSA suffer from impaired cognitive processing, memory, alertness, divided attention, and executive functioning. These deficits result in reduced capacity to process information, difficulty perceiving, encoding, storing, recalling, and retrieving information, inability to sustain attention over time, challenges in multitasking or responding to multiple stimuli, disorganization, emotional instability, impulsivity, and difficulty maintaining motivation. Sleep also plays a crucial role in brain plasticity and memory consolidation. In addition, sleep disruption impacts the activity of neurons, the formation of myelin, cellular oxidative stress, the folding of proteins, and the functioning of molecular signaling pathways. This results in the development of microinfarcts and the shrinking of the brain. In individuals with OSA, there is a decrease in both non-rapid eye movement and rapid eye movement sleep periods, leading to cognitive impairment. Moreover, OSA contributes to cerebral small vessel disease (C-SVD), which impacts tiny blood vessels such

as arteries, veins, arterioles, and capillaries, leading to a persistent decrease in blood flow and ischemic cerebral small vessel diseases like white matter hyperintensity and lacunar infarction.

It is essential to identify neurocognitive complications in OSA promptly and initiate appropriate therapy before permanent damage occurs. Studies have shown that CPAP therapy improves mental health conditions such as depression and anxiety, performance, concentration, and memory consolidation.

STUDY 1: CPAP THERAPY ON DEPRESSIVE AND ANXIETY SYMPTOMS IN PATIENTS WITH MODERATE TO SEVERE OBSTRUCTIVE SLEEP APNEA SYNDROME

The modern world is a world of speed, an unhealthy lifestyle, an obesity pandemic, and, implicitly, the increasing prevalence of developing sleep apnea syndrome. Patients who suffer from obstructive sleep apnea syndrome experience symptoms of depression and anxiety, and it is essential for healthcare providers to consider the psychological status of these individuals. According to the literature, the estimated prevalence of depressive symptoms in individuals with OSA is up to 35%, while the prevalence of anxiety is up to 32%.

Sleep disruption, low oxygen levels, and sleep deprivation can cause symptoms such as depression and anxiety. This is because these conditions increase the sensitivity of the areas in the front part of the brain that are responsible for emotions. As a result, insufficient sleep can cause an exaggerated response from these areas, leading to emotional and psychological symptoms.

Research studies have found that some literature supports a positive impact of CPAP on depressive and anxiety symptoms, while others have inconsistent results. This inconsistency may be due to the use of different scales and criteria for diagnosing depression and anxiety, which can lead to variations in the conclusions reported in different studies. Consequently, this study aims to determine how common depression and anxiety symptoms are in patients with moderate to severe obstructive sleep apnea by using two validated questionnaires, Patient Health Questionnaire-9 (PHQ-9) and Generalizes Anxiety Disorder-7 (GAD-7). Additionally, the main objective is to evaluate the effect of CPAP therapy on these psychological states over six months and a one-year follow-up period.

This study included 99 consecutive patients diagnosed with moderate to severe obstructive sleep apnea based on their apnea-hypopnea index (AHI). The average age of the participants was 56.49 ± 10.92 years. Regarding gender distribution, the study group included 66 men (67%) and 33 women (33%), and the results showed a predominance of the male sex associated with sleep apnea. According to anthropometric data, the BMI was 36.54 ± 6.4 kg/m². Neck circumference was 44.08 ± 3.82 cm; abdominal circumference was

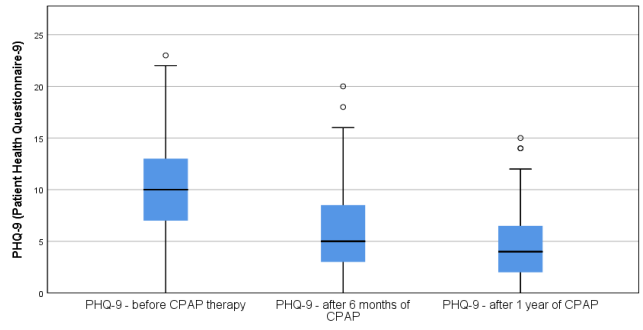
124.67 ± 14.47 cm. There was no statistically significant difference between a group of males and a group of females. A notable component of the study population consisted of obese patients with BMI>30 kg/m² (85.8%), and this factor risk showed it plays a role in OSA.

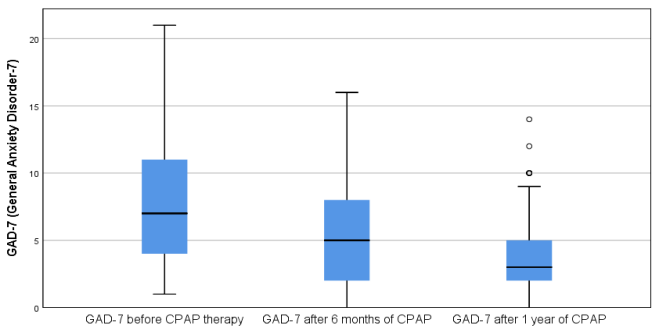
The study used the PHQ-9 questionnaire to quantify depression and found that almost half of the participants (48%) had shown clinical symptoms of depression, with a PHQ score of 10 or higher. Females manifest high scores for depression. Moreover, 27% of participants presented symptoms of clinical anxiety with a GAD-7 score of 10 or higher. There were no differences between genders.

There were multiple comorbidities in our study. The most common were hypertension (63%), ischemic heart disease (28%), diabetes mellitus (22%), COPD (16%), heart failure (14%), asthma (6%), arrhythmia (8.1%), and stroke (2%). In addition, patients with more associated comorbidities tend to have higher levels of anxiety, showed by the GAD-7 total score.

Analysis of the PHQ-9 score revealed significant correlations with BMI, AHI, ODI, ESS, [t90], and GAD-7 score. The GAD-7 score significantly correlated with AHI, ODI, and [t90]. These findings suggested that there is a link between depression and anxiety with hypoxemia, sleep fragmentation, and severity of OSA.

The PHQ-9 and GAD-7 scores showed a substantial decrease after six months and one year of CPAP usage, both in men and women. Moreover, AHI and excessive daytime sleepiness significantly improved after CPAP therapy.





In summary, the study findings have highlighted that individuals diagnosed with moderate to severe obstructive sleep apnea also have symptoms of moderate to severe depression and anxiety. In addition, women presented higher scores than men, even though the number of women was half the number of men participating in the study. Furthermore, the study revealed that adhering to continuous positive airway pressure therapy results in a substantial enhancement in both depression and anxiety symptoms using self-reported questionnaires PHQ-9 and GAD-7.

Simultaneously, there was a statistically significant association between [t90], ODI, AHI, and scores of depression and anxiety symptoms. These findings suggested that there is an underlying relationship between depression and anxiety, intermittent hypoxemia, and the severity of OSA.

Overall, the results of this study suggest that when someone shows signs of sadness and anxiety, it is essential to take into account the potential presence of obstructive sleep apnea as a possible root cause due to its widespread occurrence. Accurately diagnosing OSA and providing appropriate treatment is likely to result in an improvement in depression and anxiety symptoms.

STUDY 2: IMPACT OF CPAP THERAPY ADHERENCE ON GLOBAL COGNITION IN PATIENTS WITH MODERATE TO SEVERE OBSTRUCTIVE SLEEP APNEA: A ONE-YEAR FOLLOW-UP

Individuals with obstructive sleep apnea experience a decrease in several cognitive abilities, such as memory, attention, problem-solving, language, spatial reasoning, and reaction time. There is evidence indicating a connection between obstructive sleep apnea and cognitive impairment. However, the processes behind this link are intricate and need to be better understood. Intermittent hypoxia and sleep fragmentation cause oxidative stress, inflammation, reperfusion damage, and endothelial dysfunction, which in turn lead to changes in the brain, particularly in the areas responsible for cognitive and affective functioning.

CPAP is widely used, and it is considered the most effective treatment for obstructive sleep apnea. It effectively enhances oxygenation by lowering nocturnal breathing disturbances, daytime sleepiness, sleep-related quality of life issues, and depression and anxiety symptoms. According to the research, treatment has decreased daytime and nighttime symptoms and improved cognitive functioning. In addition, diffusion tensor imaging demonstrated a reduction in the structural integrity of white matter fibers in individuals with obstructive sleep apnea. However, after one year of continuous positive airway pressure therapy, it has been found to have a restorative effect on the specific cerebral abnormalities caused by OSA, indicating that efficacious treatment can restore cognitive abilities. These

findings indicate the significance of promptly diagnosing and treating patients with OSA to prevent cognitive deterioration.

Given the intricate interplay between obstructive sleep apnea and cognitive impairment, there is significant potential for exploring the benefits of CPAP treatment on global cognition in patients with moderate to severe OSA over a one-year follow-up.

The study included 65 participants, categorized into two groups based on their CPAP adherence: 34 patients in the CPAP group and 31 in the no-CPAP group. The average age of individuals in the CPAP group was 57.6 years, while it was 60.4 years for those in the no-CPAP group. Regarding gender distribution, the CPAP group comprised 18 men (52.9%) and 16 women (47.1%). The group without CPAP treatment consisted of 17 males (54.8%) and 14 females (45.2%). Based on the AHI categorization, 24.61% of the subjects had a moderate level of OSA (AHI = 15–29.9 events/h), whereas 75.38% had a severe level (AHI > 30 events/h).

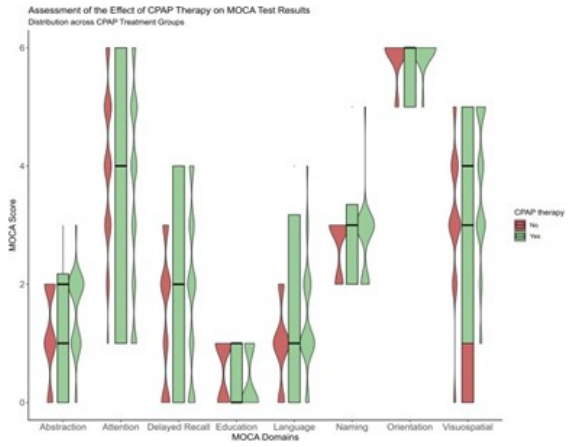
The study found that OSA patients commonly had comorbidities, with the following frequencies: arterial hypertension (98.5%), dyslipidemia (89.2%), ischemic heart disease (49.2%), heart failure (47.7%), diabetes (44.6%), asthma (24.6%), COPD (18.5%), and arrhythmias (16.9%). There was no statistical difference between the CPAP Group and no-CPAP patients according to comorbidities.

In our study, a MoCA score of less than 23 points indicates cognitive impairment. Of all the study participants, 70.76% met this criterion, with 22 individuals (64.70%) in the CPAP group and 24 individuals (77.41%) in the no-CPAP group. The MoCA score showed a strong positive connection with years of education and a negative correlation with body mass index, ESS, PHQ-9, and [t 90].

Based on a PHQ-9 score ≥ 10, which is indicative of clinical depression symptoms, our findings reveal that females (63.3%) exhibit a higher prevalence of depressive symptoms compared to males (40%). The prevalence of clinical anxiety symptoms, as indicated by a GAD-7 score greater than 10, was 34.3% among men and 23% among women.

After six months of CPAP usage, the MoCA score increased from 20.9 ± 3.5 to 22.2 ± 3.5. Significant domain improvement between groups was evidenced for visuospatial, abstraction, and delayed recall.

After one year, the CPAP group improved their total MoCA score from 20.9 ± 3.5 to 22.7 ± 3.5. The difference in scores based on domains between the groups was particularly noticeable for attention and delayed recall, with a significant variance. Moreover, a significant difference was observed in the visuospatial, language, and abstraction domains.



In comparison with the no-CPAP group, the CPAP group exhibited a substantial enhancement of MoCA score for males, with an increase in the average value from 22.1 ± 4 to 23 ± 3.8, and for females, with an increase in the average value from 21 ± 3.4 to 22.6 ± 3. Moreover, PHQ-9, GAD-7 scores, and the Epworth Sleepiness Scale (ESS) decreased significantly after CPAP therapy. In the CPAP group, after six months of therapy, AHI decreased from 48 ± 15.8 to 4.3 ± 2.4, and after one year, to 3.5 ± 2.

In summary, the results have shown that moderate to severe obstructive sleep apnea significantly affects overall cognitive function across several cognitive areas. CPAP treatment enhances overall cognitive function throughout one year of observation, with improvements, particularly in cognitive areas such as attention and delay recall, as well as visuospatial, language, and abstraction. Furthermore, the treatment effectively alleviated excessive daytime drowsiness as well as feelings of depression and anxiety, with a significant improvement in the CPAP group compared to the no-CPAP group.

Additionally, AHI at one year was negatively associated with MoCA at one year, but OSA severity at six months was positively associated with MoCA. These findings indicate that the connection between obstructive sleep apnea severity and cognitive performance may be fluid and evolve. This emphasizes the significance of continuously monitoring and managing OSA longitudinally. Moreover, future studies should consider enrolling more diverse patient cohorts and incorporating healthy control groups.

STUDY 3: A NARRATIVE REVIEW OF SELF-REPORTED SCALES TO EVALUATE DEPRESSION AND ANXIETY SYMPTOMS IN ADULT WITH OBSTRUCTIVE SLEEP APNEA PATIENTS

Obstructive sleep apnea is the prevailing and medically serious respiratory problem during sleep. The connection between OSA and mental health issues has lately received considerable attention. Depression and anxiety are quite common in people with obstructive

sleep apnea, and their presence might worsen sleep problems and reduce the likelihood of following therapy.

According to the Institute for Health Metrics and Evaluation, there are an estimated 280 million individuals globally who suffer from depression and more than 300 million individuals worldwide who exhibit symptoms of anxiety. The prevalence of depression is estimated to be 3.8% among the general population, with 5% of adults (4% of men and 6% of women) and 5.7% of persons aged 60 and above being affected.

Even if the underlying mechanism between OSA, depression, and anxiety is not very clear, literature recognizes their relationship. Several factors contribute to the relationship between depression, anxiety, and obstructive sleep apnea. OSA is defined by intermittent interruptions in breathing and frequent arousals that cause fragmented and poor-quality sleep. This leads to sleep deprivation and abnormalities in sleep structure. Insufficient sleep and low-quality sleep are factors that lead to mood disruptions, such as feelings of depression and anxiety. Neurotransmitters such as serotonin regulate both the sleep/wake cycle and mood. Neuroimaging studies indicate abnormalities in brain structure, including notable decreases in gray matter volume, particularly in regions such as the hippocampus, anterior cingulate cortex, amygdala, and frontal cortex. Episodes of apnea in obstructive sleep apnea can cause a reduction in blood oxygen levels, resulting in intermittent hypoxia. The brain can be adversely affected by chronic intermittent hypoxia and oxidative stress caused by OSA, which might impact mood regulation. In addition, individuals with obstructive sleep apnea have demonstrated a deficient immune response and aberrant activation of the inflammatory response system, leading to an elevated production of pro-inflammatory cytokines.

Scales are instruments designed to evaluate symptoms that cannot be immediately observed during a clinical examination, focusing on the patient's perspective. These surveys may include subjective elements, which capture a patient's perspective and assessment of a symptom and its impact on their daily activities. Thus, these results are considered patient-related and have the advantage of shifting focus towards the patient, which is essential for the treatment model.

This study aims to give physicians and researchers a comprehensive review of the existing scales currently available for screening depression and anxiety and measuring their intensity in patients with obstructive sleep apnea. The scales are categorized based on their kind, either as screening or rating scales, and arranged chronologically according to the year they were published. The text provides a detailed explanation and real-world examples of each scale, followed by an analysis of its psychometric features. Additionally, the strengths and limits of the instrument are examined.

Screening and rating scales for depression and anxiety.

Scales	Overview	Number of items	Scoring	Cut off	Time frame	Adminis-tration
CES-D	Screening depression	20	Responses are 4-point scales where 0 - rarely or none of the time (less than 1 day), 1- some or a little of the time (1-2 days), 2- occasionally or a moderate amount of time (3-4 days), 3- most or all of the time (5-7 days), with a total score ranging from 0 to 60	≥16	Past week	10 minutes
HADS-A HADS-D	Screening depression anxiety	14	It comprises 14 items: seven for anxiety and seven for depression and is rated from 0 to 3, according to how often the respondent has felt during the past week. Total score ranges from 0-42 and 0-21 for subscales	≥8	Past week	2-5 minutes
PHQ-9	Screening depression	9	A 4-point scale indicates the degree of severity; items are rated from 0 (not at all) to 3 (nearly daily). Total score range between 0-27	≥10	Past 2 weeks	3-5 minutes
BDI-II	Rating depression	21	It questions how respondents have felt recently. The scale is rated in an increasing ordinal severity scale, ranging from 0 to 3. The total score varies from 0 to 63.	≥11	Not establish	5-10 minutes
SDS	Rating depression	20	The standardized score is calculated by multiplying the total of the raw item scores of the 20 items by a factor of 1.25. It scored from 0 (a little of the time) to 4 (most of the time). Range 0–100, where higher scores indicate great depression.	≥53	Past several days	5-10 minutes
GAD-7	Screening anxiety	7	The patient's response options include "not at all," "several days," "more than half the days," and "nearly daily," which are assigned scores of 0, 1, 2, and 3, respectively. Mild anxiety is defined as a score of 5, while a score of 10 indicates moderate anxiety.	≥10	Past 2 weeks	3-5 minute
STAI	Rating anxiety	40	STAI-State responses on a scale of 0 to 3, ranging from "not at all" to "very much so". These responses reflect the individual's current emotional state. STAI-Trait responses range from 0 (almost never) to 3 (almost always). Scores range from 20 to 80, and higher scores indicate greater anxiety.	Not establish	State anxiety Trait anxiety	10-20 minutes
BAI	Rating anxiety	21	The total score varies from 0 to 63. A score of 0 to 7 indicates minimal anxiety, 8 to 15 indicates mild anxiety, 16 to 25 indicates moderate anxiety and 30 to 63 indicates severe anxiety.	≥16	Past week	10 minutes

The result of the study showed that the prevalence of depression and anxiety varies significantly among individuals with OSA, as per the analysis of various studies. The incidence of depression ranged from 14.4% to 88.3%, whereas anxiety ranged from 15.9% to 62.2%. A review showed the prevalence rates for depression ranged from 7% to 63%, and for anxiety, it ranged from 11% to 70%. This variation is also due to the choice of the cut-off for each study.

The most used questionnaires for depression, depending on the use in the studies involved, were:

- the Beck Depression Inventory (BDI, BDI-FS, and BDI-II), which was used in 11 studies (45.8%)
- the Hospital Anxiety and Depression Scale (HADS-D) was used in five studies (20.8%)
- the Patient Health Questionnaire-9 (PHQ-9) and the Zung Self-Rating Depression Scale (SDS) were used in three studies each (12.5%)
- the Center for Epidemiologic Studies Depression Scale (CES-D) was used in two studies (8.3%).

The most used questionnaires for anxiety, depending on the use in the studies involved, were:

- the Hospital Anxiety and Depression Scale (HADS-A) was used in five studies (20.8%),
- the Generalized Anxiety Disorder scale (GAD-7) was used in two studies (8.3%)
- the State-Trait Anxiety Inventory (STAI) was used in one study (4.1%)
- the Beck Anxiety Inventory (BAI) was used in one study (4.1%).

This narrative review provides a summary of several techniques available for screening depression and anxiety and assessing their severity in individuals with obstructive sleep apnea. When choosing the best tool to measure and evaluate depression and anxiety, it is important to consider factors such as the instrument's suitability for the study's goal, its availability, its psychometric properties, and previous use in similar study groups. Self-reported scales are simple to administer, economical, do not need significant training programs, and are less susceptible to interviewers' assumptions. However, the efficacy of these surveys depends on the respondent's desire to participate and their understanding of the questions.

The findings of our investigation revealed that the Beck Depression Inventory and the Hospital Anxiety and Depression Scale (HADS-D) were the most often employed tools for detecting depression in patients with obstructive sleep apnea. An inherent drawback of these scales is their lack of cost-free accessibility, in contrast to the PHQ-9. Moreover, the PHQ-9 possesses superiority over these scales due to its inclusion of a suicidal ideation item, which emphasizes the necessity for patients to seek assistance from expert professionals. Regarding anxiety, our findings indicate that the HADS-A questionnaire, followed by the GAD-7 questionnaire, was the most utilized, consistent with prior research.

Medical practitioners should be aware of the benefits and difficulties associated with utilizing self-reported scales to evaluate the mental state of patients with obstructive sleep apnea, as well as the significance of regular screening due to the elevated prevalence of depression and anxiety.

PERSONAL CONTRIBUTION

The scientific research objectives have been effectively achieved. The goal of evaluating the influence of CPAP therapy adherence on depression and anxiety symptoms and cognitive impairment in individuals with obstructive sleep apnea syndrome has been achieved.

Regarding the individual contributions, they were achieved as specified below:

- I have explored that long-time adhering to continuous positive airway pressure therapy results in a substantial enhancement in both depression and anxiety symptoms using self-reported questionnaires PHQ-9 and GAD-7. Moreover, I have shown a significant correlation between PHQ-9 and GAD-7 with AHI, [t90], and ODI. The findings indicate a fundamental role and an underlying mechanism of the severity of apnea and intermittent hypoxemia in depressive and anxiety symptoms.
- I have conducted an assessment of one-year follow-up adherence to CPAP therapy on global cognition using the MoCA tool. The results of this evaluation demonstrate significant improvements in global cognitive score and particularity in domains such as attention, delayed recall, visuospatial, language, and abstraction when compared with a no-CPAP group.
- The present study examined the utility of self-reported questionnaires in the context of assessing depressive and anxiety symptoms in obstructive sleep apnea syndrome among adult individuals.
- I have proposed incorporating mental state evaluations using self-reported scales into regular clinical practice for individuals diagnosed with obstructive sleep apnea.

In general, this research emphasizes the importance of adherence therapy on the well-being and cognition of individuals with obstructive sleep apnea, particularly those with moderate to severe forms of the disease.