

Obstructive Sleep Apnea and Type 2 Diabetes

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About the Author



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Introduction

Obstructive sleep apnea (OSA) and type 2 diabetes (T2D) are commonly encountered diseases in clinical practice, and there appears to be a bidirectional relationship between these 2 diseases. The presence of OSA can increase the risk of developing T2D, increase the risk of micro- and macro-vascular complications, and increase the risk of mortality. Several management strategies are available that can positively impact the outcomes of patients living with co-existing T2D and OSA. Given this bidirectional relationship, the negative consequences of untreated OSA on outcomes in T2D, along with the currently available management strategies, screening for OSA in patients with T2D should be considered.

Obstructive Sleep Apnea

OSA is the repetitive collapse or near collapse of the upper airway during sleep, which leads to periodic events of apnea (complete cessation of

breathing) and hypopnea (a substantial reduction in ventilation).¹ Repeated arousals are required to re-open the airway which leads to disrupted sleep.² The severity of OSA is directly correlated to the frequency of apnea and/or hypopnea events which are measured in number of events per hour using the Apnea-Hypopnea Index (AHI).

Patients with OSA often complain of excessive daytime sleepiness and disrupted sleep, and their bed partner can witness snoring or apnea events. Patients with T2D and OSA complain more frequently of nocturia, morning headaches, restless sleep, and leg movements when compared to patients without diabetes.² However, symptoms are not always present which is why clinicians must have a high degree of suspicion for this disease.

Risk factors for OSA include male sex, older age, the presence of obesity, micrognathia, and a higher neck circumference.¹⁻³

Relationship Between Obstructive Sleep Apnea and Type 2 Diabetes

Nocturnal hypoxia as well as frequent arousals with interrupted sleep leads to fluctuations in blood pressure and increased sympathetic nervous activity, while nocturnal hypoxemia can lead to oxidative stress and β -cell dysfunction.^{2,3} These negative physiologic consequences from OSA can lead to impaired glucose tolerance and increased insulin resistance. Furthermore, obesity is a risk factor for both OSA and T2D, and there is a direct correlation with weight and OSA severity.³

Prevalence studies of OSA have demonstrated that patients with moderate to severe OSA are more likely to have T2D.^{4,5} In fact, up to two-thirds of patients with OSA may have glucose intolerance or diabetes, and a high number of these patients may remain undiagnosed.⁵

There is also an approximately 30% higher risk for developing incident T2D in patients with OSA when compared to those without OSA. Furthermore, the severity of OSA, indicated by a higher AHI score, and a longer time spent with oxygen saturations less than 90% increase the risk of incident T2D.⁶

Patients with co-existing T2D and OSA, have a higher risk of micro- and macro-vascular complications including: ischemic heart disease, atrial fibrillation, stroke/transient ischemic attack, peripheral vascular disease, peripheral neuropathy, chronic kidney disease, and albuminuria.⁷ There is also an increased risk of mortality when both OSA and T2D are present.^{7,8}

Screening and Testing for Obstructive Sleep Apnea:

Healthcare providers should have a high clinical suspicion for OSA. Given the high prevalence of OSA, and that it poses increased risks of morbidity and mortality, patients with T2D should be screened for the presence of OSA. As screening tools for OSA, sleep questionnaires perform similarly for patients with T2D as for patients without diabetes, with the Snoring, Tiredness, Observed apnea, high blood Pressure, Body mass index, Age, Neck circumference, and Gender (STOP-BANG) and Berlin questionnaires being the most sensitive.²

The STOP-BANG questionnaire is an acronym that assigns one point for the presence of each of the following: Snoring, daytime Tiredness, Observed apneas, high blood Pressure, a Body mass index (BMI) greater than 35 kg/m², Age greater than 50 years, Neck circumference greater than 40 cm,

and male Gender. A score of 3 or greater has high sensitivity for OSA.² This questionnaire can be performed in a few minutes since it involves binary responses and only requires a few physical examination manoeuvres or measurements. The STOP-BANG questionnaire is also highly sensitive and performs similarly in patients with or without diabetes, making it a good choice for a screening tool for OSA in this population.

The Berlin questionnaire is also highly sensitive for OSA and performs similarly in patients with or without diabetes.² This questionnaire consists of 10 questions in 3 categories that evaluate: the severity of snoring (Questions 1–5), daytime sleepiness (Questions 6–9), and the presence of hypertension or obesity (Question 10). The categories for snoring or daytime sleepiness are considered positive if there are symptoms present at least 3–4 nights per week, whereas the third category is considered positive if the patient has a measured blood pressure greater than 140/90 mmHg, is currently taking anti-hypertensive medications, or has a BMI that is greater than 30 kg/m². Having at least 2 out of 3 categories positive on the Berlin questionnaire is highly sensitive for OSA.²

Patients identified as potentially having OSA, either based on clinical suspicion or screening questionnaires, should undergo diagnostic testing with an overnight sleep study.

Management Strategies

The management of patients with co-existing OSA and T2D can include non-pharmacological management, positive airway pressure therapy, as well as other devices aimed at reducing apnea/hypopnea events and improving sleep quality, pharmacologic management of diabetes, and surgical management options.

Non-Pharmacological Management

From the non-pharmacological perspective, a behavioural weight loss program in patients with obesity, OSA, and T2D have been shown to be effective in reducing their AHI scores, reducing the severity of OSA, and have led to a 3-fold increase in the chances of OSA remission.⁹ This program consisted of prescriptions for portion-controlled diets with recommended daily caloric intake as well as an activity prescription of 175 minutes per week. The changes noted in sleep apnea severity were independent of changes in hemoglobin A1c (HbA1c).

Additionally, patients should be counselled on the avoidance of sedating agents including alcohol and sedating medications.

Positive Pressure Therapy

Continuous Positive Airway Pressure (CPAP) therapy splints the airways open to prevent airway collapse, thereby improving AHI scores and improving sleep quality. Of note, the largest randomized controlled trial (RCT) to date that assessed CPAP for the prevention of cardiovascular events in those with OSA did not demonstrate a significant reduction in major cardiovascular morbidity or mortality.¹⁰ Furthermore, the rate of newly diagnosed diabetes did not significantly differ between the CPAP and usual care group in this study. However, the negative result was likely due to the low nightly hours of CPAP usage in the trial. The mean CPAP usage was 3.3 hours per night, and only 42% of the patients in the CPAP arm had an adherence of greater than 4 hours per night. To further support this theory, a recent meta-analysis demonstrated a reduction in major adverse cardiac or cerebrovascular events by 31% in patients with a CPAP adherence of at least 4 hours per night.¹¹

CPAP has been studied in patients with co-existing OSA and T2D, and has been shown to significantly reduce HbA1c levels with a direct correlation between hours of nightly CPAP usage and degree of reduction in HbA1c levels.¹² Furthermore, CPAP therapy adherence has been shown to significantly reduce healthcare resource utilization with a reduction in emergency department visits and hospitalizations.¹³ Given the dose dependent effect of CPAP therapy and the importance of adherence, a combination of therapy initiation as well as a follow-up assessment of both treatment response and barriers to adherence should be considered. Adherence and tolerability may remain a barrier for certain patients.

Other Sleep Devices and Surgical Management of OSA

Other management strategies for reducing the AHI score in those with sleep apnea include mandibular advancement devices (MAD), upper airway surgery (UAS), and positional therapy.

As their name suggests, MADs advance the mandible forward to increase airway space and prevent airway collapse. A small pilot study that examined the use of MADs in patients with OSA and T2D demonstrated a significant reduction in sleepiness and the AHI score. There was a significant decrease in HbA1c levels in patients with mild to moderate, but not severe, OSA following treatment with MADs.¹⁴ It is worth noting that although the use of MADs significantly decreased the AHI score in the severe

OSA group, their AHI score remained moderately elevated following treatment, which may explain why there was no significant difference in HbA1c levels in the treatment group.

UAS serves to surgically increase the diameter of the upper airway to prevent airway collapse. A retrospective cohort study demonstrated that patients with OSA who underwent UAS had a significantly reduced risk of developing either an impaired fasting glucose level, impaired glucose tolerance test, or other abnormal glucose finding when compared to patients who were treated with CPAP alone.¹⁵

In select patients in which the majority of their apnea and hypopnea events occur in the supine position, positional therapy with devices to promote side sleeping and prevent sleeping in the supine position can be considered on a case-by-case basis.

While the results from these small pilot and retrospective studies demonstrated benefit, more evidence is needed regarding these therapies in patients with co-existing OSA and T2D.

Pharmacologic Management of Type 2 Diabetes

On the pharmacological side, there is evidence to support both the use of the glucagon-like peptide 1 (GLP-1) receptor agonist liraglutide as well as the sodium glucose co-transporter-2 (SGLT-2) inhibitors empagliflozin and ertugliflozin to treat or prevent OSA. In a small RCT, liraglutide was found to improve the following: BMI, AHI scores, systolic blood pressure, and oxygen saturations.¹⁶ With regards to SGLT2-inhibitors, post-hoc analyses of the cardiovascular outcome trials demonstrated a relative reduction of the development of incident OSA by 47%.¹⁷ These results should be confirmed with larger and prospectively analyzed RCTs. However, the above results are promising, and the cardiovascular benefit demonstrated by SGLT-2 inhibitors¹⁸ makes this class of medications a potentially beneficial option for a comorbid population at high risk for cardiovascular complications.

- A recent trial, SURMOUNT-OSA, demonstrated superiority of tirzepatide in reducing AHI events compared to placebo in patient groups receiving PAP and not receiving PAP at baseline. Although patients with diabetes were excluded from this trial, tirzepatide is currently approved for diabetes management in Canada, and could potentially impact AHI in patients with diabetes and OSA.¹⁹

Bariatric Surgery

Finally, bariatric surgery has demonstrated positive outcomes for patients with both OSA and T2D. In a small group of patients who underwent Roux-en-Y Gastric bypass surgery, their post-operative AHI scores, BMI, and fasting glucose were all improved when compared to their pre-operative values.²⁰

The evidence from some of the above studies suggest that weight loss, whether achieved through behavioural, pharmacologic, or surgical interventions, can improve both OSA and T2D.^{9,16,20} This is in line with a previous longitudinal study demonstrating that a 10% weight loss can significantly reduce OSA severity.²¹

Conclusions

OSA is commonly associated with T2D and is highly prevalent in-patient populations with T2D. Screening tools for OSA perform similarly in patient populations with or without T2D and should therefore be used to screen for this disease. Management of co-existing T2D and OSA requires a multi-modal approach to improve glycaemic control, AHI scores, and BMI, with the aim of reducing cardiovascular morbidity and mortality. This multi-modal approach can include non-pharmacologic, positive pressure, sleep device, pharmacologic and surgical therapies.

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