The Egyptian Journal of Hospital Medicine (April 2023) Vol. 91, Page 4414-4417

Role of Tongue Fat in The Pathogenesis of Obstructive Sleep Apnea: Review Article

Ali Abdullah Amer Elfeires[1], Tarek Abdel Zaher Emara[1],
Ashraf Elsayed El-Malt[1], Mohamad Gamal nada[2], Alsayed Abdulmageed Alsayed[1]
[1]Department of Otorhinolaryngology, Faculty of Medicine, Zagazig University, Egypt
[1]Department of Radiology, Faculty of Medicine, Zagazig University, Egypt
Corresponding author: Ali Abdullah Amer Elfeires, **Mobile**: 01032911676, **Email:** aa.amer020@medicine.zu.edu.eg

ABSTRACT

Humans are fortunate to have sleep. A happy, fulfilling life depends on getting a restful night of sleep. Obstructive sleep apnea is a widespread sleep disorder is characterized by snoring loudly, difficulty breathing, and partial or complete lack of sleep. Systemic side effects from chronic obstructive sleep apnea may affect the cardiovascular system and other important body organs. Although the exact cause is unknown, a number of factors may contribute to this condition. Increased intramuscular fat may impair the tongue's capacity to act as a pharyngeal dilator muscle by changing its shape and decreasing its contractile force. More fat was found in apneic person at the base of the tongue, where the tongue's extrinsic muscles attach to the bone. Each extrinsic muscle's ability to position the tongue correctly away from the airway may be impacted by the increased fat.

INTRODUCTION

An important upper airway soft tissue risk factor for OSA is the tongue, which has a high fat content according to previous autopsy (1) and fast spin echo imaging (2) studies. However, these studies didn't focus specifically on OSA sufferers. They have demonstrated that the intramuscular fat content of the tongues of obese apneic person is extremely high (32.6%).

The average percentage of tongue fat in controls was found to be slightly higher (27.7%) than in the earlier autopsy (1) and imaging (2) studies, according to **Kim *et al.*** **(3)**. However, **Kim *et al.*** found that the masseter muscle had a low percentage of fat, suggesting that fat is not uniformly deposited in the muscles of the upper airway and that the tongue may be a unique reservoir for fat deposition**(3)**. They also found that compared to control tongues, the apneic tongue is bigger and contains more intramuscular fat. Although the differences in the overall percentage of tongue fat between cases and controls were not statistically significant after covariate adjustment (32.6% vs. 27.7%, P = 0.089), they did find statistically significant differences between apneic person and controls in the RG region of the tongue, particularly near the base. Both apneic person and controls had the same masseter muscle volume and masseter fat composition.

These findings prompt significant queries about the causes of the significant intramuscular fat percentage differences between a person's upper airway muscles and the reasons why fat is preferentially deposited in the tongue. The apneic tongue's increased fat content may have genetic roots claim **(3)**. Fat distribution phenotypes have been shown to be genetically heritable, and it has been shown that the increased fat content of the apneic tongue, as well as lower body fat deposition, are under genetic control **(4)**.

In the past, it has been shown that fat has built up in men's bellies and women's necks an effect on OSA that is related to obesity **(5)**. It has not yet been determined whether it is possible to pass on fat deposits in the tongue's upper airway muscles. Despite the fact that it has been shown OSA patients appear to preferentially deposit fat in both the tongue and the cheeks and soft palate, despite the fact that tongue size is inherited **(6)**. Significant OSA intermediate phenotypes may include increased intramuscular tongue fat and fat percentage, especially at the base of the tongue **(7)**.

Tongue Fat's Role in the Pathogenesis of OSA

People think that the tongue is the biggest and most important muscle that opens up the throat **(8)**. Four muscles outside the body (external bony origin and insertion into the base of the tongue) are the only muscles that anchor it to bone, unlike other muscles, other than that at the base. It is a distinct muscle that moves unhindered (genioglossus, hyoglossus, styloglossus, palatoglossus). longitudinal, verticalis, and transversus superior and inferior, the four muscles near the top of the tongue that start and end inside the tongue control how the tongue changes shape while these extrinsic muscles control tongue positioning. The tongue's useful abilities to maintain the patency of the airways are facilitated by the specific fiber compositions of its muscles **(9)**. Increased tongue fat, according to **Kim *et al.*,** may impair muscle function in addition to increasing The size and collapsibility are influenced by the tongue's size of the airways**(3)**. Increased intramuscular fat, in particular, may change the tongue's contractile force and shape, making it less effective as a muscle that dilates the pharynx. At the base of the tongue, where the tongue is attached to the bone by extrinsic muscles, they discovered a higher proportion of fat in apneic person. Each extrinsic muscle's ability to the tongue should be properly positioned away from the airway may be impacted by the increased fat.

The upper airway's size and shape are significantly influenced by the tongue. Increased fat at the tongue's

Received: 14/09/2022
Accepted: 17/11/2022

base may result in the tongue's retroglossal region to change shape, resulting in a smaller Risk of sleep apnea and the retroglossal airway. Airway shape has been shown to be an important mediator of airway closure during apnea. Additionally, changes in the tongue's size and shape brought on by fat may alter how readily and violently airways close (pcrit) the passive critical closing pressure technique is the gold standard for determining how easily the upper airway collapses while you're sleeping [10]. The modifications in shape required to stop apneic events could be impacted by fat infiltration at these critical junctions. Apneic person experienced task failure more quickly than controls in a tongue force fatigability test that required participants to maintain repeated 90 percent of their maximum force protrusion isometric contractions.

Relationship between OSA and Obesity

The primary risk factor for OSA is obesity though the exact nature of this connection is unclear. Weight loss causes both lean mass and fat mass to decrease, but fat mass does so more than twice as much as lean mass [12].

It has also been shown that fat accumulates faster than fat-free tissue when a person puts on weight. As a result, the link between obesity and OSA may be influenced by an increase in both fatty and muscular tissue. Due to fat infiltration, there may be a secondary increase in muscle tissue in obese people. According to these results, obesity affects upper airways of apneic person in ways other than through fat buildup in the fat pads of the parapharynx. Using conventional Regardless of BMI, apneic person have more fat deposited in the soft palate than controls according to T1-weighted spin echo MRI [7]. **Ando *et al.***, who discovered that OSA patients had a mean tongue fat NIR of 17.4% as opposed to 16.0% in the control group, came to a similar conclusion **[13]**. **Kim *et al.*** found no discernible between the OSA and difference in tongue fat group and the control patients [3]. The information from **Kim *et al.*** showed a significant difference in tongue fat percentage before adjusting for age, BMI, sex, and race. It's possible that ageing played a role in the male group's increased tongue fat [3]. These findings led to the hypothesis that age and sex, in addition to BMI, may be important factors in tongue fat deposition.

Despite the fact that the BMIs of OSA patients and healthy individuals were similar the body fat percentage in OSA patients who are male, for both sexes was noticeably higher in comparison to the male control patients. This finding suggests that a specific type of fat tissue deposition may exist in men with OSA. Therefore, it was believed that one of the distinctive fat tissue depositions in male OSA patients was the greater fat deposition of the tongue [13].

Tongue Fat NIR and Age Relationship

In order to identify aspiration risk factors in the elderly, **Butler *et al.* [14]** examined in 2012 the tongue's tissue composition. They came to the conclusion that lower isometric strength was linked to more obesity in the back of the tongue. The accumulation of fat tissue in the tongue was thought to be the cause brought on by ageing, obesity, and muscular hypotonia may have an impact on the development and aggravation of OSA. Male OSA patients had higher tongue fat than male control patients, according to **Ando *et al.***, and tongue fat increased significantly with age **[13]**. Men who have a specific fat deposition may experience OSA due to age-related tongue atrophy, according to **Ando *et al.* [13].**

NIR of the Relationship Between Body Fat Percentage and Tongue Fat

OSA patients' body composition was compared to that of control patients in 2009 by **Bruno *et al*. [15].** Dual-energy x-ray absorptiometry was used to examine the oral region's tissue composition, and the results revealed that In comparison to the control group, OSA patients had significantly less fat-free mass.

Previous research's findings have provided evidence in favor of the idea that tongue fat has an impact on respiration and deglutition. Additionally, according to **Welch *et al.***, losing weight causes the parapharyngeal fat pads and lateral pharyngeal wall to shrink, which widens the upper airway **[16]**. According to this study, there is a direct correlation between rising body fat levels and rising tongue fat.

The Connection Between Tongue Fat NIR and OSA Severity (AHI)

According to **Ando *et al.***, there was no discernible relationship between the NIR of In men with OSA, tongue fat and AHI are linked **[13]**. However, among OSA patients, there was a very strong positive correlation who were female. Male OSA patients had significantly more tongue fat than male control patients did, and it increased as the body fat percentage increased. Additionally, among all OSA BMI and body fat % were significantly positively correlated in patients.

Shigeta *et al.* found that as BMI increased, the tongue volume increased as well **[17]**. These findings supported the theory that fat deposition causes an increase in tongue fat volume in patients suffering from OSA. Because the fat deposition of the tongue is one of the risk factors for the development of OSA in men, it was previously believed that the greater fat deposition of the tongue was one of the specific fat tissue depositions in male OSA patients.

There was a significant correlation between tongue fat and body fat, but there was no discernible difference in tongue fat and OSA severity among the female OSA patients based on OSA status. Obesity and OSA have long been associated, and in both sexes, the severity of the condition is positively correlated with BMI [18].

In the study done by **Ando *et al.***, tongue fat increased along with body fat percentage **[13]**. However, among the male OSA patients, there was no correlation between tongue fat and the severity of the condition. It's possible that men and women respond differently to gender-based differences in tongue fat distribution. Despite the fact that fat builds up in the tongue with weight gain, women typically have lower Mallam Pati scores, suggesting that fat does not play as much of a role in the female tongue as it does in the male tongue [1,19].

OSA generally affects 2% to 5% of adult females and 3% to 7% of adult males, and it is associated with daytime sleepiness [20, 21].

Menopause is the reason for the decline in the sex-related protective effect, according to **Bonsignore *et al.*** who compared the sex disparities related to the risk factor for OSA **[22]**. Female hormones, particularly progesterone, have a significant influence on the upper airway dilator muscle's activity, and postmenopausal women have lower genioglossus activity.

It's possible that the tongue's extrinsic muscles are underactive the initiator of a fatty transformation. An additional study examined the experimental menopause model's histopathologic changes in the rat base of the tongue. One hypothesis states that menopause results in Lymphocyte infiltration, polymorphonuclear leukocyte infiltration, and subepithelial changes are all noticeable histopathologic modifications in the base of the tongue edema, similar to those seen in OSA patients [23].

Loss of weight has an impact on the surrounding soft tissues and upper airway calibre.

The shape of the two measurements of the upper airway were the RP airway and the volumes of the tongue fat, pterygoid, and lateral walls. that changed with weight loss. Other upper airway measurements, however, did not change. The anatomy of the upper airways may therefore be affected differently by weight loss; the cause is unknown, but genetics may be involved [10].

The volume of adipose tissue shrinks with weight loss. Therefore, a decrease in tongue fat was anticipated. Even though MRI couldn't find any fat deposits in the pterygoid and lateral walls, reductions were still seen in these structures (despite the fact that intramyocellular lipid droplets in the pharyngeal constrictors that make up the lateral walls have been seen under electron microscopy) [24].

The ways that losing It is likely that the way that weight affects soft tissues differs depending on whether the tissues are primarily made of fat or not [25]. Analysis has shown that losing weight causes a reduction in muscle mass and volume, which may account for the volume reductions in the pterygoid and lateral walls. Other possible causes besides Two potential explanations for the change in lateral wall volume include smaller parapharyngeal fat pads, which provided space for the lateral walls, and/or the tracheal tug, which created tension and narrowed the lateral walls as a result of increased lung volume with weight loss[26].

An edematous reaction could be brought on by the repeated trauma of obstruction in OSA. Weight loss enhances OSA, which reduces pharyngeal tissue inflammation and trauma. This would explain why the volumes of the lateral wall and pterygoid decreased, but it does not explain why the volume of the soft palate did not change. Given that the fat, high-resolution palate is present. Dixon imaging might be necessary to find effects that are fat-specific, such as those seen in the tongue. As an alternative, it has been shown that people who have apnea have a fibrosed and inflamed soft palate, and losing weight shouldn't be able to undo this fibrosis. Ultimately, the complexity of these relationships is highlighted by variations in the changes of various upper airway soft tissues with weight loss. Understanding the causes of these variations could shed light on OSA heterogeneity and help in the development of customized treatments[27].

Potential Therapeutic Target: Tongue Fat

AHI levels rising and tongue fat levels falling in this study had statistically significant positive correlations. Mediation analyses identified changes in tongue fat as the primary upper airway mediator between weight loss and AHI decline. Even though the connection between tongue size and tongue fat reduction is unknown, it could improve tongue function or calibrate the upper airways. In particular, there was a muscle lipid content and force, speed, and power were in direct opposition to one another. Fat can also enter muscle bundles and how they impact muscle power. Muscle function was also negatively impacted by obesity. Therefore, less tongue fat ought to make muscles work better and perhaps keep you from collapsing while you sleep. The results show that, regardless of the mechanism, OSA treatments that reduce tongue fat might be effective [25, 28].

Despite not having been thoroughly investigated, there are many possible treatments. Dixon MRI should be performed both before and after these interventions to evaluate the viability and efficacy of each. Exercises for the upper airways reduce AHI and improve OSA[29]; one potential mechanism is a decrease in tongue fat. More research is required, but it's possible that different weight loss plans with various dietary compositions will have different effects on tongue fat. Treatments with cold may also be able to reduce tongue fat. For instance, Adipocytes are lysed using a non-invasive cooling technique called cryolipolysis and can be utilized to safely and effectively reduce belly and Submental fat; a related procedure may also be utilized to reduce tongue fat[45, 46]. The data set the stage for investigations into these treatments using either animal or human studies, despite the fact that they are unproven.

Ingargiola *et al.* and **Lipner** found that the reasons why upper airway surgery does not treat OSA more effectively [30, 31]. Patients with OSA have received treatment using comblation by lowering the size of the tongue, but its efficacy is constrained. Coblation vaporises all types of soft tissue without distinguishing using radiofrequency and water to create a plasma, distinguish between fat and muscle. Therefore, their findings that tongue fat volume serves a specific purpose may help to elucidate the observed inefficiency. The effectiveness of comblation may be improved if only fat tissue was eliminated.

REFERENCES

1. **Nashi N, Kang S, Barkdull C *et al*. (2007):** Lingual fat at autopsy. Laryngoscope, 117:1467–1473.
2. **Humbert A, Reeder B, Porcaro J *et al*. (2008):** Simultaneous estimation of tongue volume and fat fraction using IDEAL-FSE. J. Magn. Reson. Imaging, 28:504–508.
3. **Kim M, Keenan T, Jackson N *et al*. (2014):** Tongue fat its relationship to obstructive sleep apnea. Sleep, 37910):1639-1648.
4. **Malis C, Rasmussen L, Poulsen P *et al.* (2005):** Total and regional fat distribution is strongly influenced by genetic factors in young and elderly twins. Obes. Res., 13:2139–2145.
5. **Simpson L, Mukherjee S, Cooper N *et al.* (2010):** Sex differences in the association of regional fat distribution with the severity of obstructive sleep apnea. Sleep, 33:467–474.
6. **Schwab J, Pasirstein M, Kaplan L *et al*. (2006):** Family aggregation of upper airway soft tissue structures in normal subjects and patients with sleep apnea. Am. J. Respir. Crit. Care Med., 173:453–463.
7. **Li Y, Na L, Ye J *et al.* (2012):** Upper airway fat tissue distribution differences in patients with obstructive sleep apnea and controls as well as its effect on retropalatal mechanical loads. Respir. Care, 57:1098–1105.
8. **White P (2006):** Sleep apnea. Proc. Am. Thorac. Soc., 3:124–128.
9. **Saboisky P, Butler E, Fogel B *et al.* (2006):** Tonic and phasic respiratory drives to human genioglossus motoneurons during breathing. J. Neurophysiol., 95:2213–2221.
10. **Wang H, Keenan T, Wiemken A *et al*. (2020):** Effect of weight loss on upper airway anatomy and the apnea–hypopnea index. The importance of tongue fat. American journal of respiratory and critical care medicine, 201(6): 718-727.
11. **Eckert J, Lo L, Saboisky P *et al*. (2011):** Sensorimotor function of the upper-airway muscles and respiratory sensory processing in untreated obstructive sleep apnea. J. Appl. Physiol., 111:1644–1653.
12. **Beavers M, Miller E, Rejeski J *et al.* (2013):** Fat mass loss predicts gain in physical function with intentional weight loss in older adults. J. Gerontol. A. Biol. Sci. Med. Sci., 68:80–86.
13. **Ando E, Shigeta Y, Ishikawa C *et al.* (2019):** Evaluation of fat tissue deposition within the tongue via near-infrared interactance. J. Dent. Sleep Med., 6(4): 13-28.
14. **Butler G, Lintzenich R, Leng X *et al.* (2012):** Tongue adiposity and strength in healthy older adults. Laryngoscope, 122(7):1600-1604.
15. **Bruno E, Alessandrini M, Napolitano B *et al.* (2009):** Dual-energy X-ray absorptiometry analysis of body composition in patients affected by OSAS. Eur. Arch. Otorhinolaryngol., 266(8):1285-1290.
16. **Welch C, Foster D, Ritter T *et al.* (2002):** A novel volumetric magnetic resonance imaging paradigm to study upper airway anatomy. Sleep, 25(5):532-542.
17. **Shigeta Y, Ogawa T, Ando E *et al*. (2011):** Influence of tongue/ mandible volume ratio on oropharyngeal airway in Japanese male patients with obstructive sleep apnea. Oral Surg Oral Med. Oral. Pathol. Oral. Radiol. Endod., 111:239–243.
18. **Jugé L, Olsza I, Knapman L *et al.* (2021):** Effect of upper airway fat on tongue dilation during inspiration in awake people with obstructive sleep apnea. Sleep, 44(12): 192-199.
19. **Davidson T, Patel M (2008):** Waist, circumference and sleep disordered breathing. Laryngoscope, 118(2):339-347.
20. **Punjabi M (2008):** The Epidemiology of Adult Obstructive Sleep Apnea. Proc. Am. Thorac Soc., 5(2):136-143.
21. **Mirrakhimov E, Sooronbaev T, Mirrakhimov M (2013):** Prevalence of obstructive sleep apnea in Asian adults: a systematic review of the literature. BMC Pulm. Med., 13:10-22.
22. **Bonsignore R, Saaresranta T, Riha L (2019):** Sex differences in obstructive sleep apnoea. European Respiratory Review, 28(154): 213-224.
23. **Deveci I, Sürmeli M, Senem H *et al.* (2013):** Effects of polycystic ovary syndrome and menopause on rat soft palate and base of tongue. Otolaryngol Head Neck Surg., 148(4):595-601.
24. **Choi J, Files C, Zhang T *et al*. (2016):** Intramyocellular lipid and impaired myofiber contraction in normal weight and obese older adults. J. Gerontol. A Biol. Sci. Med. Sci., 71:557–564**.**
25. **Cava E, Yeat C, Mittendorfer B (2017):** Preserving healthy muscle during weight loss. Adv. Nutr., 8:511–519.
26. **Yoshimura E, Kumahara H, Tobina T *et al*. (2014):** Aerobic exercise attenuates the loss of skeletal muscle during energy restriction in adults with visceral adiposity. Obes. Facts., 7:26–35.
27. **Barbarroja-Escudero J, Asunsolo-Del-Barco A, Sanchez-Gonzalez J *et al*. (2019):** Heterogeneous predisposing factors and etiology of edema of the uvula in a Spanish population. J. Investig. Allergol. C`lin Immunol., 29:280–286.
28. **Therkelsen E, Pedley A, Hoffmann U *et al.* (2016):** Intramuscular fat and physical performance at the Framingham Heart Study. Age (Dordr)., 38:31-44.
29. **Verma K, Johnson R, Goyal M *et al.* (2016):** Oropharyngeal exercises in the treatment of obstructive sleep apnoea: our experience. Sleep Breath, 20:1193–1201.
30. **Ingargiola J, Motakef S, Chung T *et al.* (2015):** Cryolipolysis for fat reduction and body contouring: safety and efficacy of current treatment paradigms. Plast. Reconstr. Surg., 135:1581–1590.
31. **Lipner R (2018):** Cryolipolysis for the treatment of submental fat: review of the literature. J. Cosmet. Dermatol., 17:145–151.