Hindawi
Acta Neurologica Scandinavica
Volume 2023, Article ID 4310809, 8 pages
https://doi.org/10.1155/2023/4310809

Research Article

Sarcopenia and Hypoxia in Patients with Obstructive Sleep Apnea

Jinseung Kim[1], **Ho-Joon Lee**[2], **Dong Ah. Lee**[3] **and Kang Min Park**[3]

[1]*Department of Family Medicine, Busan Paik Hospital, Inje University College of Medicine, Republic of Korea*
[2]*Department of Radiology, Haeundae Paik Hospital, Inje University College of Medicine, Busan, Republic of Korea*
[3]*Department of Neurology, Haeundae Paik Hospital, Inje University College of Medicine, Busan, Republic of Korea*

Correspondence should be addressed to Kang Min Park; smilepkm@hanmail.net

Received 17 October 2023; Revised 27 November 2023; Accepted 28 November 2023; Published 6 December 2023

Academic Editor: Paul Cumming

Objectives. Obstructive sleep apnea (OSA) is associated with a variety of health issues. Both OSA and sarcopenia are associated with metabolic disorders; however, there is limited literature assessing the correlation between them. Therefore, we aimed to investigate sarcopenia using temporal muscle thickness (TMT) in patients with obstructive sleep apnea (OSA) and the association between sarcopenia and hypoxia. *Methods*. We enrolled patients with OSA and healthy controls. Both groups underwent brain magnetic resonance imaging (MRI) scans, including three-dimensional T1-weighted imaging. TMT, a marker for sarcopenia, was obtained based on the T1-weighted imaging and compared between the groups. Additionally, we analyzed the correlation between TMT and clinical factors in patients with OSA. *Results*. In total, 40 patients with OSA and 52 healthy controls were evaluated. There was no difference in TMT between patients with OSA and healthy controls (10.425 ± 2.13 vs. 10.400 ± 1.94 mm, $p = 0.953$). In the correlation analysis, age was negatively correlated with TMT ($r = -0.356$, $p = 0.023$), and lowest oxygen saturation ($r = -0.558$, $p < 0.001$) in patients with OSA. *Conclusion*. Our results demonstrated negative correlations between TMT and lowest oxygen saturation in the patients with OSA. These findings suggest potential relationships between sarcopenia and hypoxia in patients with OSA. Thus, these results underline the importance of maintaining oxygen saturation in patients with OSA by implementing active treatment. This study also demonstrates the feasibility of sarcopenia assessment by measuring TMT through conventional head MRI in patients with various neurological disorders.

1. Introduction

Obstructive sleep apnea (OSA) is defined by intermittent collapse of the upper airway, a phenomenon contingent upon the individual's sleep state. This leads to recurring instances of reduced or halted ventilation, causing hypoxia, hypercapnia, and arousals from sleep [1]. The prevalence of OSA ranges from 9 to 38% among the adult population, with a higher occurrence in men compared with that in women [2, 3]. However, the fundamental pathophysiology of OSA is intricate and varies among individuals. Key pathophysiological elements that influence the severity of OSA include anatomical impediments within the upper airway, a diminished threshold for respiratory arousal, elevated loop gain leading to unstable respiratory control, and inadequate responsiveness of the upper airway dilator muscles [4]. Additionally, OSA is associated with a spectrum of persistent health issues, such as cardiovascular risks, metabolic disorders, and psychiatric conditions [5–7].

Sarcopenia is a progressive muscle disorder characterized by rapid loss of muscle mass and function. This condition has been linked to various detrimental health consequences such as fractures, reduced functionality, and increased mortality [8]. In community-dwelling individuals aged ≥ 60 years, the estimated global prevalence of sarcopenia is approximately 10%, slightly higher than previously observed [9]. Sarcopenia, not limited to the elderly, can begin in midlife and is prevalent in various populations, including those with cancer, chronic kidney and liver disease, and metabolic disorders, serving as a significant prognostic indicator for survival and clinical complications in these patients [10–13].

Sarcopenia is initially diagnosed by assessing muscle strength, such as grip strength [14]. Subsequent diagnosis involves measuring muscle mass, primarily estimated through dual-energy X-ray absorptiometry for lean mass, combined with other tools such as bioelectrical impedance analysis and computed tomography scans [15]. However, the assessment of skeletal muscle mass and function is based on additional examinations that result in a higher radiation dose for the patient, in addition to health care costs, or prolonged clinical examinations.

Moreover, recent studies have established a significant correlation between temporal muscle thickness (TMT) and the risk of developing sarcopenia. TMT, obtained on routinely performed brain magnetic resonance imaging (MRI), has been shown to estimate skeletal muscle mass. Thus, it has been explored as a new proxy indicator for identifying sarcopenia risk in individuals with neurological conditions [16, 17]. Previous studies have demonstrated a strong correlation between TMT and both hand grip strength and skeletal muscle mass, as well as good interrater reliability, making it a reliable marker for assessing sarcopenia [16–18]. Notably, TMT assessment can be conveniently performed using routine brain computed tomography or MRI protocols or retrospectively, providing an optimal method for assessing sarcopenia. Furthermore, the measurement of TMT has proven effective in investigating the impact of sarcopenia on prognosis among patients with brain tumors [19, 20].

Previous literature indicates that among community-dwelling older adults, women with poor sleep quality exhibit a heightened risk of sarcopenia [21]. Moreover, OSA and sarcopenia are recognized for their association with metabolic disorders, and OSA is often accompanied by hypertension and diabetes, which are risk factors for sarcopenia [22]. Therefore, we might expect sarcopenia to be more common in patients with OSA compared to healthy individuals. However, there have been limited studies exploring the association between sarcopenia and OSA, yielding contradictory results [23–25]. Moreover, there is a notable dearth of specific research examining the precise correlation between them using TMT. Therefore, this study is aimed at evaluating the presence of sarcopenia in patients with OSA by employing TMT measurements. Our hypothesis posited a clear and distinct relationship between OSA and sarcopenia. Furthermore, we investigated the association between sarcopenia and hypoxia in patients with OSA.

2. Methods

2.1. Participants. This study was conducted at a tertiary care hospital with the approval of the institutional review board. Patients with OSA who agreed to participate in this study were enrolled between September 2018 and August 2023. Participants who met the following specific criteria for OSA were included: (1) confirmed diagnosis of OSA based on polysomnography (PSG) results, demonstrating an apnea-hypopnea index (AHI) exceeding five, along with accompanying symptoms such as excessive sleepiness or chronic snoring and (2) availability of three-dimensional (3D) T1-weighted (T1-WI) MRI data. We excluded patients with OSA with (1) presence of any other medical or neurological disorders, aside from OSA, or (2) presence of any structural brain lesions, as confirmed by visual inspection of brain MRI scans. Clinical and PSG data were collected from patients with OSA. Healthy individuals were included as a control, matched in terms of age and sex to the patients with OSA. These individuals had no history of medical or neurological disorders and exhibited normal brain MRI findings upon visual examination. Although PSG was not conducted for these healthy participants, none of them reported snoring or displayed any symptoms of OSA.

2.2. MRI Acquisition. Both patients with OSA and the healthy control group underwent brain MRI scans using identical sequences performed on a three-tesla MRI scanner equipped with a 32-channel head coil (AchievaTx, Phillips Healthcare, Best, The Netherlands). The 3D T1-WI images were acquired using the same sequences in both groups. Additionally, patients underwent axial T2-weighted images to detect structural brain lesions. The 3D T1-WI image was acquired in the sagittal plane, using a turbo-field echo sequence with the following parameters: TI = 1300 ms, repetition time/echo time = 8.6/3.96 ms, flip angle = 8°, and an isotropic voxel size of 1 mm^3.

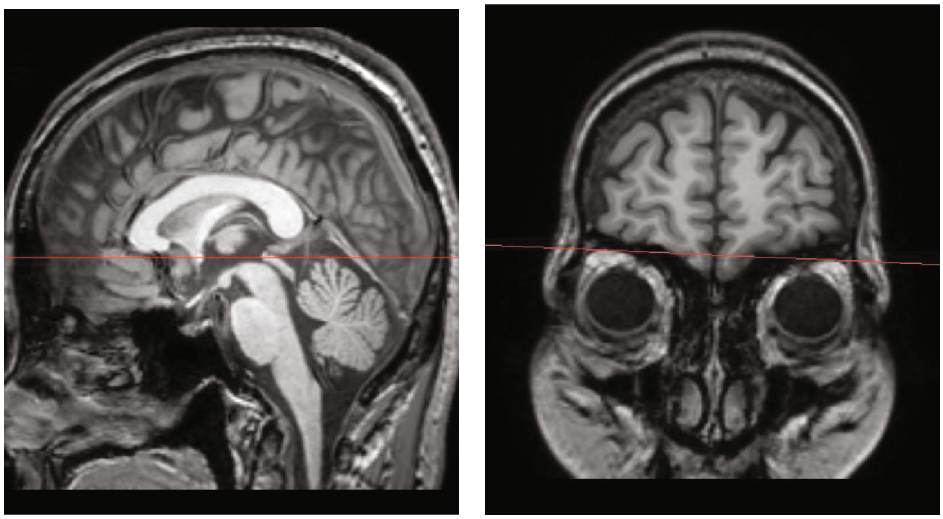
2.3. Temporal Muscle Thickness Measurement. TMT was measured on 3D T1-WI images on the right and left sides by a board-certified radiologist (H.J.L) with 9 years of subspecialty experience in neuroradiology. The images were reformatted to an axial plane parallel to the anterior commissure-posterior commissure line. Thereafter, TMT was measured perpendicular to the long axis of the temporalis muscle, using the orbital roof and the Sylvian fissure as landmarks. Image reformatting and measurements were performed using 3D Slicer (version 5.4.0, https://www.slicer.org) [26, 27]. The measurements for each side were averaged for use in further analysis (Figure 1).

2.4. Statistical Analysis. We employed the independent samples *t*-test to compare age and TMT between the groups, and Fisher's exact test to analyze sex differences. The Pearson correlation test was used for correlation analysis between TMT and clinical factors. All statistical analyses were performed using MedCalc® software (version 20.014, MedCalc Software, Ostend, Belgium; accessible at https://www.medcalc.org; 2021). Statistical significance was set at $p < 0.05$.

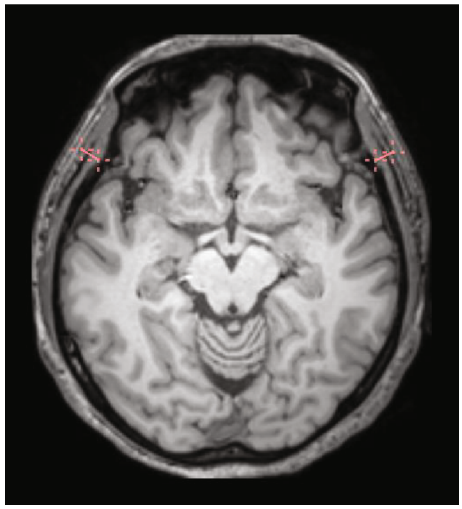
3. Results

3.1. Clinical Characteristics and Polysomnographic Findings in Participants. We included 40 patients with OSA and 52 healthy controls. No significant differences in age and sex were found between the two groups. Table 1 presents the clinical characteristics and PSG findings in patients with OSA. Eighty percent of patients with OSA were male.

3.2. Difference of the Temporal Muscle Thickness between Patients with OSA and Healthy Controls. No difference was found in TMT between patients with OSA and healthy controls (10.425 ± 2.13 vs. 10.400 ± 1.94 mm; $p = 0.953$) (Figure 2).



(a) (b)



(c)

Figure 1: Illustration of temporalis muscle thickness measurement procedure. (a) Images were reformatted to the axial plane parallel to the anterior commissure-posterior commissure line. (b) The view was navigated to the orbital roof level. (c) Thickness measurements of the temporalis muscle were taken on both sides, using the Sylvian fissure as the anterior-posterior reference point.

Table 1: Clinical characteristics and polysomnographic findings in participants.

	Patients with obstructive sleep apnea ($N = 40$)	Healthy controls ($N = 52$)	p value
Clinical data			
Age ± SD, years	61.5 ± 14.8	61.9 ± 8.5	0.870
Male, N (%)	32 (80.0)	40 (76.9)	0.724
Body mass index (kg/m^2) (interquartile range)	25.2 (23.9–27.1)		
Epworth sleepiness scale (interquartile range)	6 (3–9)		
Polysomnographic data			
Sleep time ± SD (minutes)	349.5 ± 54.3		
Sleep efficiency (%) (interquartile range)	77.1 (71.8–85.1)		
Total apnea-hypopnea index (interquartile range)	15.4 (9.9–24.9)		
Average oxygen saturation ± SD (%)	94.3 ± 1.2		
Lowest oxygen saturation (%) (interquartile range)	85.0 (82.5–88.7)		

SD: standard deviation.

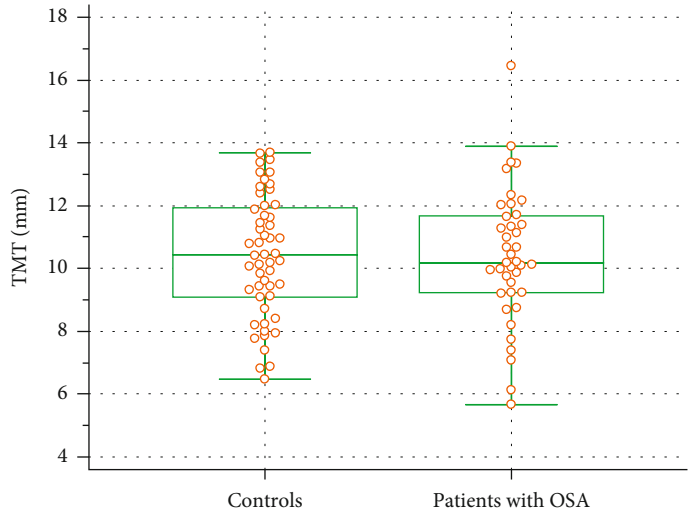


Figure 2: Difference in temporal muscle thickness between patients with obstructive sleep apnea and healthy controls. The figure shows that the temporal muscle thickness is not different between patients with obstructive sleep apnea and healthy controls (10.425 vs. 10.400 mm, $p = 0.953$). TMT: temporal muscle thickness; OSA, obstructive sleep apnea.

3.3. Correlation Analysis between Temporal Muscle Thickness and Clinical Factors. Age and lowest oxygen saturation were negatively correlated with TMT ($r = -0.356$, $p = 0.023$; $r = -0.558$, $p < 0.001$, respectively) in patients with OSA (Figure 3). However, other clinical factors, such as body mass index ($r = 0.309$, $p = 0.052$), Epworth sleep scale ($r = 0.217$, $p = 0.179$), sleep efficiency ($r = 0.077$, $p = 0.636$), AHI ($r = 0.048$, $p = 0.767$), average oxygen saturation ($r = 0.020$, $p = 0.935$), and sleep time ($r = 0.128$, $p = 0.429$), were not correlated with TMT.

4. Discussion

In the present study, we investigated the difference in the presence of sarcopenia using TMT measurement between 40 patients with OSA and 52 healthy controls. Contrary to our initial hypothesis, there was no significant difference in TMT between the two groups. However, our results demonstrated a negative correlation between age and TMT, as well as between the lowest oxygen saturation and TMT in patients with OSA.

Our results are consistent with those of previous studies using dual-energy X-ray absorptiometry, wherein OSA was strongly associated with total and upper body obesity, but not with sarcopenia in patients with nondialyzed chronic kidney disease [23, 25]. Traditionally, OSA has been characterized and measured mainly based on the frequency of apneas and hypopneas during sleep, known as the AHI [28–30]. However, in our study, AHI did not correlate with the TMT measurement, but hypoxia alone showed a negative correlation with TMT. This suggests that hypoxia is more strongly associated with sarcopenia than the severity of OSA.

Clinical and epidemiological investigations have shown a standalone correlation between OSA and occurrences of cardiovascular events, suggesting that OSA might instigate cardiometabolic dysregulation [31–33]. Two primary patterns of hypoxemia have been established. First, patients with OSA often exhibit short, intermittent, high-frequency hypoxemia, characterized by a cyclical pattern of oxygen desaturation lasting 15–60 seconds followed by reoxygenation, persisting for 8–9 hours during sleep and extending over weeks to months or longer. Second, sustained, or low-frequency hypoxemia, with oxygen saturation ranging between 80 and 85% and lasting from a few minutes to hours, is observed during rapid ascent and descent from altitude as well as in chronic lung disease during sleep [34]. Persistent and continuous hypoxemia, prevalent at high altitudes or in cases of chronic lung disease, can trigger both adaptive and maladaptive reactions. These responses may involve heightened erythropoiesis and the development of pulmonary hypertension. Conversely, intermittent hypoxia typically induces maladaptive reactions, distinctly modulating hypoxia-inducible factors 1 and 2 [35]. Chronic obstructive pulmonary disease is a lung condition resulting in diminished tissue oxygenation, consequently inducing a state of tissue hypoxia. In patients with chronic obstructive pulmonary disease, skeletal muscle fiber size is reduced compared to that of healthy individuals [36]. Muscle size reduction is likely a result of changes in molecular pathways that control both muscle growth and breakdown. The mTORC1 signaling pathway, a widely studied anabolic pathway, is activated in skeletal muscle in response to nutrients, growth factors, and muscle loading. This activation leads to an enhanced mRNA translational capacity, ultimately promoting muscle growth [37]. Research conducted in mice revealed that a brief intermittent hypoxia regimen, a characteristic feature of OSA, induced significant oxygen fluctuations in the liver, closely resembling the variations in SpO_2 levels. The oscillations in oxygen levels were mitigated in muscle tissue and significantly reduced in adipose tissue in both lean and obese mice. These findings indicate that OSA intensifies tissue-level hypoxia [38]. The heightened hypoxia within adipose tissue could represent a significant mechanism contributing to cardiometabolic dysfunction in

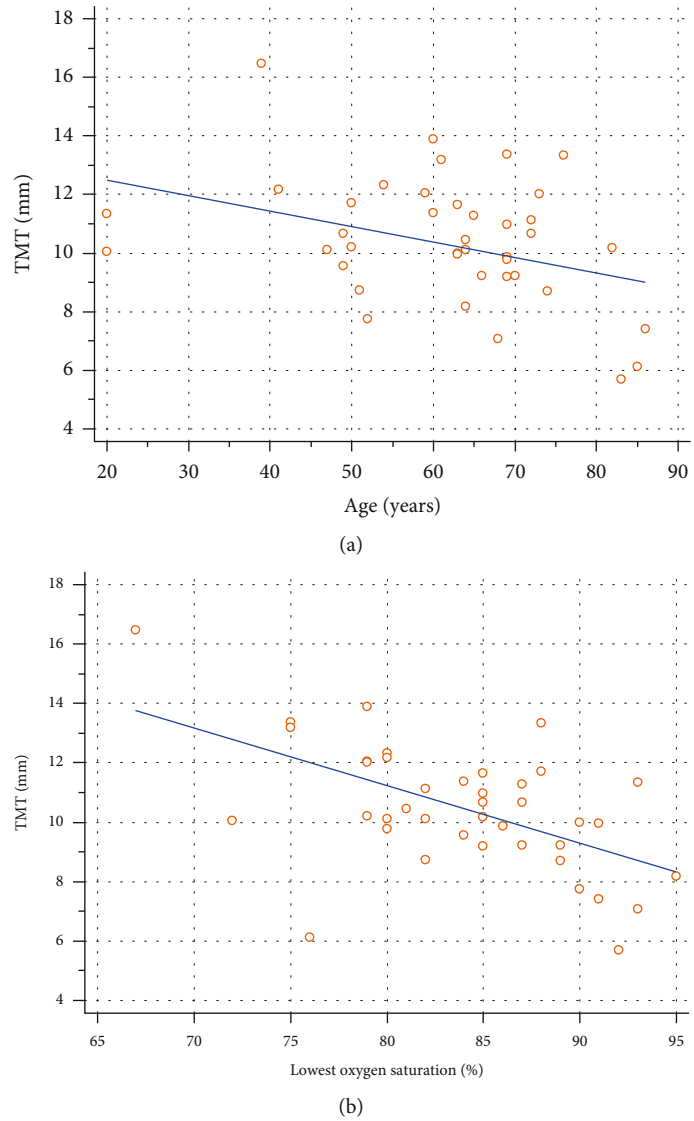


FIGURE 3: Results of the correlation analysis. The figures represent a negative correlation between age and temporal muscle thickness ($r = -0.356$, $p = 0.023$) (a) and a negative correlation between lowest oxygen saturation and temporal muscle thickness ($r = -0.558$, $p < 0.001$) (b) in patients with obstructive sleep apnea. TMT: temporal muscle thickness.

OSA. This heightened hypoxia is a primary initiator of processes such as lipolysis, chronic inflammation, infiltration of macrophages, reduction in adiponectin levels, increased leptin levels, adipocyte cell death, endoplasmic reticulum stress, and impaired mitochondrial function [39].

Hypoxemia resulting from OSA triggers the activation of arterial sympathetic nerves and the renin-angiotensin-aldosterone system, primarily driving the pathophysiology underlying complications such as cardiovascular morbidity and mortality. Notably, angiotensin II/angiotensin II type 1 receptor activity also contributes to fibrotic, atrophic, and inflammatory effects on muscles [40]. Age-related sleep changes, encompassing sleep apnea, insomnia, reduced sleep efficiency, and disrupted circadian rhythms, elevate cortisol levels, impair endothelial function, and induce arousal and insulin resistance, while diminishing growth hormone, insulin-like growth factor 1 secretion, and protein synthesis, culminating in a hormonal imbalance that skews muscle metabolism towards catabolism and contributes to sarcopenia [41]. Moreover, prolonged hypoxia has an adverse impact on skeletal muscle protein metabolism [42–44]. In cases where protein breakdown exceeds synthesis, there is a decline in skeletal muscle mass and in the cross-sectional area of myofibers, ultimately resulting in diminished muscle strength and function [45, 46]. Therefore, hypoxia should be recognized as a potent initiator of inflammation. Additionally, cellular responses to hypoxia hinge on the transcription factor hypoxia-inducible factor 1α. While inactive in normoxemic conditions, this dimeric protein becomes active in the presence of hypoxia [47]. Together, these aspects may explain our results which showed a negative correlation between the degree of hypoxia and TMT in OSA patients.

Nonetheless, this study encountered several limitations. First, as this was a single-center study with a relatively small

sample size, generalizing the findings to the general population is challenging. Second, due to the study's cross-sectional design, the establishment of a definitive temporal relationship between hypoxia and sarcopenia was not possible. Third, despite incorporating a control group without OSA symptoms, PSG examinations were not conducted, potentially allowing for the inclusion of individuals with undiagnosed OSA. Fourth, TMT is a well-known marker for sarcopenia and is associated with hand grip strength, indicating its potential to reflect skeletal muscle mass. However, we were unable to directly measure muscle strength, muscle mass, and physical performance, which is crucial for diagnosis of sarcopenia. Finally, factors such as body mass index (BMI) or lifestyle factors may have caused bias, which may affect the TMT in patients with OSA and healthy controls. However, a previous study demonstrated sarcopenia as an independent factor for TMT, even after adjusting for age, sex, and BMI [18].

Despite these limitations, this was the first study to investigate sarcopenia in patients with OSA compared to healthy controls. We identified negative correlations between TMT and lowest oxygen saturation in the patients with OSA. Thus, these results underline the importance of maintaining oxygen saturation in patients with OSA by implementing active treatment, such as positive airway pressure. This study also demonstrates the feasibility of sarcopenia assessment by measuring TMT through conventional head MRI in patients with various neurological disorders. This study marks the pioneering exploration of the association between OSA and sarcopenia using the assessment of TMT through brain MRI in patients with OSA. It could be better studied to measure and compare TMT again after treating OSA with large a sample size in the future.

5. Conclusion

We observed a negative correlation between TMT and lowest oxygen saturation in the patients with OSA. This suggests a potential association between sarcopenia and hypoxia in patients with OSA. Thus, these results underline the importance of maintaining oxygen saturation in patients with OSA by implementing active treatment. This study also demonstrates the feasibility of sarcopenia assessment by measuring TMT through conventional head MRI in patients with various neurological disorders.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

Neither of the authors has any conflict of interest to disclose.

Authors' Contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Jinseung Kim, Ho-Joon Lee, Dong Ah Lee, and Kang Min Park. The first draft of the manuscript was written by Kang Min Park, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. Jinseung Kim and Ho-Joon Lee contributed equally to this study.

Acknowledgments

This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HR21C1003).

References

[1] J. A. Dempsey, S. C. Veasey, B. J. Morgan, and C. P. O'Donnell, "Pathophysiology of sleep apnea," *Physiological Reviews*, vol. 90, no. 1, pp. 47–112, 2010.

[2] E. V. Reddy, T. Kadhiravan, H. K. Mishra et al., "Prevalence and risk factors of obstructive sleep apnea among middle-aged urban Indians: a community-based study," *Sleep Medicine*, vol. 10, no. 8, pp. 913–918, 2009.

[3] S. Tufik, R. Santos-Silva, J. A. Taddei, and L. R. A. Bittencourt, "Obstructive sleep apnea syndrome in the Sao Paulo epidemiologic sleep study," *Sleep Medicine*, vol. 11, no. 5, pp. 441–446, 2010.

[4] D. J. Eckert and A. Malhotra, "Pathophysiology of adult obstructive sleep apnea," *Proceedings of the American Thoracic Society*, vol. 5, no. 2, pp. 144–153, 2008.

[5] L. F. Drager, S. M. Togeiro, V. Y. Polotsky, and G. Lorenzi-Filho, "Obstructive sleep apnea: a cardiometabolic risk in obesity and the metabolic syndrome," *Journal of the American College of Cardiology*, vol. 62, no. 7, pp. 569–576, 2013.

[6] A. G. Wheaton, G. S. Perry, D. P. Chapman, and J. B. Croft, "Sleep disordered breathing and depression among U.S. adults: National Health and Nutrition Examination Survey, 2005-2008," *Sleep*, vol. 35, no. 4, pp. 461–467, 2012.

[7] M. Olaithe, R. S. Bucks, D. R. Hillman, and P. R. Eastwood, "Cognitive deficits in obstructive sleep apnea: insights from a meta-review and comparison with deficits observed in COPD, insomnia, and sleep deprivation," *Sleep Medicine Reviews*, vol. 38, pp. 39–49, 2018.

[8] A. J. Cruz-Jentoft and A. A. Sayer, "Sarcopenia," *The Lancet*, vol. 393, no. 10191, pp. 2636–2646, 2019.

[9] G. Shafiee, A. Keshtkar, A. Soltani, Z. Ahadi, B. Larijani, and R. Heshmat, "Prevalence of sarcopenia in the world: a systematic review and meta- analysis of general population studies," *Journal of Diabetes & Metabolic Disorders*, vol. 16, no. 1, pp. 1–10, 2017.

[10] L. Feng, Q. Gao, K. Hu et al., "Prevalence and risk factors of sarcopenia in patients with diabetes: a meta-analysis," *The Journal of Clinical Endocrinology & Metabolism*, vol. 107, no. 5, pp. 1470–1483, 2022.

[11] X. Shu, T. Lin, H. Wang et al., "Diagnosis, prevalence, and mortality of sarcopenia in dialysis patients: a systematic review and meta-analysis," *Journal of Cachexia, Sarcopenia and Muscle*, vol. 13, no. 1, pp. 145–158, 2022.

[12] X. Tantai, Y. Liu, Y. H. Yeo et al., "Effect of sarcopenia on survival in patients with cirrhosis: a meta-analysis," *Journal of Hepatology*, vol. 76, no. 3, pp. 588–599, 2022.

[13] S. S. Shachar, G. R. Williams, H. B. Muss, and T. F. Nishijima, "Prognostic value of sarcopenia in adults with solid tumours: a meta-analysis and systematic review," *European Journal of Cancer*, vol. 57, pp. 58–67, 2016.

[14] H. C. Roberts, H. J. Denison, H. J. Martin et al., "A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach," *Age and Ageing*, vol. 40, no. 4, pp. 423–429, 2011.

[15] F. Buckinx, F. Landi, M. Cesari et al., "Pitfalls in the measurement of muscle mass: a need for a reference standard," *Journal of Cachexia, Sarcopenia and Muscle*, vol. 9, no. 2, pp. 269–278, 2018.

[16] A. Steindl, J. Leitner, M. Schwarz et al., "Sarcopenia in neurological patients: standard values for temporal muscle thickness and muscle strength evaluation," *Journal of Clinical Medicine*, vol. 9, no. 5, p. 1272, 2020.

[17] J. Leitner, S. Pelster, V. Schöpf et al., "High correlation of temporal muscle thickness with lumbar skeletal muscle cross-sectional area in patients with brain metastases," *PLoS One*, vol. 13, no. 11, article e0207849, 2018.

[18] M. Nozoe, H. Kubo, M. Kanai et al., "Reliability and validity of measuring temporal muscle thickness as the evaluation of sarcopenia risk and the relationship with functional outcome in older patients with acute stroke," *Clinical Neurology and Neurosurgery*, vol. 201, article 106444, 2021.

[19] J. Furtner, A. S. Berghoff, O. M. Albtoush et al., "Survival prediction using temporal muscle thickness measurements on cranial magnetic resonance images in patients with newly diagnosed brain metastases," *European Radiology*, vol. 27, no. 8, pp. 3167–3173, 2017.

[20] S. Huq, A. M. Khalafallah, M. A. Ruiz-Cardozo et al., "A novel radiographic marker of sarcopenia with prognostic value in glioblastoma," *Clinical Neurology and Neurosurgery*, vol. 207, article 106782, 2021.

[21] X. Hu, J. Jiang, H. Wang, L. Zhang, B. Dong, and M. Yang, "Association between sleep duration and sarcopenia among community-dwelling older adults: a cross-sectional study," *Medicine*, vol. 96, no. 10, article e6268, 2017.

[22] P. Han, H. Yu, Y. Ma et al., "The increased risk of sarcopenia in patients with cardiovascular risk factors in suburb-dwelling older Chinese using the AWGS definition," *Scientific Reports*, vol. 7, no. 1, p. 9592, 2017.

[23] J. F. R. Fernandes, M. I. B. Silva, C. P. Loivos et al., "Obstructive sleep apnea in non-dialyzed chronic kidney disease patients: association with body adiposity and sarcopenia," *Nutrition*, vol. 57, pp. 282–289, 2019.

[24] T. Matsumoto, K. Tanizawa, R. Tachikawa et al., "Associations of obstructive sleep apnea with truncal skeletal muscle mass and density," *Scientific Reports*, vol. 8, no. 1, p. 6550, 2018.

[25] R. D. Piovezan, C. Hirotsu, R. Moizinho et al., "Associations between sleep conditions and body composition states: results of the EPISONO study," *Journal of Cachexia, Sarcopenia and Muscle*, vol. 10, no. 5, pp. 962–973, 2019.

[26] A. Fedorov, R. Beichel, J. Kalpathy-Cramer et al., "3D Slicer as an image computing platform for the quantitative imaging network," *Magnetic Resonance Imaging*, vol. 30, no. 9, pp. 1323–1341, 2012.

[27] R. Kikinis and S. Pieper, "3D Slicer as a tool for interactive brain tumor segmentation," *Annual International Conference of the IEEE Engineering in Medicine and Biology*, vol. 2011, pp. 6982–6984, 2011.

[28] E. Shahar, "Apnea-hypopnea index: time to wake up," *Nature and Science of Sleep*, vol. 6, pp. 51–56, 2014.

[29] D. A. Pevernagie, B. Gnidovec-Strazisar, L. Grote et al., "On the rise and fall of the apnea– hypopnea index: a historical review and critical appraisal," *Journal of Sleep Research*, vol. 29, no. 4, article e13066, 2020.

[30] D. C. Lim, D. R. Mazzotti, K. Sutherland et al., "Reinventing polysomnography in the age of precision medicine," *Sleep Medicine Reviews*, vol. 52, article 101313, 2020.

[31] T. Young, L. Finn, P. E. Peppard et al., "Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort," *Sleep*, vol. 31, no. 8, pp. 1071–1078, 2008.

[32] N. M. Punjabi, B. S. Caffo, J. L. Goodwin et al., "Sleep-disordered breathing and mortality: a prospective cohort study," *PLoS Medicine*, vol. 6, no. 8, article e1000132, 2009.

[33] J. M. Marin, S. J. Carrizo, E. Vicente, and A. G. Agusti, "Long-term cardiovascular outcomes in men with obstructive sleep apnoea- hypopnoea with or without treatment with continuous positive airway pressure: an observational study," *The Lancet*, vol. 365, no. 9464, pp. 1046–1053, 2005.

[34] N. R. Prabhakar, "Invited review: oxygen sensing during intermittent hypoxia: cellular and molecular mechanisms," *Journal of Applied Physiology*, vol. 90, no. 5, pp. 1986–1994, 2001.

[35] N. R. Prabhakar and G. L. Semenza, "Adaptive and maladaptive cardiorespiratory responses to continuous and intermittent hypoxia mediated by hypoxia-inducible factors 1 and 2," *Physiological Reviews*, vol. 92, no. 3, pp. 967–1003, 2012.

[36] M. J. Mador and E. Bozkanat, "Skeletal muscle dysfunction in chronic obstructive pulmonary disease," *Respiratory Research*, vol. 2, no. 4, pp. 216–224, 2001.

[37] S. R. Kimball, "Integration of signals generated by nutrients, hormones, and exercise in skeletal muscle[1234]," *The American Journal of Clinical Nutrition*, vol. 99, no. 1, pp. 237s–242s, 2014.

[38] C. Reinke, S. Bevans-Fonti, L. F. Drager, M.-K. Shin, and V. Y. Polotsky, "Effects of different acute hypoxic regimens on tissue oxygen profiles and metabolic outcomes," *Journal of Applied Physiology*, vol. 111, no. 3, pp. 881–890, 2011.

[39] J. Ye, "Emerging role of adipose tissue hypoxia in obesity and insulin resistance," *International Journal of Obesity*, vol. 33, no. 1, pp. 54–66, 2009.

[40] Z. N. Jin and Y. X. Wei, "Meta-analysis of effects of obstructive sleep apnea on the renin-angiotensin-aldosterone system," *Journal of Geriatric Cardiology*, vol. 13, no. 4, pp. 333–343, 2016.

[41] R. D. Piovezan, J. Abucham, R. V. Dos Santos, M. T. Mello, S. Tufik, and D. Poyares, "The impact of sleep on age-related sarcopenia: possible connections and clinical implications," *Ageing Research Reviews*, vol. 23, no. Part B, pp. 210–220, 2015.

[42] R. Rathor, G. Suryakumar, and S. N. Singh, "Diet and redox state in maintaining skeletal muscle health and performance at high altitude," *Free Radical Biology and Medicine*, vol. 174, pp. 305–320, 2021.

[43] G. Biolo, T. Cederholm, and M. Muscaritoli, "Muscle contractile and metabolic dysfunction is a common feature of sarcopenia of aging and chronic diseases: from sarcopenic obesity to cachexia," *Clinical Nutrition*, vol. 33, no. 5, pp. 737–748, 2014.

[44] C. Di Giulio, G. Petruccelli, G. Bianchi, M. Cacchio, and V. Verratti, "Does hypoxia cause sarcopenia? Prevention of hypoxia could reduce sarcopenia," *Journal of Biological Regulators & Homeostatic Agents*, vol. 23, no. 1, pp. 55–58, 2009.

[45] F. G. Di Girolamo, N. Fiotti, Z. Milanović et al., "The aging muscle in experimental bed rest: a systematic review and meta-analysis," *Frontiers in Nutrition*, vol. 8, article 633987, 2021.

[46] G. Biolo, B. Massolino, F. G. Di Girolamo et al., "Intensive insulin therapy increases glutathione synthesis rate in surgical ICU patients with stress hyperglycemia," *PLoS One*, vol. 13, no. 1, article e0190291, 2018.

[47] H. K. Eltzschig and P. Carmeliet, "Hypoxia and inflammation," *New England Journal of Medicine*, vol. 364, no. 7, pp. 656–665, 2011.