Current Allergy and Asthma Reports (2019) 19: 34
https://doi.org/10.1007/s11882-019-0865-3

OTITIS (DP SKONER, SECTION EDITOR)

Role of Obesity in Otorhinolaryngologic Diseases

Su Young Jung[1] · Dong Choon Park[2] · Sang Hoon Kim[3] · Seung Geun Yeo[3]

Published online: 3 June 2019

Abstract

Purpose of Review Obesity is a major public health problem associated with various diseases. Improving obesity control and achieving greater patient satisfaction are critical unmet needs. Various otorhinolaryngologic diseases can have negative effects on quality of life or actual health status depending on their type. Over the past decade, the relationship between obesity and otorhinolaryngologic conditions has been investigated. The purpose of this review was to discuss the relationship between obesity and otorhinolaryngological diseases.

Recent Findings This is a narrative review on the current state of incidence, effects, and associated mechanisms between obesity and otorhinolaryngologic diseases. In various otologic diseases, otitis media (OM) and hearing loss (HL) are associated with obesity. In rhinologic parts, chronic rhinosinusitis (CRS) and obstructive sleep apnea (OSA) were significantly associated with obesity. Most of these diseases are reported to have higher susceptibility and severity as body mass index (BMI) increases. However, the incidence of head and neck cancer (HNC) was inversely associated with obesity, especially central adiposity. The relevance of obesity in laryngopharyngeal reflux disease (LPR) and allergic rhinitis (AR) has yet to be clarified, and this remains controversial.

Summary This review provides a comprehensive overview of the current state of incidence, effects, and associated mechanisms between obesity and otorhinolaryngologic diseases. Various otorhinolaryngological diseases are related to obesity. As obesity can be a negative risk factor in these otorhinolaryngologic diseases, early diagnosis and treatment of these diseases in obese patients will be critical.

Keywords Obesity · Overweight · BMI · Otorhinolaryngology · Head and neck cancer · Related diseases

Introduction

Obesity is a major global health problem. Its prevalence has tripled over the last decade in every age. People are generally considered obese when the body mass index (BMI) measured by dividing people's weight by the square of a person's height is greater than 30 kg/m^2. A range of 25–30 kg/m^2 is defined as overweight. Some East Asian countries use lower values. The obesity epidemic in the USA has reached staggering proportions. An estimated 30% of the adult population in the USA is obese, and another 20% are overweight according to defined BMI cutoffs. Obesity has been reported to increase annual healthcare spending on a patient basis and to account for approximately $ 113.9 billion in medical resource consumption [1, 2]. Obesity leads to musculoskeletal overload and chronic diseases such as diabetes, hypertension, and hyperlipidemia through metabolic syndrome, which in turn leads to atherosclerotic diseases including coronary heart disease, heart failure, cerebrovascular disease, and chronic renal disease [3]. Obesity is the accumulation of abnormal or excessive fat that may interfere with the maintenance of an optimal state of health [1]. Recent studies suggest that obesity may be a systemic chronic inflammatory condition [4]. Excessive macronutrients in adipose tissues stimulate the release of inflammatory mediators such as tumor necrosis factor-α (TNF-α) and interleukin 6 (IL-6), and the production of adiponectin. This generates predisposition to a proinflammatory state and oxidative stress [5, 6]. Indeed, obesity is associated with a variety of inflammatory conditions [7, 8]. Recent evidence suggests

This article is part of the Topical Collection on *Otitis*

✉ Seung Geun Yeo
yeo2park@gmail.com

[1] Department of Otorhinolaryngology-Head and Neck Surgery, Myongji Hospital, Hanyang University College of Medicine, Goyang, South Korea

[2] Department of Obstetrics and Gynecology, St. Vincent's Hospital, The Catholic University of Korea, Suwon, South Korea

[3] Department of Otorhinolaryngology-Head & Neck Surgery, School of Medicine, Kyung Hee University, Hoegi-dong, Dongdaemun-gu, Seoul 130-702, South Korea

that allergic rhinitis (AR) and chronic sinusitis (CRS) are chronic inflammatory rather than infectious diseases of the nasal cavity and sinuses, and show pathophysiologic mechanisms similar to those of asthma, a typical chronic inflammatory disease of the lower respiratory tract [9, 10]. These diseases are caused by a mechanism similar to that of airway inflammation observed in asthma [11]. The effects of obesity on AR or CRS have been studied extensively [12–29]. In addition, the relationship between obstructive sleep apnea (OSA) and obesity has been reported in various studies associated with metabolic syndrome [30–44]. There have been various reports on the relationship between obesity and otitis media (OM) [18, 27, 45–52] and hearing loss (HL) [53–60]. It has been speculated that laryngopharyngeal reflux (LPR) is also associated with obesity by a mechanism similar to that of gastroesophageal reflux disease (GERD) [61]. Thus, various otorhinolaryngological diseases seem to be associated with obesity (Table 1). To our best knowledge, there has yet to be a systematic evaluation of the literature on the relationship between obesity and various otorhinolaryngological diseases.

In this article, we address this gap in knowledge by reviewing research on the relationship between obesity and otorhinolaryngologic diseases, and summarize the mechanisms by which obesity affects each disease.

Main Pathophysiology of Obesity

Obesity, which is broadly defined as excess body weight for a given height, is an ongoing global health concern, as it is associated with increased risk of numerous chronic diseases. A recent analysis of data from 195 countries revealed that the prevalence of obesity has doubled in more than 70 countries since 1980, and over 600 million adults were obese in 2015, with high BMI accounting for 4 million deaths globally [62••, 63].

Excess adiposity typically evolves slowly, with a long-term positive energy balance. An obese person with stable weight, as compared with a person with normal weight, has larger fat and lean mass, along with higher resting energy expenditure, cardiac output, blood pressure, and greater pancreatic β-cell mass [64, 65]. Insulin secretion in the fasting state and after a glucose load increases linearly with BMI [66].

Obesity is accompanied by increased numbers of macrophages and other immune cells in adipose tissue, partly due to tissue remodeling in response to apoptosis of adipocytes [67]. These immune cells secrete proinflammatory cytokines, which contribute to the insulin resistance that is often present in patients with obesity. Visceral adipose tissue is a smaller storage compartment for lipids than is subcutaneous adipose tissue, with omental and mesenteric fat mechanistically linked to many of the metabolic disturbances and adverse outcomes associated with obesity [68, 69]. Obesity is often accompanied by an increase in pharyngeal soft tissues, which can block airways during sleep and lead to OSA [70]. An increase in intra-abdominal pressure purportedly accounts for the elevated risks of GERD or LPR [71].

Chronic overactivity of the sympathetic nervous system is present in some obese patients and may partially account for several pathophysiological processes, including high blood pressure [65]. Chronic renal diseases, stroke, and cardiovascular disease all have high blood pressure as their main pathophysiological mechanism alongside the cluster of findings associated with insulin resistance, obesity-associated dyslipidemia, and diabetes. Adipocytes synthesize adipokines (cell-signaling proteins) and hormones, the secretion rates and effects of which are influenced by the distribution and amount of adipose tissue present. Excessive secretion of proinflammatory adipokines by adipocytes and macrophages within adipose tissue leads to a low-grade systemic inflammatory state in some individuals with obesity [69]. Thus, obesity causes a variety of diseases through various pathological mechanisms. In particular, dysregulation of the immune system, induction

Table 1 Various otorhinolaryngologic diseases associated with obesity

Diseases	Subtypes
Otitis media	Otitis media with effusion (OME)
	Chronic otitis media (COM)
	Acute otitis media (AOM)
	Recurrent otitis media (ROM)
	Tasty dysfunction (associated with OM)
Hearing loss	Sensorineural hearing loss (SNHL)
	Sudden sensorineural hearing loss (SSNHL)
	Age-related hearing loss (ARHL)
	Noise-induced hearing loss (NIHL)
Chronic rhinosinusitis (CRS)	
Obstructive sleep apnea (OSA)	
Laryngopharyngeal reflux (LPR)	
Head and neck cancers (HNC)	

of a chronic inflammatory state, high blood pressure, and progression of atherosclerotic processes due to increased insulin resistance are thought to be related to otorhinolaryngological diseases.

Association Between Obesity and Otologic Diseases

Otitis Media

OM refers to inflammatory diseases of the middle ear, regardless of cause or pathological mechanism [72]. In children, OM is the leading cause of visits to the doctor, antibiotic prescription, and performance of surgical procedures, as well as being the most common cause of HL [73, 74]. There is a substantial overlap between the established risk factors for childhood obesity and OM. Obesity and OM are associated with male predominance, low socioeconomic status, immune dysfunction, and inflammation that characterizes each disease. This overlap implies a relationship between obesity and OM, and has catalyzed research over the past decade [75]. Table 2 provides details of studies investigating OM and obesity that have been included in this review. Various studies have been conducted in relation to OM and obesity in children. In 2007, Kim et al. [52] revealed the association between OM with effusion (OME) and obesity in children, and various studies subsequently reported similar results [18, 27, 45–52]. A prospective, non-randomized, case-control study investigated the association between OM and obesity in children. The experimental group comprised 155 children aged 2 to 7 years that received unilateral or bilateral ventilation tube insertion for the treatment of OME. The control group comprised 118 children with no history of OME that underwent operations for conditions other than ear diseases. Differences in BMI, serum triglyceride (TG), and total cholesterol (TC) concentrations between the experimental and control groups were analyzed. BMI and TC level, but not mean serum TG level, were significantly higher in the experimental group than in the control group. Based on these results, the authors concluded that childhood obesity may be associated with the occurrence of OME. However, the frequency of ventilation tube insertion did not significantly differ between the obese and non-obese subgroups in this study [52]. In 2011, there was a case-control study of the association between obesity and OM in 190 children who underwent surgery for non-ear related diseases and 140 children who underwent ventilation tube insertion. The prevalence of obesity was significantly higher in the OME group than in the control group ($P < 0.05$). However, BMI did not significantly differ between groups, according to standard body weight. The authors concluded that pediatric obesity may have an effect on the development of OME, but pediatric overweight may not be associated with occurrence of OME [51]. One limitation of the study was that it did not correct for the influence of socioeconomic status on risk factors for OM. To address this, Kuhle et al. conducted a prospective cohort study of 3399 children aged 10–11 years [47]. Relative to normal weight children, obese children had more healthcare provider contacts for serous otitis media (SOM) and higher odds of having repeated SOM. Socioeconomic factors, history of breastfeeding, presence of an allergic disorder, or chronic adenoid/tonsil disorder did not influence the association between obesity and SOM. Based on these results, the authors concluded that there is a clear association between childhood obesity and SOM that cannot be explained by confounding socioeconomic factors or clinically associated disorders [47]. Another study evaluated data gathered from a prospective cohort of 530 children from 1991 to 1996. In this study, the authors reported a significantly increased risk of obesity in infants undergoing ventilation tube insertion for OM when adjusting for birth weight, maternal prenatal smoking, maternal education status, and socioeconomic status [49]. In another case-control study of 146 children, the prevalence of overweight or obesity was higher in children with OME, according to weight for height percentiles ($P = 0.012$) [45].

Several studies have examined the mechanisms underlying obesity's effects on OM. A prominent hypothesis is that obesity-induced chronic inflammatory changes affect the production, secretion, and biological reactions of various cytokines. Obesity is characterized by low-grade systemic inflammation, as obese individuals show greater expression of inflammatory markers, especially C-reactive protein and interleukin (IL)-6 [4–6]. Adipokine is a protein secreted by adipose tissue (mainly adipocytes) along with leptin and adiponectin (resistin, adipsin, and visfatin). Other inflammatory mediators secreted by adipose tissue and adipocytes include TNF-α, IL-1, IL-6, IL-8, IL-18, monocyte chemoattractant protein-1, white adipose tissue-derived IL-1 receptor antagonist, and macrophage inflammatory protein-1 [4, 6]. In obese patients, the average levels of these cytokines are increased. Altered systemic and local adipokine concentrations have been reported in obese individuals with various inflammatory/autoimmune conditions. Increased inflammatory cytokine production caused by altered T cell responses, production of interferon-γ, and elevated leptin concentrations can alter host immunity and increase the risk of infection. Based on these findings, it is suggested that obesity-related changes in inflammatory mediators and repeated infections can increase the risk of OME [76].

Previous research reporting increased incidence of OM in obese children has catalyzed additional studies in this field. One study examined the relationship between dietary patterns, BMI, and OM. In this study, BMI was high in children with dietary intake related to excessive adiposity, and the incidence of OM was higher in this group. Overall, these findings support an association between high OM

Table 2 Studies assessing the association between otologic diseases and obesity

Authors and reference	Country	Study design	No.	Age	Otologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
Kim TH, et al. [18]	Korea	Cross-sectional study	585	Over 20 years	COM	BMI	Mean BMIs were significantly higher in the COM group than in the control group (24.45 ± 2.72 vs 3.22 ± 3.01 kg/m^2, $P < 0.05$)	Mean BMI and the prevalence of obesity were elevated in the three groups of patients with COM
Sidell D, et al. [27]	USA	Cross-sectional analysis	42,100,000	School-age children (average age: 12.2 years)	AOM	BMI	Utilizing an adjusted multivariate model, childhood obesity was found to be associated with AOM (OR, 1.44; 95% CI 1.08 to 1.93; $P = 0.033$)	Childhood obesity appears to be associated with the development of AOM
Kaya S, et al. [45]	Turkey	Case-control study	146 (60 children with OME, 86 healthy children)	2–10 years	OME	BMI, weight for height and weight z-score	The prevalence of overweight or obesity was higher in children with OME, according to weight for height percentiles ($P = 0.012$)	Overweight and obesity may be risk factors for developing OME, or vice versa
Choi HG, et al. [46]	Korea	Cross-sectional study	4359 (80 children with OME, 4297 healthy children)	4–12 years	OME	BMI, distribution of fat intake	BMI category was not associated with OME. The distribution of fat intake was associated with OME (every 10% increase of fat calories/total calories: adjusted for age, sex, and other factors; OR = 1.392, 95% CI 1.054 to 1.839, $P = 0.020$)	A high-fat diet was associated with OME and may represent a confounding factor between obesity and OME
Kuhle S, et al. [47]	Canada	Prospective cohort study	3399	10–11 years	SOM	BMI	Relative to normal weight children, obese children had more healthcare provider contacts for SOM (adjusted incidence rate ratio 2.03, 95% CI 1.66 to 2.49) and had higher odds to have repeated SOM (adjusted OR = 2.27, 95% CI 1.54 to 3.35). Socioeconomic factors, a history of breastfeeding, presence of an allergic disorder, or chronic adenoid/tonsil disorder did not change the association between obesity and SOM	There is a clear association between childhood obesity and otitis media that cannot be explained by confounding socioeconomic factors or clinically associated disorders
Shin IH, et al. [48]	Korea	Prospective, non-randomized, case-control study	84 (OME: 42, control: 42)	3–7 years	OME: change in taste function	BMI	BMI was significantly higher in the OME than in the control group ($P = 0.02$). EGM showed that the anterior part of the tongue had a significantly higher taste threshold in the OME than in the control group (anterior right, $P = 0.03$; anterior left, $P = 0.04$). Chemical taste test results revealed that sweet and salty tastes were significantly lower in the OME group (sweet, $P = 0.02$; salty, $P = 0.04$)	OME can cause changes in taste; these changes may be related to pediatric obesity
Nelson HM, et al. [49]	USA	Prospective cohort study	538	0–2 years	ROM	WFL	11.4% of children had a WFL measure at 2 years of age ≥ 95th percentile. Those children with a history of tympanostomy tube treatment had a significantly increased risk of	The findings of this study are consistent with the hypothesis and prior research that ROM treated with tympanostomy

Table 2 (continued)

Authors and reference	Country	Study design	No.	Age	Otologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
							having a WFL ≥ 95th percentile after controlling for birthweight, maternal prenatal smoking, maternal education, and family income (OR = 3.32, 95% CI 1.43 to 7.72)	tubes is associated with overweight status
Seaberg RM, et al. [50]	Canada	Retrospective cohort study.	142	5–18 years	AOM: chorda tympani nerve function	BMI	There was no significant association between the history of AOM and BMI	No relationship between AOM and elevated BMI was demonstrated
Kim SH, et al. [51]	Korea	Prospective, non-randomized, case-control study	330 (AOM: 140, control: 190)	2–7 years	OME	BMI	The prevalence of obesity was significantly higher in the OME group than in the control group ($P < 0.05$). However, BMI did not differ significantly between groups, according to standard body weight	Pediatric obesity may have an effect on the development of OME, but pediatric overweight may not be associated with occurrence of OME
Kim JB, et al. [52]	Korea	Prospective, non-randomized, case-control study	273 (OME: 155, control: 122)	2–7 years	OME	BMI	BMI (22.0 ± 3.4 vs 16.3 ± 2.4) ($P = 0.01$) and was significantly higher in the OME group than in the control group	Childhood obesity may be associated with the occurrence of OME
Scinicariello F, et al. [53]	USA	Cross-sectional study (based on NHANES)	1469	12–19 years	HL (NIHL, SFHL, HFHL)	BMI	Obese adolescents had a higher adjusted OR for NIHL (OR = 1.93; 95% CI 1.33 to 2.81) and HFHL (OR = 1.95; 95% CI 1.19 to 3.21)	Being obese was associated with NIHL and HL
Hwang JH, et al. [54]	Taiwan	Prospective cross-sectional study	690	47–66 years	ARHL	WC (> 90 cm male and > 80 cm female)	WC was an independent risk factor of ARHL even after adjustment for BMI, particularly for low and high frequencies in males younger than 55 years and for high frequencies in female subjects older than 55 years	WC is independently associated with HL, but this differs by age and gender
Lee JS, et al. [55]	Korea	Case-controlled study with a longitudinal prospective study	1296 (SSNHL: 324, control: 972)	35–65 years	SSNHL	BMI	BMI was significantly higher in patients with SSNHL compared with control subjects ($P < 0.05$). BMI was an independent risk factor of treatment outcome, as patients with BMI ≥ 27.5 were less likely to achieve complete recovery than those with BMI < 27.5 ($P < 0.05$)	Increased BMI is significantly associated with the prevalence of SSNHL and its prognosis
Hwang JH [56]	Taiwan	Retrospective cohort study	254	40–70 years	SSNHL	BMI (≥25 kg/m^2)	BMI (OR = 1.04, 95% CI = 0.964–1.131, $P = 0.292$) was not significantly associated with the recovery of SSNHL for all subjects, after adjusting for all considered variables	Obesity/overweight appeared to have no significant effect on the prognosis of SSNHL

Table 2 (continued)

Authors and reference	Country	Study design	No.	Age	Otologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
Lalwani AK, et al. [57]	USA	Retrospective cross-sectional study	1488	12–19 years	SNHL	BMI	Obesity was associated with a 1.85-fold increase in the odds of unilateral low-frequency SNHL (95% CI 1.10 to 3.13) after controlling for multiple hearing-related covariates	Obesity in childhood is associated with higher hearing thresholds across all frequencies and an almost twofold increase in the odds of low-frequent HL
Curhan SG, et al. [58]	USA	Retrospective longitudinal analysis	68,421	25–42 years	HL	BMI, WC	Compared with that for women with BMI < 25 kg/m^2, the multivariate-adjusted RR for women with BMI ≥ 40 was 1.25 (95% CI 1.14 to 1.37). Compared with that for women with waist circumference < 71 cm, the multivariate-adjusted RR for waist circumference > 88 cm was 1.27 (95% CI 1.17 to 1.38)	Higher BMI and larger waist circumference are associated with increased risk of HL in women
Kim TS, et al. [59]	Korea	Prospective cross-sectional study	662	40–82 years	ARHL	BMI, WC, visceral adipose tissue	After adjusting for age, systemic disease, and other variables, a positive association between visceral adipose tissue area and average hearing threshold was observed in women	Visceral adipose tissue is positively associated with ARHL in women over 40 years
Barrenäs ML, et al. [60]	Sweden	Prospective longitudinal register study	245,092	0–80 years	SNHL	BMI	Compared with conscripts with average BMI, overweight was associated with 30%, obesity with 99%, and overweight if born light for gestational age with 118% higher risk of SNHL	Increased BMI was associated with a doubled risk of SNHL

COM chronic otitis media, *BMI* body mass index, *AOM* acute otitis media, *OR* odds ratio, *CI* confidence interval, *OME* otitis media with effusion, *SOM* suppurative otitis media, *EGM* electrogustometry, *ROM* recurrent otitis media, *WFL* weight-for-length, *NHANES* National Health and Nutrition Examination Survey, *HL* hearing loss, *NIHL* noise-induced hearing loss, *SFHL* speech frequency hearing loss, *HFHL* high frequency hearing loss, *ARHL* age-related hearing loss, *WC* waist circumference, *SSNHL* sudden sensorineural hearing loss, *SNHL* sensorineural hearing loss, *RR* relative risk

exposure and elevated adiposity in preschoolers [77]. Another study examined the effect of obesity on the relationship between OM and taste disorders. Histopathological analysis of the degree of fibrosis of the perineurium of the chorda tympani nerve in OM patients suggested that inflammation of middle ear lesions caused progressive dysfunction, and resulting damage of the chorda tympanic nerve may underlie taste disorders in OM patients [78]. Another study reported that taste dysfunction may be more frequent and more severe in obese patients with OM. In this study, chemical taste testing and electrogustometry were used to assess taste function in a pediatric population. BMI was significantly higher in patients with OME than in non-OME controls. In this study, OME patients showed significantly higher taste thresholds for salty and sweet tastes. Based on these results, it was hypothesized that taste dysfunction influenced OME patients to intake more food in order to attain the same intensity of taste as that of the control group. Further, OME patients were thought to ingest more calories and be at increased risk for developing obesity [48].

Hearing Loss

HL is the most important and frequent symptom of ear disease due to partial or complete dysfunction of the auditory pathway from the ear to the cerebral auditory cortex [79]. HL is a major public health problem and was recently ranked as the fifth leading cause of years lived with disability, exceeding other chronic diseases such as diabetes, dementia, and chronic obstructive pulmonary disease. There are several types of HL, ranging from temporary to permanent losses that can be either congenital or acquired. Sensorineural HL (SNHL) refers to either damage to the outer or inner hair cells in the organ of Corti located within the cochlea, or nerve damage along the auditory nerve (the eighth cranial nerve). Examples of SNHL include age-related hearing loss (ARHL) and sudden sensorineural hearing loss (SSNHL) [80]. ARHL (or presbyacusis) is the most prevalent sensory impairment in the elderly population. According to recent statistics, more than 70% of people over 70 years old, and over 40% of people over 50 years old, experience some type of hearing dysfunction [81•]. ARHL is predominantly sensorineural dysfunction of hearing, so the effects on older listeners may be loss of the ability to correctly interpret sounds, especially in complex listening environments. Therefore, ARHL is not limited to hearing deficits alone, but rather to difficulty in comprehension and understanding of speech, that can have significant effects on quality of life. Obesity is an independent risk factor for ARHL, with increased BMI enhancing the severity of SNHL. Adipose tissue is thought to act as endocrine tissue, secreting hormones and cytokines, with obesity-induced inflammation causing end-organ damage by affecting atherosclerosis, insulin resistance, and energy metabolism [82]. Therefore, obesity-associated atherosclerosis may lead to reduced cochlear blood flow by inducing stiffening and constriction of internal auditory arteries. This process may ultimately lead to hearing loss through the induction of stria vascularis and cell death [82•]. SSNHL is usually defined as a reduction in hearing threshold of 30 dB HL or more, occurring over a 72-h period in three consecutive frequencies of pure tone audiometry (PTA). SSNHL is considered to be idiopathic, with several potential causes reported, including viral or immunologic [83]. Another cause for concern is microangiopathy, which is an interruption in the vascular supply to the cochlea (a highly metabolic organ) that causes SSNHL. As the blood supplied to the cochlea derives from the labyrinthine artery without collateral arterial blood flow, the cochlea is vulnerable to transient ischemia [82]. Obesity has been proposed as a predisposing factor to SSNHL, potentially via cochlear microvascular circulation mechanisms. Obesity can induce atherosclerotic changes or alter the stiffness and/or elasticity of blood vessels, thereby inducing microangiopathy. Each pathologic change in the inner ear can increase the likelihood of SSNHL. Semipermanent changes in blood vessels are thought to have a negative association with outcomes in patients with SSNHL [82]. Table 2 describes reports investigating the relationship between HL and obesity.

According to a study on the association between ARHL and obesity, waist circumference (WC), a measurement item for defining central obesity, is independently associated with HL, but this differs by age and gender. In this study, PTA at low, pure, and high frequencies were assessed in 690 men and women aged between 35 and 86 years old. The proportion of normal hearing was higher in women. When comparing individuals with central adiposity to those without, hearing at low frequency was impaired in men over 55 years; at high frequency, there was hearing impairment in women aged over 55 years. Factors significantly associated with HL at both low and high frequencies included waist circumference, age, BMI, smoking, coronary artery disease, and chronic renal failure. Even after adjustment for BMI, WC was an independent risk factor for ARHL, particularly for low and high frequencies in males younger than 55 years and for high frequencies in female subjects older than 55 years [56]. However, in contrast to this, another study reported that visceral adipose tissue was positively linked with hearing threshold in obese women. The authors recruited 662 participants aged over 40 years and performed computerized tomography scanning for fat measurements and extracting total and visceral adipose tissue, PTA, morphometry, and medical questionnaires. Positive associations were observed between female PTA-low and PTA-high thresholds

and visceral adipose tissue. They concluded that a suitable approach for preventing the acceleration of ARHI in women could be to reduce visceral adiposity [57], but further studies on visceral adipose tissue are necessary.

There are two studies focused solely on obesity and SSNHL. A matched case-control study in 2015 examined patients attending a university hospital between 2009 and 2012. The experimental group consisted of 324 participants (mean age, 49.64 years old) diagnosed with unilateral SSNHL. Group data on 972 control participants were obtained from the Korean National Health and Nutrition Examination Survey. BMI was significantly higher in patients with SSNHL than in control subjects ($P < 0.05$). BMI was an independent risk factor for treatment outcome, as patients with BMI ≥ 27.5 were less likely to achieve complete recovery than those with BMI < 27.5 ($P < 0.05$). The authors concluded that increased BMI is significantly associated with the prevalence of SSNHL and its prognosis. They proposed that elevated blood lipid levels are a risk factor for SSNHL, although contradictory evidence has indicated that the association between lipid profiles and SSNHL is inconclusive [54]. Another study collected clinical and audiometric data from 254 adults who were reported to have had unilateral SSNHL. These patients were divided into two groups based on BMI; patients with BMI < 25 or ≥ 25 kg/m^2 were categorized as the non-obesity and overweight/obese groups, respectively. In this study, BMI was not significantly associated with recovery of SSNHL in all subjects after adjusting for all considered variables, implying that obesity/overweight had no significant effect on the prognosis of SSNHL [55]. This is contrary to previous studies, and the authors speculated that these negative results may be due to the lack of WC data and different BMI cutoff points in the Asian population. However, further analyses are required to clarify these discrepancies.

In a prospective longitudinal register study, information on Swedish conscripts' birth characteristics was obtained from the Swedish Birth Register and linked to the Swedish Conscript Register using the males' unique personal identification numbers. Compared to that for average BMI, there was a 30, 99, and 118% higher risk of SNHL associated with overweight, obesity, and overweight if born light for gestational age, respectively. Conscripts born light for gestational age had a 41% increased risk, independent of later growth patterns. Based on these results, the authors concluded that increased BMI was associated with double the risk of SNHL [59].

Two studies have reported a correlation between obesity and HL in adolescents. Lalwani et al. investigated whether obese children were at greater risk of SNHL than non-obese children. In this study, hearing thresholds in 1488 adolescents aged 12–19 years were compared between normal weight and overweight/obesity groups. Obesity was associated with a 1.85-fold increase in the odds of unilateral low-frequency SNHL after controlling for multiple hearing-related covariates. The authors concluded that obesity in childhood is associated with higher hearing thresholds across all frequencies and an almost twofold increase in the odds of low-frequency HL [58]. Another cross-sectional study of 1469 adolescents aged 12–19 years reported similar results. This study investigated whether obesity was associated with audiometric notches indicative of noise-induced hearing loss (NIHL), speech frequency hearing loss (SFHL), and high frequency hearing loss (HFHL) in adolescent participants of the National Health and Nutrition Examination Survey 2007–2010. Obese adolescents had a higher adjusted odds ratio (OR) of having NIHL and HFHL, suggesting that being obese was associated with certain types of HL (especially NIHL and HFHL) [60]. To summarize, obesity is associated with the onset of various forms of sensory neural deafness, most of which show negative effects.

Association Between Obesity and Rhinologic Diseases

Allergic Rhinitis and Chronic Rhinosinusitis

The nasal cavity and sinuses are classified as the upper airway and experience pathophysiological mechanisms similar to those of the lower airway, such as the trachea or lungs [11]. Obesity is a well-known risk factor and aggravating factor of asthma, one of the most common chronic inflammatory diseases of the lower respiratory tract. In this regard, the hypothesis that AR and CRS, which are typical chronic inflammatory diseases of the nasal cavity and sinus, are related to obesity has been corroborated by numerous studies [12–29]. Obesity is reported to cause immune disorders and increase levels of inflammatory mediators [84]. Adiponectin is the most abundant adipokine and is representative of "anti-inflammatory" adipokines. It has various metabolic, anti-inflammatory, and anti-proliferative effects. Obesity implies that plasma adiponectin levels are low, and inflammation may increase in obesity if adiponectin levels are reduced [85]. Leptin is an adipose-derived energy regulating hormone. Circulating leptin is positively correlated with body fat percentage and body fat mass [13, 86]. Osteopontin (OPN) is expressed in human eosinophils. OPN levels are increased after granulocyte-macrophage colony-stimulating factor (GM-CSF) and IL-5 activation [12]. These factors may be related to the deterioration of allergic inflammation, which is a chronic inflammatory reaction.

AR and CRS have an annual prevalence of 7.9 and 4.9%, respectively, and are among the most common chronic diseases affecting the adult patient population in the USA, resulting in health care costs of $1492 and $2449 per patient per year, respectively [19]. In particular, AR has high prevalence depending on age. According to a phase III clinical

study of childhood asthma and allergies, the global prevalence of AR in children ranges from 0.8 to 14.9% between the ages of 6 and 7 years, and from 1.4 to 39.7% between the ages of 13 and 14 [87]. Like other chronic inflammatory diseases, the prevalence of these diseases is also increasing.

Studies on the association between AR and CRS and obesity have indicated that increased BMI is associated with the presence of AR and CRS (Table 3) [12–29]. According to a cross-sectional analysis of a medical panel survey of 229.3 ± 4.6 million adult Americans published in 2013, an increased prevalence of adult obesity was associated with both AR and CRS. In this study, increasing BMI as a continuous variable was significantly associated with the presence of both AR and CRS [19]. Similar results in children have been reported. According to a questionnaire-based survey of 3327 children aged 2–14 years, the prevalence of AR and atopic dermatitis was higher in obese children than in asthma, food allergies, and drug allergies. And in this study, obesity affected the incidence of AR, especially in girls [16]. In two case-control studies of pediatric AR patients in China, the expression of leptin and OPN in the obese group was increased, suggesting that the symptoms of AR were more severe in the obese group with increased leptin and OPN [12, 13]. Obesity may be involved in the regulation of eosinophils through leptin and OPN. In addition, several studies have reported that increased BMI is significantly associated with the presence of AR in children. Collectively, these findings suggest that obesity is a factor that increases the incidence or exacerbates symptoms of AR or CRS [14, 15, 17, 18, 20, 21].

In contrast, some studies have reported no significant or negative correlation between obesity and AR [25–29]. According to one epidemiologic study in Japan, childhood obesity was negatively associated with AR prevalence, especially among boys [29]. A questionnaire was distributed to the parents of 50,086 Japanese school children to assess whether and how childhood obesity is associated with allergic diseases. A significant association was detected between lower BMI and AR, as well as a significantly lower prevalence of AR among children with obesity, especially boys. No association between obesity and disease severity was observed for AR. Similar results were observed in a population-based cross-sectional study for adults [28]. According to one study, the prevalence of AR is increased by sporting activities, and the incidence of new rhinitis in school children is increasing. Children with more sporting activity tend to suffer from AR. The authors suggested that increased exposure to pollen during sporting activities or transdermal absorption of inhalant allergens may be enhanced through barrier-disrupted skin during sporting activities, leading to nasal allergy inflammation [88]. In addition, some studies have reported that obesity may have a different impact on AR, depending on gender and age [24].

In summary, the role of obesity in the development of CRS is relatively well defined, and there is a negative association between obesity and CRS. In contrast, although obesity and AR are associated, the directionality of association remains unclear and should be clarified in future studies.

Obstructive Sleep Apnea and Other Forms of Sleep-Disordered Breathing

Individuals spend approximately one third of their lives on average sleeping, which is essential for health and well-being. Sleep-disordered breathing (SDB), a major cause of sleep disturbances in a wide range of abnormal conditions ranging from simple snoring to OSA, can have detrimental effects on physical or mental health. OSA is a disorder in which the upper airway is repeatedly blocked, resulting in oxygen saturation and awakening during sleep [89, 90]. OSA affects approximately 13% of men, 6% of women aged 30–70 years old, and 1–4% of children [91]. Recent studies have shown that OSA is closely related to metabolic syndrome and has pathophysiologically overlapping mechanisms [91–93].

Obesity is one of five components comprising metabolic syndrome. Metabolic syndrome is strongly linked to obesity and is also a well-known risk factor for OSA. Therefore, several mechanisms have been suggested to explain the biological plausibility of OSA, independent of obesity, increasing the risk of metabolic syndrome [92]. These mechanisms may be associated with cytokines, oxidative stress, intermittent hypoxia, and selective activation of systemic inflammatory reactions. Repeated obstructive events cause intermittent hypoxia in OSA. Repaid reoxygenation of transiently ischemic tissues can damage tissues and release reactive oxygen species, the cause of oxidative stress. Intermittent hypoxia and resultant oxidative stress have been proposed as a pathogenic pathway between OSA and disturbance of glucose homeostasis, hyperlipidemia, insulin resistance, and hypercholesterolemia. Inflammatory cytokines (e.g., IL-6 or TNF-α) that are triggered by intermittent hypoxia and sleep fragmentation have been postulated as a putative mechanism underpinning metabolic syndrome. Inflammatory cytokines may also impair insulin action in peripheral tissues and increase insulin resistance, dyslipidemia, and hypertension in OSA [93]. Therefore, obesity and OSA appear to have a synergistic, negative effect on glucose metabolism. Furthermore, intermittent hypoxemia has been shown to produce beta cell dysfunction as well as insulin resistance [91, 93]. Another way in which the pathophysiological mechanisms may overlap is inflammation. Several studies have proposed that OSA in both adults and children is a disease of inflammation. Intermittent airway obstruction places mechanical stress on mucosa that promotes local airway inflammation and systemic overexpression of proinflammatory cytokines [92, 93].

Recently, clinicians are recognizing that the development of OSA and subsequent sleep fragmentation may contribute to accelerated weight gain. Many patients report rapid increases

Table 3 Studies assessing the association between rhinologic diseases and obesity

Authors and reference	Country	Study design	No.	Age	Rhinologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
Liu W, et al. [12]	China	Case-control study	60	5–10 years	AR	BMI	AR children with obesity had higher TNSS score than did AR children without obesity. Serum leptin and OPN levels were significantly higher in AR children than in controls, especially in obese children ($P < 0.05$)	Upregulation of leptin and OPN in obese children with AR was correlated with the count and activation (ECP level) of eosinophil inflammation when compared with non-obese children with AR or controls, suggesting that obesity may be involved in the regulation of eosinophils through leptin and OPN
Zeng Q, et al. [13]	China	Case-control study	60	7–12 years	AR	BMI	TNSS was significantly higher in obese children with AR than in non-obese children with AR ($P < 0.05$). Both serum leptin and OPN concentrations were significantly increased in children with AR compared with normal controls, especially in patients with obesity ($P < 0.05$)	Leptin and OPN were significantly upregulated in obese children with AR
Liu W, et al. [14]	China	Cross-sectional study	3126	Adults	AR	BMI, WC, WHR, PBF	The symptom score (9.5 ± 3.1 vs 8.2 ± 3.5, $P < 0.05$) and medication score (3.6 ± 1.6 vs 2.9 ± 1.8, $P < 0.05$) were significantly higher in obese children with AR than in non-obese children with AR	Obesity exacerbates inflammation and contributes to disease severity in AR
Lim MS, et al. [15]	Korea	Cross-sectional study	53,769 (AR patient: 9018)	15.0 ± 0.0 years	AR	BMI	In AR, OR was significantly higher in overweight groups than in other groups based on multiple logistic regression analysis (OR = 1.05; 95% CI 0.99 to 1.12; $P = 0.025$)	Overweight was positively correlated with AR
Lei Y, et al. [16]	China	Cross-sectional study	3327	2–14 years	AR	BMI	Obesity (OR = 1.33) increased the prevalence of AR. Obesity (OR = 1.48) affected the incidence of AR in girls	Obesity increased the prevalence of AR in children
Park DY, et al. [17]	Korea	Cross-sectional study	97	Adults	AR	BMI	The association between histamine skin reactivity (wheal size) and BMI was present in multivariate analysis, adjusted for age, sex, atopy, smoking history, and season	Histamine skin reactivity increased with BMI (degree of obesity)
	Korea		585	Over 20 years	CRS	BMI		

Table 3 (continued)

Authors and reference	Country	Study design	No.	Age	Rhinologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
Kim TH, et al. [18]		Cross-sectional study					Mean BMIs in the CRS group were significantly higher than in the control group (24.68 ± 3.25 vs 3.22 ± 3.01 kg/m2, $P < 0.05$). The rates of obesity were significantly higher in the CRS group than in the control group (42.9 vs 24.3%, $P < 0.05$)	Mean BMI and prevalence of obesity were elevated in three groups of patients with representative CRS
Bhattacharyya N. [19]	USA	Cross-sectional analysis of medical panel survey	229.3 ± 4.6 million adult Americans (unweighted $N = 46{,}617$),	Over 18 years	AR, CRS	BMI (≥ 30.0 kg/m^2)	The aOR for AR when obesity was present was 1.22 ($P < 0.001$, 95% CI 1.12 to 1.33) and CRS was 1.31 ($P < 0.001$, 95% CI 1.18 to 1.45). Increasing BMI as a continuous variable was significantly associated with the presence of both AR (OR = 1.023, $P < 0.001$) and CRS (OR = 1.022, $P < 0.001$)	Increased prevalence of adult obesity was associated with both AR and CRS
Huang SL, et al. [20]	Taiwan	Cross-sectional study	1459	13.78 ± 0.36 years	AR	BMI	Girls in the highest BMI quintile had higher prevalence of atopy and rhinitis symptoms. Girls in the lowest BMI quintile had lower prevalence of BHR and wheezing	BMI was a significant predictor of atopy, allergic symptoms, and BHR in teenage girls
Saadeh D, et al. [21]	France	Cross-sectional study	6733	9–11 years	AR	BMI	After adjustment for confounding factors, lifetime and past-year AR were associated with high BMI in wheezing children (aOR = 1.63, [1.09 to 2.45] and aOR = 2.20, [1.13 to 4.27])	High BMI was associated with lifetime and past-year AR
Chung SD, et al. [22]	Taiwan	Cross-sectional study	22,963 (CRS: 5734, control: 17,202)	18–80 years	CRS	BMI	Obesity was significantly associated with CRS (aOR = 2.50, 95% CI 1.90 to 3.30, $P < 0.05$)	Subjects with CRS have an increased prevalence of obesity
Matsumoto M, et al. [23]	Japan	Cross-sectional study	11,917	18–25 years	PAR, SAR	BMI	The prevalence of PAR was not associated with BMI. Low BMI was significantly associated with high SAR prevalence ($P < 0.05$)	Comparisons between PAR and SAR revealed that the conditions are differentially associated with BMI
Han YY, et al. [24]	USA	Cross-sectional study	8165 (2358 children and 4906 adults)	≥ 6 years	AR	BMI	In adults, being overweight or obese was associated with increased odds of non-AR (aOR = 1.43, 95% CI 1.06	In adults, obesity is associated with increased odds of non-AR, particularly in males.

Table 3 (continued)

Authors and reference	Country	Study design	No.	Age	Rhinologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
							to 1.93, $P = 0.02$). In children, central obesity was associated with reduced odds of AR (aOR = 0.35, 95% CI 0.19 to 0.64, $P < 0.01$)	In children, central obesity is associated with reduced odds of AR, regardless of gender
Kanagalingam S, et al. [25]	USA	Randomized, double-masked, placebo--controlled study	236	21–68 years	AR	BMI	Obesity had no effect on the severity of sinonasal disease symptoms in asthmatics (SNOT 22 score [mean ± SD] 35.4 ± 18.5, 40.2 ± 22.8, and 39.1 ± 21.7, $P = 0.43$, in lean, overweight, and obese participants, respectively), or on nasal, bronchial, or systemic markers of allergic inflammation	Obesity does not affect severity of sinonasal disease in patients with asthma
Sybilski AJ, et al. [26]	Poland	Questionnaire-based survey	18,617	Children: (1) 6–7 years, (2) 13–14 years Adult: 20–44 years	AR	BMI	Overweight (OR = 0·81) and obesity (OR = 0·76) reduced the prevalence of AR in men	Higher BMI was negatively associated with the prevalence of AR in overweight and obese man
Sidell D, et al. [27]	USA	Cross-sectional analysis	42.1 million (unweighted $N = 510,623$)	School-age children	AR, CRS	BMI	Utilizing an adjusted multivariate model, childhood obesity was found to be no associated with AR and CRS	Childhood obesity appears to be associated with the development of AOM; however, an association between obesity and AR or CRS was not demonstrated
Konno S, et al. [28].	Japan	A population-based, cross-sectional study	22,819	20–79 years	Rhinitis	BMI	Particularly in the 20- to 44-year age group, obesity was negatively associated with rhinitis without asthma	Obesity may have different effects on the development of rhinitis
Kusunoki T, et al. [29]	Japan	Cross-sectional study	50,086	7–15 years	AR	BMI	Significant associations were found between lower BMI and AR/AC ($P < 0.0001$). Significantly lower prevalence of AR/AC ($P = 0.002$) was observed in children with obesity, and AR ($P = 0.04$) and AR/AC ($P = 0.0004$) among boys with obesity than those without obesity	Childhood obesity has negative associations with AR prevalence, especially among boys
Andersen IG, et al. [30]	Denmark	Cross-sectional study	139	7–18 years	OSA	BMI SDS	OSA prevalence was 44.6% in children with overweight/obesity compared with 9.1% in the normal weight group	Children with overweight/obesity had a significantly higher

Table 3 (continued)

Authors and reference	Country	Study design	No.	Age	Rhinologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
							($P = 0.0002$). Relative risk of OSA was 4.9 (95% CI 1.6 to 14.7). A generalized linear regression adjusted for the same variables revealed an association between BMI SDS and AHI (a one-unit increase in the BMI SDS equaled an average increase in the AHI of 35% [95% CI 19 to 53%, $P < 0.0001$])	prevalence of OSA when compared with a normal weight group. Increased BMI SDS was associated with increased AHI
Evangelisti M, et al. [31]	Italy	Cross-sectional study	248	8.08 years	SDB	BMI	Obese children showed higher ODI and lower nadir SaO_2 compared to non-obese children ($P < 0.05$). ODI and nadir SaO_2 correlated with obesity ($P < 0.05$)	Obese children with SDB have more significant oxygen desaturation
Mathew R, et al. [32]	USA	Retrospective review study	90	Over 18 years	OSA	BMI	BMI was the only significant predictor of HAR (aOR = 0.138; $P = 0.002$) in a linear regression model with natural log transformation of the HAR performed for age, gender, race, and BMI	Extremely obese patients manifest OSA with a preponderance of hypopneas
Kim H, et al. [33]	Korea	Retrospective review study	297	19–87 years	OSA	BMI	The oxygen desaturation index was different in patients who were treated with MAD and surgery. Obese patients with severe OSA showed an unfavorable response to CPAP treatment. For CPAP compliance, obese patients showed a tendency to be highly compliant with CPAP treatment at 12 months when compared to non-obese patients	Obesity may be a factor in determining the success or failure of treatment. Obesity may be a predictive factor for CPAP compliance
Arnardottir ES, et al. [34]	Iceland	Cross-sectional study	452	54.3 ± 10.6 years	OSA	BMI	Leptin levels were more strongly correlated with BMI. No relationship was detected between sleep apnea severity and leptin levels, assessed within three BMI groups (BMI < 30, BMI 30–35, and BMI > 35 kg/m^2)	Obesity and gender are the predominant determinants of leptin levels
Antczak J, et al. [35]	Germany	Retrospective chart review	38 (13 non-obese, 13 obese, and 12 severely obese male)	Adults	OSA (CPAP therapy)	BMI	In diagnostic polysomnography, obese and severely obese subjects showed increases in AHI and NREM-1 sleep, and decreases in min SaO_2, REM sleep, and partial SWS, when compared with the non-obese group. On the second night under CPAP, normalization of AHI and rebound of REM	After long-term CPAP therapy, no deleterious effects of obesity on sleep quality are apparent in sleep apnea patients

Table 3 (continued)

Authors and reference	Country	Study design	No.	Age	Rhinologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
							and SWS occurred, which were more pronounced in the severely obese than in the non-obese and obese group	
Daltro C, et al. [36]	Brazil	Cross-sectional study	108	37.1 ± 10.2 years	OSA	BMI	The calculated AHI ranged widely from 2.5 to 128.9 events/h. Sleep apnea was detected in 93.6% of the sample, wherein 35.2% had mild, 30.6% moderate, and 27.8% severe apnea	There was a high frequency of sleep apnea in this group of morbidly obese patients, for whom it was very important to request PSG, thus enabling therapeutic management and prognostication
Redline S, et al. [37]	USA	Community-based genetic epidemiologic study	399	2–18 years	SDB	BMI	SDB of moderate level was significantly associated with obesity (OR = 4.59; 95% CI 1.58 to 13.33) and African-American race (OR = 3.49; 95% CI 0.156 to 8.32) but not with sex or age	These data suggest the importance of obesity as risk factors for SDB in children and adolescents
Newman AB, et al. [38]	USA	Multicenter, longitudinal cohort study	2968	Adults	SDB	Weight change	Both men and women had a greater increase in RDI with weight gain than a decrease in RDI with weight loss	Modest changes in weight were related to an increase or decrease in SDB, and this association was stronger in men than in women
Peppard PE, et al. [39]	USA	Longitudinal population-based prospective cohort study	690	Adults	SDB	Weight change	A 10% increase in weight predicted a six-fold (95% CI 2.2 to 17.0) increase in the odds of developing moderate-to-severe SDB	Clinical and public health programs that result in even modest weight control are likely to be effective in managing SDB and reducing new occurrence of SDB
Punjabi NM, et al. [40]	USA	Prospective cross-sectional study	150	Over 45 years	SDB	BMI, determination of body fat	After adjusting for BMI and percent body fat, an AHI over five events/h was associated with an increased risk of having impaired or diabetic glucose tolerance (OR = 2.15, 95% CI 1.05 to 4.38)	SDB is a prevalent condition in mildly obese men and is independently associated with glucose intolerance and insulin resistance
Richman RM, et al. [41]	USA	Prospective cross-sectional study	108 women	Over 18 years	OSA	BMI	There was a significant positive correlation for RDI and BMI ($r = 0.71$; $P < 0.001$)	Obese women should be considered at risk of OSA
Vgontzas AN, et al. [42]	USA		378 (obese group: 250, age- and	Adults	OSA	BMI	Obese patients, both men and women, without OSA demonstrated a	Severely or morbidly obese men are at extremely high

Table 3 (continued)

Authors and reference	Country	Study design	No.	Age	Rhinologic disease	Anthropometric measurement for obesity assessment	Results	Conclusions
		Prospective case series with historical controls	sex-matched control group: 128)				significant degree of sleep disturbance when compared with non-obese controls	risk for sleep apnea and should be routinely evaluated in the sleep laboratory for this condition, while for severely or morbidly obese women, the physician should include a thorough sleep history in clinical assessment
Shinohara E, et al. [43]	Japan	Prospective study	37	Adults	OSA	VAT	Ratio of VAT was significantly greater in OSA patients compared to that in non-OSA patients. It was also closely correlated with an increase in apnea index	Visceral fat accumulation is an important risk indicator for OSA in obese subjects
Young T, et al. [44]	USA	Prospective cohort study	5616	40–98 years	SDB	BMI	Male sex, age, BMI, neck girth, snoring, and repeated breathing pause frequency were independent, significant correlates of an AHI of 15 or greater. The OR (95% CI) for an AHI of 15 or greater versus an AHI less than 15 were 1.6 and 1.5, respectively, for 1-SD increments in BMI and neck girth	BMI was associated with SDB, and high prevalence of obesity and morbid obesity was high in patients with sleep apnea

AR allergic rhinitis, *BMI* body mass index, *TNSS* total nasal symptom score, *OPN* osteopontin, *ECP* eosinophil cationic protein, *WC* waist circumference, *WHR* waist-to-height ratio, *PBF* body fat percentage, *OR* odds ratio, *CI* confidence interval, *CRS* chronic rhinosinusitis, *aOR* adjusted odds ration, *PAR* perennial allergic rhinitis, *SAR* seasonal allergic rhinitis, *SNOT22* Sino-Nasal Outcome Test 22, *AC* allergic conjunctivitis, *OSA* obstructive sleep apnea, *BMI SDS* body mass index standard deviation score, *AHI* apnea-hypopnea index, *SDB* sleep-disordered breathing, *ODI* oxygen desaturation index, SaO_2 oxygen saturation, *HAR* hypopnea/apnea ratio, *MAD* mandible advancement device, *CPAP* continuous airway positive pressure, *NREM* non-rapid eye movement sleep, *REM* rapid eye movement sleep, *SWS* slow wave sleep, *PSG* polysomnography, *RDI* respiratory distress index, *VAT* visceral adipose tissue

Table 4 Studies assessing the association between laryngologic/head and neck diseases and obesity

Authors and reference	Country	Study design	No.	Age	Laryngologic/ head and neck disease	Anthropometric measurement for obesity assessment	Results	Conclusions
Rodrigues MM, et al. [61]	Brazil	Observational retrospective cross--sectional study	105 (obese: 39, non--obese: 66)	18–80 years	LPR in OSA patients	BMI	In the obese group, the mean RSI was 6.7 in patients with mild OSA and 11.53 in patients with moderate-to-severe OSA ($P < 0.05$)	LPR, OSA, and obesity are positively correlated
Halum SL, et al. [96]	USA	Retrospective study	285	Adults	LPR	BMI	Abnormal pharyngeal reflux did not correlate with increasing BMI; however, abnormal esophageal reflux events correlated with increasing BMI ($P = 0.002$). The mean number of pharyngeal reflux events was not elevated in obese patients, whereas the mean number of esophageal reflux events was significantly elevated in obese patients ($P = 0.02$) when compared with non-obese patients	Pharyngeal reflux is not associated with increasing BMI or obesity in LPR patients
Etemadi A, et al. [97]	USA	Prospective cohort study	218,854	50–71 years	HNC	BMI, WHR	There was an inverse association between HNC and BMI, which was almost exclusively among current smokers (HR = 0.76 per 5-unit increase; 95% CI 0.63 to 0.93). In addition, direct association with WHR (HR = 1.16 per 0.1-unit increase; 95% CI 1.03 to 1.31), particularly for cancers of the oral cavity (HR = 1.40; 95% CI 1.17 to 1.67)	The risk of HNC was inversely associated with leanness in current smokers, and directly with abdominal obesity
Maasland DH, et al. [98]	Netherlands	Case-cohort study	120,852	55–69 years	HNC	BMI	BMI at baseline was inversely associated with risk of HNC overall, with a multivariate rate ratio of 3.31 (95% CI 1.40 to 7.82). The association between BMI at age 20 and HNC risk appeared to be positive	BMI at baseline was inversely associated with HNC risk. For BMI at age 20, a positive rather than inverse association was shown
Gaudet MM, et al. [99]	INHANCE	Large pooled analysis of 17 case-control studies	12,716 cases and 17,438 controls	12–94 years	HNC	BMI	Adjusted ORs (95% CIs) were elevated for people with BMI at reference ≤ 18.5 kg/m^2 (2.13, 1.75 to 2.58) and reduced for BMI > 25.0–30.0 kg/m^2 (0.52, 0.44 to 0.60) and BMI ≥ 30 kg/m^2 (0.43, 0.33 to 0.57), compared to those with normal weight	Leanness was associated with increased HNC risk regardless of smoking and drinking status, although reverse causality cannot be excluded. The reduced risk among overweight or obese people may indicate body size is a modifier of the risk associated with smoking and drinking

Table 4 (continued)

Authors and reference	Country	Study design	No.	Age	Laryngologic/ head and neck disease	Anthropometric measurement for obesity assessment	Results	Conclusions
Ward HA, et al. [100•]	10 countries in Europe (Denmark, France, Germany, Greece, Italy, Norway, the Netherlands, Spain, Sweden, and the UK)	Prospective cohort study	363,094	25–70 years	HNC	BMI, WC, WHR	Among men, a BMI < 22.5 kg/m2 was associated with higher HNC risk (HR 1.62, 95% CI 1.23 to 2.12). WC and WHR were associated with greater risk of HNC among women, (WC per 5 cm: HR 1.08, 95% CI 1.02 to 1.15; WHR per 0.1 unit: HR 1.64, 95% CI 1.38 to 1.93). Among men, WC and WHR were associated with HNC only upon additional adjustment for BMI (WC per 5 cm: HR 1.16, 95% CI 1.07 to 1.26; WHR per 0.1 unit: HR 1.42, 95% CI 1.21 to 1.65)	Central adiposity, particularly among women, may have a stronger association with HNC risk

LPR laryngopharyngeal reflux, *BMI* body mass index, *OSA* obstructive sleep apnea, *HNC* head and neck cancer, *WHR* waist-to-hip ratio, *CI* confidence interval, *INHANCE* International Head and Neck Cancer Epidemiology, *HR* hazard ratio

in weight in the year prior to OSA diagnosis [89, 90]. It is estimated that 58% of moderate-to-severe OSA is due to obesity [38, 39]. In severe obesity (BMI ≥ 40 kg/m^2), the prevalence of sleep apnea is estimated to vary between 40 and 90% [39]. In addition, the severity of sleep apnea was greater than that found in leaner clinical populations [34, 38]. These results are similar for both adults and children [30–33]. In conclusion, the effects of obesity on sleep apnea susceptibility are related to the distribution of adiposity between central and peripheral compartments. Central obesity accounts for the strong male predominance of this disorder, whereas peripheral adiposity may protect women from developing sleep apnea [32, 37, 38, 43]. Obesity and particularly central adiposity can increase sleep apnea susceptibility by increasing upper airway mechanical loads and/or decreasing compensatory neuromuscular responses [91–93]. These effects may be mediated by circulating adipokines, which influence body fat distribution and CNS activity [92]. Based on the results of various studies related to weight loss, it is suggested that as patients with sleep apnea lose weight, improvements in upper airway function and disease severity are likely related to the amount and patterns of weight loss [38–44].

Association Between Obesity and Laryngologic Disease or Head and Neck Tumors

Laryngopharyngeal Reflux Disease

LPR is defined as the retrograde flow of stomach contents to the larynx and pharynx whereupon this material comes into contact with the upper aerodigestive tract. Stomach content reflux outside of the esophagus and into respiratory organs most commonly manifests as laryngeal symptoms such as coughing, hoarseness, dysphagia, globus, and sore throat, but there can be signs of nose, sinus, and lung infections [94]. Unlike the esophageal mucosa, the laryngeal and pharyngeal mucosa have no such protective mechanism, and acid nutrient activity causes mucosal lesions. Therefore, laryngeal symptoms are the most complex, and most LPR patients are treated by an otolaryngologist. Epidemiological studies have indicated that the prevalence of this syndrome is extremely high; it has characteristics of an outbreak and is one of the most common causes of patient visits to doctors [94, 95]. LPR requires a multifaceted treatment approach as it can be accompanied by complications such as reflux laryngitis, stenotic stenosis, laryngeal cancer, granuloma, contact ulcer, and vocal cord paralysis. Among them, obesity is known to increase intra-abdominal pressure and directly increase stomach acid reflux [94, 95]. However, there are no definitive reports on the relationship between obesity and LPR alone. According to an observational retrospective cross-sectional

study in 105 adults, OSA, LPR, and obesity reciprocally affected each other's symptoms. In particular, the severity of LPR increased with the severity of OSA in the obese group (Table 4) [62••]. One limitation of this study was that it did not assess the relationship between LPR and obesity alone. As previously mentioned, the relevance of OSA to obesity is well established, and it is likely that OSA served as a confounding factor in the analysis of the relationship between LPR and obesity. In contrast, a retrospective study of 285 adults reported that pharyngeal reflux in LPR patients was not associated with increased BMI or obesity. That is, abnormal pharyngeal reflux did not correlate with increased BMI; however, abnormal esophageal reflux events correlated with increased BMI ($P = 0.002$). The mean number of pharyngeal reflux events was not elevated in obese patients, whereas the mean number of esophageal reflux events was significantly elevated in obese patients ($P = 0.02$) [96]. These results provide evidence that obesity may have different mechanisms in LPR and GERD. Nonetheless, weight loss and low-fat/carbohydrate diets are recommended in LPR treatment guidelines [94, 95].

Head and Neck Cancers

Cancers of the oral cavity, pharynx, and larynx (known collectively as head and neck cancers, or HNC) are the sixth most common form of cancer worldwide [97, 98]. Table 4 summarizes a representative cohort study of HNC and obesity. According to another prospective cohort study, 218,854 participants aged 50 to 71 were cancer-free at baseline (1995 and 1996) and had valid anthropometric data. In this study, 779 incident HNCs occurred. There was an inverse association between HNC and BMI, which was almost exclusively among current smokers, and diminished as initial years of follow-up were excluded. The authors reported a direct association with waist-to-hip ratio (WHR). Further, height was directly associated with total HNC ($P = 0.020$). It was concluded that the risk of HNC was inversely associated with leanness among current smokers and directly associated with abdominal obesity and height [97]. A large cohort study in Netherlands investigated the association between BMI, BMI at age 20 years, and changes in BMI during adulthood with risk of HNC. A total of 120,852 participants completed a questionnaire on diet and other cancer risk factors, including anthropometric measurements, at baseline in 1986. After 20.3 years of follow-up, 411 HNC cases and 3980 subcohort members were available for case-cohort analysis using Cox proportional hazards models. BMI at baseline was inversely associated with overall risk of HNC, with a multivariate rate ratio of 3.31 for subjects with a BMI < 18.5 kg/m^2 when compared to participants with a BMI of 18.5 to 25 kg/m^2. The association between BMI at age 20 and HNC risk was positive. The authors concluded that BMI at baseline was inversely associated with HNC risk. However, a positive association between BMI at age 20 and HNC risk was observed. Based on these results, low BMI seems to be associated with risk of HNC [98]. In addition, a large pooled analysis of 17 case-control studies with 12,716 cases and 17,438 controls showed that leanness (BMI < 18.5 kg/m^2) was associated with increased HNC risk, regardless of smoking and drinking status [99]. The inverse association between BMI and HNC may be due to the excessively low absolute muscle mass in lean patients that is unable to withstand the abnormal physiology of cancer cells in the body [97–99]. In a more recent multicenter prospective cohort study, among 363,094 participants with measured anthropometry, 837 incident cases of HNC were observed. Among men but not women, a BMI < 22.5 kg/m^2 was associated with higher HNC risk. WC and WHR were associated with greater risk of HNC among women. After stratification by smoking status, an association for WHR was observed only among smokers ($P = 0.004$). Among men, WC and WHR were associated with HNC only upon additional adjustment for BMI. The authors concluded that central adiposity but not BMI, particularly among women, may have a stronger association with HNC risk than previously estimated [100•]. Therefore, it may be important to establish standard anthropometry for defining obesity in HNC patients as appropriate.

Conclusion

We have summarized the current knowledge on the association between obesity and otorhinolaryngologic diseases. Various otorhinolaryngological disorders, especially OM, HL, CRS, and OSA, showed a clear association with obesity. Although there were differences according to disease type, obesity has been reported to be a risk factor for these diseases. The severity of obesity was found to increase with severity of each disease. However, the incidence of HNC was inversely associated with obesity, especially central adiposity. The relevance of obesity in LPR and AR has not yet been clarified, and controversy remains. Therefore, if a patient with a target disease (such as OM, HL, CRS, or OSA) is obese, it may be necessary to diagnose and treat the target diseases more aggressively.

Funding Information This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (NRF 2017R1D1A1B3030021) (NRF-2018R1A6A1A03025124).

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Ryan DH, Kahan S. Guideline recommendations for obesity management. Med Clin North Am. 2018;102(1):49–63.
2. Tsai AG, Williamson DF, Glick HA. Direct medical cost of overweight and obesity in the USA: a quantitative systematic review. Obes Rev. 2010;12(1):50–61.
3. Sturm R, Ringel JS, Andreyeva T. Increasing obesity rates and disability trends. Health Aff (Millwood). 2004;23(2):199–205.
4. Greenberg AS, Obin MS. Obesity and the role of adipose tissue in inflammation and metabolism. Am J Clin Nutr. 2006;83(2):461S–5S.
5. Monteiro R, Azevedo I. Chronic inflammation in obesity and the metabolic syndrome. Mediators Inflamm. 2010;2010:289645.
6. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. Annu Rev. Immunol. 2011;29:415–45.
7. Harper JW, Zisman TL. Interaction of obesity and inflammatory bowel disease. World J Gastroenterol. 2016;22(35):7868–81.
8. Gupta S, Lodha R, Kabra SK. Asthma, GERD and obesity: triangle of inflammation. Indian J Pediatr. 2018;85(10):887–92.
9. Lee S, Lane A. Chronic rhinosinusitis as a multifactorial inflammatory disorder. Curr Infect Dis Rep. 2011;13(2):159–68.
10. Bassiouni A, Naidoo Y, Wormald PJ. When FESS fails: the inflammatory load hypothesis in refractory chronic rhinosinusitis. Laryngoscope. 2012;122(2):460–6.
11. Krouse JH, Brown RW, Fineman SM, Han JK, Heller AJ, Joe S, et al. Asthma and the unified airway. Otolaryngol Head Neck Surg. 2007;136(5S):S75–106.
12. Liu W, Zeng Q, Chen Y, Luo RZ. Role of leptin/osteopontin axis in the function of eosinophils in allergic rhinitis with obesity. Mediators Inflamm. 2018;24(2018):9138904. https://doi.org/10.1155/2018/9138904.
13. Zeng Q, Luo X, Han M, Liu W, Li H. Leptin/osteopontin axis regulated type 2T helper cell response in allergic rhinitis with obesity. EBioMedicine. 2018;32:43–9. https://doi.org/10.1016/j.ebiom.2018.05.037.
14. Liu W, Zeng Q, Zhou L, Luo R, Dong H. Association of leptin with disease severity and inflammation indicators in Chinese obese children with allergic rhinitis. Pediatr Allergy Immunol. 2018;29(2):186–93.
15. Lim MS, Lee CH, Sim S, Hong SK, Choi HG. Physical activity, sedentary habits, sleep, and obesity are associated with asthma, allergic rhinitis, and atopic dermatitis in Korean adolescents. Yonsei Med J. 2017;58(5):1040–6.
16. Lei Y, Yang H, Zhen L. Obesity is a risk factor for allergic rhinitis in children of Wuhan (China). Asia Pac Allergy. 2016;6(2):101–4.
17. Park DY, Kim YS, Kim JH, Kang JW. Association of body mass index and other factors with histamine skin reactivity in adults with allergic nasal symptoms. Am J Rhinol Allergy. 2015;29(6):e160–3.
18. Kim TH, Kang HM, Oh IH, Yeo SG. Relationship between otorhinolaryngologic diseases and obesity. Clin Exp Otorhinolaryngol. 2015;8(3):194–7.
19. Bhattacharyya N. Associations between obesity and inflammatory sinonasal disorders. Laryngoscope. 2013;123(8):1840–4.
20. Huang SL, Shiao G, Chou P. Association between body mass index and allergy in teenage girls in Taiwan. Clin Exp Allergy. 1999;29(3):323–9.
21. Saadeh D, Salameh P, Caillaud D, Charpin D, de Blay F, Kopferschmitt C, et al. High body mass index and allergies in schoolchildren: the French six cities study. BMJ Open Respir Res. 2014;24(1):e000054. https://doi.org/10.1136/bmjresp-2014-000054.
22. Chung SD, Chen PY, Lin HC, Hung SH. Comorbidity profile of chronic rhinosinusitis: a population-based study. Laryngoscope. 2014;124(7):1536–41.
23. Matsumoto M, Konno S, Kimura H, Takei N, Kimura H, Shimizu K, et al. Associations of current wheeze and body mass index with perennial and seasonal allergic rhinitis in young adults. Int Arch Allergy Immunol. 2018;176(2):143–9.
24. Han YY, Forno E, Gogna M, Celedón JC. Obesity and rhinitis in a nationwide study of children and adults in the United States. J Allergy Clin Immunol. 2016;137(5):1460–5.
25. Kanagalingam S, Shehab SS, Kaminsky DA, Wise RA, Lang JE, Dixon AE. Effect of obesity on sinonasal disease in asthma. J Asthma. 2018;55(5):525–31.
26. Sybilski AJ, Raciborski F, Lipiec A, Tomaszewska A, Lusawa A, Furmańczyk K, et al. Obesity—a risk factor for asthma, but not for atopic dermatitis, allergic rhinitis and sensitization. Public Health Nutr. 2015;18(3):530–6.
27. Sidell D, Shapiro NL, Bhattacharyya N. Obesity and the risk of chronic rhinosinusitis, allergic rhinitis, and acute otitis media in school-age children. Laryngoscope. 2013;123(10):2360–3.
28. Konno S, Hizawa N, Fukutomi Y, Taniguchi M, Kawagishi Y, Okada C, et al. The prevalence of rhinitis and its association with smoking and obesity in a nationwide survey of Japanese adults. Allergy. 2012;67(5):653–60.
29. Kusunoki T, Morimoto T, Nishikomori R, Heike T, Ito M, Hosoi S, et al. Obesity and the prevalence of allergic diseases in schoolchildren. Pediatr Allergy Immunol. 2008;19(6):527–34.
30. Andersen IG, Holm JC, Homøe P. Obstructive sleep apnea in children and adolescents with and without obesity. Eur Arch Otorhinolaryngol. 2019;276(3):871–8.
31. Evangelisti M, Shafiek H, Rabasco J, Forlani M, Montesano M, Barreto M, et al. Oximetry in obese children with sleep-disordered breathing. Sleep Med. 2016;27–28:86–91.
32. Mathew R, Castriotta RJ. High hypopnea/apnea ratio (HAR) in extreme obesity. J Clin Sleep Med. 2014;10(4):391–6.
33. Kim H, Kim MS, Lee JE, Kim JW, Lee CH, Yoon IY, et al. Treatment outcomes and compliance according to obesity in patients with obstructive sleep apnea. Eur Arch Otorhinolaryngol. 2013;270(11):2885–90.
34. Arnardottir ES, Maislin G, Jackson N, Schwab RJ, Benediktsdottir B, Teff K, et al. The role of obesity, different fat compartments and sleep apnea severity in circulating leptin levels: the Icelandic Sleep Apnea Cohort study. Int J Obes (Lond). 2013;37(6):835–42.
35. Antczak J, Horn B, Richter A, Jernajczyk W, Bodenschatz R, W Schmidt EW. The influence of obesity on sleep quality in male sleep apnea patients before and during therapy. J Physiol Pharmacol. 2008;59(Suppl 6):123–34.
36. Daltro C, Gregorio PB, Alves E, Abreu M, Bomfim D, Chicourel MH, et al. Prevalence and severity of sleep apnea in a group of morbidly obese patients. Obes Surg. 2007;17(6):809–14.
37. Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children. Associations with obesity, race, and respiratory problems. Am J Respir Crit Care Med. 1999;159(5 Pt 1):1527–32.
38. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. Arch Intern Med. 2005;165(20):2408–13.

39. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA. 2000;284(23):3015–21.
40. Punjabi NM, Sorkin JD, Katzel LI, Goldberg AP, Schwartz AR, Smith PL. Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. Am J Respir Crit Care Med. 2002;165(5):677–82.
41. Richman RM, Elliott LM, Burns CM, Bearpark HM, Steinbeck KS, Caterson ID. The prevalence of obstructive sleep apnoea in an obese female population. Int J Obes Relat Metab Disord. 1994;18(3):173–7.
42. Vgontzas AN, Tan TL, Bixler EO, Martin LF, Shubert D, Kales A. Sleep apnea and sleep disruption in obese patients. Arch Intern Med. 1994;154(15):1705–11.
43. Shinohara E, Kihara S, Yamashita S, Yamane M, Nishida M, Arai T, et al. Visceral fat accumulation as an important risk factor for obstructive sleep apnoea syndrome in obese subjects. J Intern Med. 1997;241(1):11–8.
44. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, et al. Sleep Heart Health Study Research Group. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med. 2002;162(8):893–900.
45. Kaya S, Selimoğlu E, Cureoğlu S, Selimoğlu MA. Relationship between chronic otitis media with effusion and overweight or obesity in children. J Laryngol Otol. 2017;131(10):866–70.
46. Choi HG, Sim S, Kim SY, Lee HJ. A high-fat diet is associated with otitis media with effusion. Int J Pediatr Otorhinolaryngol. 2015;79(12):2327–31.
47. Kuhle S, Kirk SF, Ohinmaa A, Urschitz MS, Veugelers PJ. The association between childhood overweight and obesity and otitis media. Pediatr Obes. 2012;7(2):151–7.
48. Shin IH, Park DC, Kwon C, Yeo SG. Changes in taste function related to obesity and chronic otitis media with effusion. Arch Otolaryngol Head Neck Surg. 2011;137(3):242–6.
49. Nelson HM, Daly KA, Davey CS, Himes JH, Synder DJ, Bartoshuk LM. Otitis media and associations with overweight status in toddlers. Physiol Behav. 2011;102(5):511–7.
50. Seaberg RM, Chadha NK, Hubbard BJ, Gordon KA, Allemang BA, Harrison BJ, et al. Chorda tympani nerve function in children: relationship to otitis media and body mass index. Int J Pediatr Otorhinolaryngol. 2010;74(12):1393–6.
51. Kim SH, Park DC, Byun JY, Park MS, Cha CI, Yeo SG. The relationship between overweight and otitis media with effusion in children. Int J Obes (Lond). 2011;35(2):279–82.
52. Kim JB, Park DC, Cha CI, Yeo SG. Relationship between pediatric obesity and otitis media with effusion. Arch Otolaryngol Head Neck Surg. 2007;133(4):379–82.
53. Scinicariello F, Carroll Y, Eichwald J, Decker J, Breysse PN. Association of obesity with hearing impairment in adolescents. Sci Rep. 2019;9(1):1877. https://doi.org/10.1038/s41598-018-37739-5.
54. Hwang JH, Wu CC, Hsu CJ, Liu TC, Yang WS. Association of central obesity with the severity and audiometric configurations of age-related hearing impairment. Obesity (Silver Spring). 2009;17(9):1796–801.
55. Lee JS, Kim DH, Lee HJ, Kim HJ, Koo JW, Choi HG, et al. Lipid profiles and obesity as potential risk factors of sudden sensorineural hearing loss. PLoS One. 2015;10(4):e0122496. https://doi.org/10.1371/journal.pone.0122496.
56. Hwang JH. Role of obesity on the prognosis of sudden sensorineural hearing loss in adults. Otolaryngol Head Neck Surg. 2015;153(2):251–6.
57. Lalwani AK, Katz K, Liu YH, Kim S, Weitzman M. Obesity is associated with sensorineural hearing loss in adolescents. Laryngoscope. 2013;123:3178–84.
58. Curhan SG, Eavey R, Wang M, Stampfer MJ, Curhan GC. Body mass index, waist circumference, physical activity, and risk of hearing loss in women. Am J Med. 2013;126(12):1142.e1–8.
59. Kim TS, Park SW, Kim do Y, Kim EB, Chung JW, So HS. Visceral adipose tissue is significantly associated with hearing thresholds in adult women. Clin Endocrinol (Oxf). 2014;80(3):368–75.
60. Barrenas ML, Jonsson B, Tuvemo T, Hellstrom PA, Lundgren M. High risk of sensorineural hearing loss in men born small for gestational age with and without obesity or height catch-up growth: a prospective longitudinal register study on birth size in 245 000 Swedish conscripts. J Clin Endocrinol Metab. 2005;90(8):4452–6.
61. Rodrigues MM, Dibbern RS, Santos VJ, Passeri LA. Influence of obesity on the correlation between laryngopharyngeal reflux and obstructive sleep apnea. Braz J Otorhinolaryngol. 2014;80(1):5–10.
62.•• The GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, et al. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med. 2017;377(1):13–27. **Showed on the impact of obesity on the health of humankind in the last 25 years. The prevalence of obesity has been steadily increasing, and the mortality rate associated with this disease has also increased**.
63. Heymsfield SB, Wadden TA. Mechanisms, pathophysiology, and management of obesity. N Engl J Med. 2017;376(15):1492.
64. Heymsfield SB, Gonzalez MC, Shen W, Redman L, Thomas D. Weight loss composition is one-fourth fat-free mass: a critical review and critique of this widely cited rule. Obes Rev. 2014;15(4):310–21.
65. Hall JE, da Silva AA, do Carmo JM, Dubinion J, Hamza S, Munusamy S, et al. Obesity-induced hypertension: role of sympathetic nervous system, leptin, and melanocortins. J Biol Chem. 2010;285(23):17271–6.
66. Ferrannini E, Camastra S, Gastaldelli A, Maria Sironi A, Natali A, Muscelli E, et al. Beta-cell function in obesity: effects of weight loss. Diabetes. 2004;53(Suppl 3):S26–33.
67. Grant RW, Dixit VD. Adipose tissue as an immunological organ. Obesity (Silver Spring). 2015;23(3):512–8.
68. Shen W, Wang Z, Punyanita M, Lei J, Sinav A, Kral JG, et al. Adipose tissue quantification by imaging methods: a proposed classification. Obes Res. 2003;11(1):5–16.
69. Tchkonia T, Thomou T, Zhu Y, Karagiannides I, Pothoulakis C, Jensen MD, et al. Mechanisms and metabolic implications of regional differences among fat depots. Cell Metab. 2013;17(5):644–56.
70. Ashrafian H, Toma T, Rowland SP, Harling L, Tan A, Efthimiou E, et al. Bariatric surgery or non-surgical weight loss for obstructive sleep apnoea? A systematic review and comparison of meta-analyses. Obes Surg. 2015 Jul;25(7):1239–50.
71. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. Ann Intern Med. 2005;143(3):199–211.
72. Klein JO. The burden of otitis media. Vaccine. 2000;19(Suppl 1):S2–8.
73. Coker TR, Chan LS, Newberry SJ, Limbos MA, Suttorp MJ, Shekelle PG, et al. Diagnosis, microbial epidemiology, and antibiotic treatment of acute otitis media in children: a systematic review. JAMA. 2010;304(19):2161–9.
74. Teele DW, Klein JO, Rosner B. Epidemiology of otitis media during the first seven years of life in children in greater Boston: a prospective cohort study. J Infect Dis. 1989;160(1):83–94.
75. Ahmed S, Arjmand E, Sidell D. Role of obesity in otitis media in children. Curr Allergy Asthma Rep. 2014;14(11):469.
76. Lee SK, Yeo SG. Relationship between pediatric obesity and otitis media with effusion. Curr Allergy Asthma Rep. 2009;9(6):465–72.

77. Peracchio HL, Henebery KE, Sharafi M, Hayes JE, Duffy VB. Otitis media exposure associates with dietary preference and adiposity: a community-based observational study of at-risk preschoolers. Physiol Behav. 2012;106(2):264–71.
78. Griffith IP. Observations on the pathology of chorda tympani nerve in temporal bone sections. J Laryngol Otol. 1977;91(2):151–7.
79. Nash SD, Cruickshanks KJ, Klein R, Klein BE, Nieto FJ, Huang GH, et al. The prevalence of hearing impairment and associated risk factors: the Beaver Dam Offspring Study. Arch Otolaryngol Head Neck Surg. 2011;137(5):432–9.
80. Owens E, Talbott CB, Schubert ED. Vowel discrimination of hearing-impaired listeners. J Speech Hear Res. 1968;11(3):648–55.
81.• Dhanda N, Taheri S. A narrative review of obesity and hearing loss. Int J Obes (Lond). 2017;41(7):1066–73. **Study showing that obesity can increase the incidence of some kind of hearing loss in general population**.
82. Jung SY, Shim HS, Hah YM, Kim SH, Yeo SG. Association of metabolic syndrome with sudden sensorineural hearing loss. JAMA Otolaryngol Head Neck Surg. 2018;144(4):308–14.
83. Stachler RJ, Chandrasekhar SS, Archer SM, Rosenfeld RM, Schwartz SR, Barrs DM, et al. American Academy of Otolaryngology-Head and Neck Surgery. Clinical practice guideline: sudden hearing loss. Otolaryngol Head Neck Surg. 2012;146(3 Suppl):S1–35.
84. Boulet LP. Obesity and atopy. Clin Exp Allergy. 2015;45(1):75–86.
85. Medoff BD, Okamoto Y, Leyton P, Weng M, Sandall BP, Raher MJ, et al. Adiponectin deficiency increases allergic airway inflammation and pulmonary vascular remodeling. Am J Respir Cell Mol Biol. 2009;41(4):397–406.
86. Bouloumie A, Marumo T, Lafontan M, Busse R. Leptin induces oxidative stress in human endothelial cells. FASEB J. 1999;13(10):1231–8.
87. Strachan D, Sibbald B, Weiland S, Aït-Khaled N, Anabwani G, Anderson HR, et al. Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). Pediatr Allergy Immunol. 1997;8(4):161–76.
88. Ulrik CS. Asthma and obesity: is weight reduction the key to achieve asthma control? Curr Opin Pulm Med. 2016;22(1):69–73.
89. Gharibeh T, Mehra R. Obstructive sleep apnea syndrome: natural history, diagnosis, and emerging treatment options. Nat Sci Sleep. 2010;2:233–55.
90. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep disordered breathing in adults. Am J Epidemiol. 2013;177(9):1006–14.
91. Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):242–52.
92. Lam JC, Mak JC, Ip MS. Obesity, obstructive sleep apnoea and metabolic syndrome. Respirology. 2012;17(2):223–36.
93. Xu S, Wan Y, Xu M, Ming J, Xing Y, An F, et al. The association between obstructive sleep apnea and metabolic syndrome: a systematic review and meta-analysis. BMC Pulm Med. 2015;15:105. https://doi.org/10.1186/s12890-015-0102-3.
94. Campagnolo AM, Priston J, Thoen RH, Medeiros T, Assunção AR. Laryngopharyngeal reflux: diagnosis, treatment and latest research. Int Arch Otorhinolaryngol. 2014;18(2):184–91.
95. Sidhwa F, Moore A, Alligood E, Fisichella PM. Diagnosis and treatment of the extraesophageal manifestations of gastroesophageal reflux disease. Ann Surg. 2017;265(1):63–7.
96. Halum SL, Postma GN, Johnston C, Belafsky PC, Koufman JA. Patients with isolated laryngopharyngeal reflux are not obese. Laryngoscope. 2005;115(6):1042–5.
97. Etemadi A, O'Doherty MG, Freedman ND, Hollenbeck AR, Dawsey SM, Abnet CC. A prospective cohort study of body size and risk of head and neck cancers in the NIH-AARP diet and health study. Cancer Epidemiol Biomarkers Prev. 2014;23(11):2422–9.
98. Maasland DH, van den Brandt PA, Kremer B, Schouten LJ. Body mass index and risk of subtypes of head-neck cancer: the Netherlands Cohort Study. Sci Rep. 2015;5:17744. https://doi.org/10.1038/srep17744.
99. Gaudet MM, Olshan AF, Chuang SC, Berthiller J, Zhang ZF, Lissowska J, et al. Body mass index and risk of head and neck cancer in a pooled analysis of case-control studies in the International Head and Neck Cancer Epidemiology (INHANCE) Consortium. Int J Epidemiol. 2010;39(4):1091–102.
100.• Ward, HA WPA, Muller DC, Steffen A, Johansson M, Norat T, et al. Measured adiposity in relation to head and neck cancer risk in the European Prospective Investigation into Cancer and Nutrition. Cancer Epidemiol Biomarkers Prev. 2017;26(6):895–904. **Study showing thatstrategies to reduce obesity may beneficially impact head and neck cancer incidence**.