International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

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ARTICLE TITLE	OBESITY AS A MODIFIABLE DETERMINANT OF THYROID DYSFUNCTION, STRUCTURAL CHANGES, AND THYROID CANCER
DOI	https://doi.org/10.31435/ijitss.4(48).2025.4647
RECEIVED	27 November 2025
ACCEPTED	27 December 2025
PUBLISHED	30 December 2025
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OBESITY AS A MODIFIABLE DETERMINANT OF THYROID DYSFUNCTION, STRUCTURAL CHANGES, AND THYROID CANCER

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ABSTRACT

Introduction: Obesity has become a global health problem with rapidly increasing prevalence across all age groups. Accumulating evidence suggests that excess adiposity affects thyroid function and morphology and may contribute to the rising incidence of thyroid cancer. This review summarizes current knowledge on the interplay between obesity, thyroid physiology, thyroid structural alterations, and thyroid cancer risk.
Methods: A comprehensive literature search was conducted using PubMed and Google Scholar, focusing on systematic reviews and meta-analyses. Keywords such as "obesity", "body mass index", "thyroid nodules", "thyroid cancer", "bariatric surgery", and "GLP-1 RA" guided the search. Selected studies were qualitatively analyzed.
Results: Obesity was strongly associated with elevated TSH, thyroid hypertrophy, increased thyroid volume, and higher prevalence of nodules, often with more suspicious cytology. Meta-analyses showed that each 5-unit increase in BMI corresponds to an increase up to a 30% in thyroid cancer risk, particularly for papillary, follicular, and anaplastic subtypes. Mechanisms include hyperleptinemia, chronic inflammation, insulin resistance, altered estrogen signaling, and oxidative stress. Weight-loss interventions, including bariatric surgery and GLP-1 receptor agonists, were associated with the improvements of thyroid function and morphology.
Conclusions: Obesity is a significant and modifiable determinant of thyroid dysfunction and thyroid cancer. Effective weight management may reverse obesity-related thyroid alterations and should be integrated into clinical care and preventive strategies.

KEYWORDS

Obesity, Body Mass Index, Thyroid Nodules, Thyroid Cancer, Bariatric Surgery, GLP-1 RA

CITATION

Klaudia Baran, Aleksandra Grygorowicz, Michał Ględa, Michał Szyszka, Weronika Radecka, Weronika Kozak, Agnieszka Szreiber, Karol Grela, Karolina Nowacka, Kamil Jabłoński, Anna Woźniak. (2025). Obesity as a Modifiable Determinant of Thyroid Dysfunction, Structural Changes, and Thyroid Cancer. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4647

Introduction

The prevalence of obesity has increased significantly in recent decades in both adult and pediatric populations (Blüher, 2019; Tung et al, 2023). Some studies indicate that obesity has become a global epidemic and is a major worldwide health problem (Blüher, 2019; Lin & Li, 2021; Mahmoud, 2022). The etiopathogenesis of obesity is a complex issue comprising genetic, socioeconomic and cultural influences. Nevertheless, modification of lifestyle habits, patterns of consumption and urban development have become key factors that meaningfully contribute to its progressive prevalence (Mahmoud, 2022). Obesity should be treated as a chronic multisystem disease associated with a decreased quality of life and increased mortality (Lin, & Li, 2021; Sarma, Sockalingam, & Dash, 2021). It is not only the risk factor for noncommunicable diseases such as coronary artery disease, hypertension, chronic kidney disease, hyperlipidemia, type 2 diabetes mellitus or musculoskeletal disorders, but also a condition associated with a higher risk of malignancy, including thyroid cancer (TC) (Lin & Li, 2021; Pati et al, 2023).

The objective of this review is to provide readers with updated information on obesity and its impact on thyroid function and morphology among adult patients, to present the relationship between obesity and TC development and to summarize recent evidence on obesity treatment, both surgical and non-surgical, and its impact on thyroid function.

Methodology

This review aims to provide the latest scientific findings regarding obesity and thyroid morphology and function. A literature search was conducted using PubMed and Google Scholar. Most evidence is derived from meta-analyses and systematic reviews. Specific keywords such as "obesity", "body mass index", "thyroid nodules", "thyroid cancer", "bariatric surgery", "GLP-1 RA" were used in the search strategy. Thoroughly selected studies were examined and qualitatively analyzed.

Obesity - Definition And Epidemiology

Definition

According to the World Health Organization (WHO) guidelines, the diagnosis of obesity in adults is based on the Body Mass Index (BMI) (WHO, 2000). BMI is calculated as the weight in kilograms divided by the square of the height in metres (kg/m2). Overweight is characterised as a BMI in the range 25.00–29.99 and obesity as a BMI greater than or equal to 30.00. Then it is further classified into three severity levels: class I (BMI 30.00–34.99), class II (BMI 35.00–39.99) and class III (BMI ≥ 40.00) (WHO, 2000; Lin, & Li, 2021). The International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) extends the WHO classification by subdividing obesity into five classes: classes I–III correspond to those defined by the WHO, class IV (formerly termed "super obesity") includes individuals with a BMI of 50.0–59.99 kg/m², and class V (previously "super–super obesity") includes individuals with a BMI ≥ 60.0 kg/m² (Salminen et al, 2024). The classifications are presented in Table 1.

Table 1. Classifications of body weight in adults based on Body Mass Index (BMI).

Classification	WHO	IFSO
Underweight	<18.50	<18.50
Normal range	18.50 – 24.99	18.50 – 24.99
Overweight	25.00-29.99	25.00 – 29.99
Obesity	≥30.00	≥ 30.00
Class I	30.00-34.99	30.00 – 34.99
Class II	35.00-39.99	35.00 – 39.99
Class III	≥40.00	40.00 – 49.99
Class IV	–	50.00 – 59.99
Class V	–	≥ 60.00

BMI is considered as a sufficiently reliable diagnostic measurement for population-level assessments and many individual patients. Nevertheless, some studies suggest that accurate diagnosis of obesity in an individual may require other anthropometric assessments beyond body weight alone (e.g., waist circumference, percent body fat, and android/visceral fat) (Fitch & Bays, 2022). Quoted limitations of using BMI as the only indicator of adiposity include its imperfect correlation with individual body composition, failure to account for variations in muscle mass, misclassification of obesity in muscular individuals and underestimation of adiposity among patients with sarcopenia (Fitch & Bays, 2022). However BMI is indicated as a reasonable and simple initial screening tool for a majority of patients (Fitch & Bays, 2022).

Epidemiology

Obesity is currently perceived as a global pandemic (Blüher, 2019). In 2022 over 890 million adults were obese what corresponds to about 16% of adults aged 18 years and older worldwide who were diagnosed with obesity in 2022 (WHO, 2025). According to the report of the WHO the worldwide prevalence of obesity has nearly tripled over the past five decades and it is estimated that by 2030 over one billion adults globally will be obese (WHO, 2023). Due to its well-documented and indisputable negative impact on human health, at the 75th World Health Assembly in 2022, Member States prepared and adopted new recommendations for the prevention and management of obesity (WHO, 2023). Stopping the increasing obesity prevalence is one of the Global Targets for Noncommunicable Diseases (WHO, 2023).

The Relationship Between Obesity and Thyroid Function and Morphology

Leptin and TSH correlation

Obesity is a multisystem disease that affects the function of many organs in the human body, including the thyroid. Thyroid-stimulating hormone (TSH) levels are positively correlated with the amount of adipose tissue (Biondi, 2024; Santini et al, 2014). Leptin, adipocytokine produced by adipose tissue, participates in the expression of the thyrotropin-releasing hormone (TRH) in the paraventricular nucleus (PVN) and arcuate nucleus (ARC), and regulates the hypothalamus–pituitary–thyroid axis (Biondi, 2024). As a result of hyperleptinemia caused by excess adiposity, the hypothalamus–pituitary–thyroid axis activates resulting in elevated TSH plasma concentration (Santini et al, 2014). An observational study assessing weight change during 11-year follow-up among 4,649 individuals without previous thyroid disease treatment indicated that 0.6 kg weight gain in women (95% CI = 0.4–0.9, $p < 0.01$) and a 0.7 kg weight gain in men (95% CI = 0.02–1.3, $p = 0.04$) were associated with an increase of 1 mIU/L of TSH (Bjergved et al, 2014). This association is further supported by the fact that TSH levels decrease following weight loss achieved through bariatric surgery or diets with a caloric deficit (Guan et al, 2017; Santini et al, 2014). Moreover, due to TSH receptor expression on adipocytes, elevated TSH results in stimulated leptin secretion. A complex positive-feedback interaction therefore links leptin with serum TSH. (Baranowska-Bik & Bik, 2020; Biondi, 2024).

TSH in obese patients

Thyroid stimulating hormone (TSH), a glycoprotein hormone synthesized in the pituitary gland, is a regulatory element of the hypothalamus–pituitary–thyroid axis. It is secreted by the anterior pituitary gland in both basal and pulsatile patterns. The synthesis and release of TSH are essential for thyroid hormone production and secretion and are regulated by TRH as well as by negative feedback from circulating triiodothyronine (T3) and thyroxine (T4). TSH stimulates hypertrophy and hyperplasia of thyrocytes, enhances iodine uptake and thyroglobulin production and contributes to modulation of immune response (Wu et al, 2022). However, permanently increased TSH serum level, as observed in many patients diagnosed with obesity, may lead to overstimulation, excessive hyperplasia, and the development of focal thyroid lesions, resulting in overall thyroid enlargement (Szczepanek-Parulska et al, 2016).

Hiperinsulinemia and thyroid gland

Insulin is an anabolic peptide hormone regulating glucose homeostasis. Hyperinsulinemia and the subsequent development of insulin resistance are well-documented consequences of weight gain. High energy intake promotes excessive fatty acid storage in white adipose tissue, leading to adipose tissue dysfunction, chronic inflammation, and impaired insulin sensitivity, which in turn stimulates pancreatic β-cells to increase insulin secretion, resulting in hyperinsulinemia and the progression of insulin resistance (Mastrototaro & Roden, 2021). Several reviews have shown that hyperinsulinemia exerts a growth-stimulatory effect on thyrocytes and insulin resistance is an acknowledged risk factor for the development of thyroid goiter, including nodular goiter (Chen, Xu, Renko, & Derwahl, 2012). A study conducted among 413 residents of Georgia demonstrated that the mean thyroid volume was significantly higher in patients with insulin resistance compared to controls (20.52 ± 6.39 cm³ vs. 15.25 ± 6.55 cm³, $p < 0.001$) (Lomtadze, Giorgadze, Janjgava, Kacharava, & Taboridze, 2023).

Obesity and thyroid autoimmunity

Several studies have evaluated the association between leptin levels and autoimmune thyroid disease in obese individuals (Marzullo et al, 2010; Song et al, 2019). The results suggest that thyroid peroxidase antibodies (TPOAb) are more frequently detected in obese patients, and an increased leptin concentration may be associated with Hashimoto thyroiditis, regardless of bioanthropometric parameters (Marzullo et al, 2010). A meta-analysis of 14 studies reported a causal relationship between obesity and subclinical hypothyroidism. Obese individuals exhibited an increased risk of subclinical hypothyroidism (OR = 1.70, 95% CI = 1.42–2.03; $p < 0.001$) and a significant association with Hashimoto thyroiditis (OR = 1.91, 95% CI = 1.10–3.32, $p = 0.022$), supporting the concept that adiposity constitutes a risk factor for both Hashimoto thyroiditis and subclinical hypothyroidism (Song et al, 2019). Elevated leptin levels may play a key role by modulating immune activity and inflammatory pathways, potentially contributing to increased TPOAb production (Song et al, 2019).

Thyroid nodules in obese patients

Over recent decades, the global prevalence of thyroid nodules has increased substantially (Pemayun, 2016). Although this trend is largely attributed to the widespread availability and frequent use of thyroid ultrasonography, the escalating global prevalence of obesity and accumulating evidence on the effects of adipose tissue on thyroid morphology highlight the need to further examine the role of obesity in the development of thyroid alterations. In a retrospective analysis of 310 patients, Demetriou et al (2025) evaluated the potential association between obesity and the occurrence of thyroid nodules. Overweight and obese individuals (BMI ≥ 25 kg/m²) exhibited a tendency toward a higher number of nodules compared with individuals of normal BMI (4.25 ± 2.42 vs. 3.66 ± 1.93, p = 0.05). Furthermore, patients with BMI ≥ 25kg/m² demonstrated significantly poorer fine-needle aspiration (FNA) outcomes than those with BMI < 25 kg/m² (p = 0.029), with a notable difference in the proportion of Thy4–Thy5 categories (p = 0.04). Lesion risk assessment was conducted according to the UK RCPath terminological system, as presented in Table 2.

Table 2. UK RCPath terminology system in thyroid fine-needle aspiration (Poller, Cochand-Priollet, & Trimboli, 2021)

Thy1	Non-diagnostic for cytological diagnosis
Thy1c	Non-diagnostic for cytological diagnosis—cystic lesion
Thy2	Non-neoplastic
Thy2c	Non-neoplastic—cystic lesion
Thy3a	Neoplasm possible—atypia/non-diagnostic
Thy3f	Neoplasm possible, suggesting follicular neoplasm
Thy4	Suspicious of malignancy
Thy5	Malignant

In another study, Fokou et al (2025) analyzed 294 patients diagnosed with Hashimoto toxicosis and found that individuals with BMI ≥ 25 kg/m² had a significantly higher rate of suspicious or malignant cytology (Thy4–Thy5) compared with those with BMI < 25 kg/m² (27.03% vs. 18.18%, p < 0.01). These findings collectively suggest a positive correlation between obesity and an increased risk of thyroid malignancy.

Thyroid Cancer - Epidemiology, Classification and Risk Factors

Epidemiology

TC is the most common endocrine malignancy worldwide and represents a growing public health challenge. It affects women disproportionately and is the second most frequent cancer in young adult females (Bray et al, 2018). Globally, TC ranks ninth among all malignancies, and its incidence, particularly that of papillary thyroid carcinoma, has risen markedly over recent decades (Wirth et al, 2021). Although advances in diagnostic methods, including high-resolution ultrasonography and improved cytological assessment, have contributed to the increased detection of small thyroid lesions, they do not fully explain this trend. Data from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute in the United States have shown an increased incidence of even larger, clinically apparent tumors between 1980 and 2005, which are detectable without advanced diagnostic techniques (Enewold et al, 2009). These observations suggest that additional factors may be involved in the rising incidence of TC. The available evidence indicates that TC development is likely influenced by a combination of improved detection and broader epidemiological shifts linked to environmental and metabolic factors.

Classification

TC comprises a heterogeneous group of malignancies that differ substantially in histological subtype, clinical behavior, and prognosis. Differentiated TC represent the vast majority of cases, with papillary thyroid carcinoma (PTC) being the most prevalent subtype, accounting for approximately 85–90% of all TC (Zhang & Xu, 2024). PTC typically exhibits indolent behavior and excellent long-term survival, although aggressive variants and advanced disease with lymph nodes or distant metastases may occur. Follicular thyroid carcinoma (FTC) constitutes the second most common subtype, representing 10–15% of cases, with a higher prevalence in iodine-deficient regions. Compared with PTC, FTC demonstrates a greater tendency for vascular invasion and distant metastases, particularly to the lungs and bones (Shen et al, 2024). Medullary thyroid carcinoma (MTC), arising from parafollicular C cells, accounts for approximately 3–5% of TC and may occur

sporadically or as part of hereditary syndromes, most notably multiple endocrine neoplasia type 2 (Forma et al, 2025). Anaplastic thyroid carcinoma (ATC) is the rarest subtype, accounting for about 2% of cases, yet it is responsible for a disproportionate number of TC–related deaths due to its highly aggressive nature, rapid progression, and poor response to therapy (Li, Zhang, Zhou, & Du, 2022).

Risk factors

Numerous studies are currently underway to better characterize the risk factors associated with TC. Increasing attention has been directed toward identifying environmental, metabolic, hormonal, and genetic influences that may drive carcinogenesis (Franchini et al, 2022). Understanding these factors is essential for improving risk stratification, informing preventive strategies, and elucidating the complex mechanisms underlying thyroid tumor initiation and progression. The most important risk factors include iodine deficiency and radiation exposure (Mirkatouli, Hirota, & Yoshinaga, 2023). However, additional contributors such as dietary factors, exposure to endocrine-disrupting chemicals and other xenobiotics, estrogen exposure, cigarette smoking, diabetes, obesity, metabolic syndrome, and insulin resistance have also been proposed (Derwahl & Nicula, 2014; Lee, Chai, & Yi, 2021; Dong et al, 2022; Ma, et al, 2015; Zhao et al, 2012; Rezzónico, Rezzónico, Pusiol, Pitoia, & Niepomniszcze, 2009). These conditions may disrupt the organism's epigenetic status and influence health by altering gene expression patterns (Nettore et al, 2019). Many of these factors are strongly linked to increased body weight, suggesting that excess adiposity may play an important role in TC development.

Molecular Links Between Obesity and Thyroid Cancer

In recent decades, the global rise in obesity has renewed scientific interest in understanding its impact on the incidence and progression of various malignancies, including TC. Although a single unifying mechanism has not been identified, the currently available studies strongly suggest that obesity induces a constellation of endocrine, metabolic, inflammatory, and molecular alterations that not only contribute to the development of focal lesions and hypothyroidism, as mentioned in previous paragraphs. Performing together they can also create a microenvironment favorable to the neoplastic transformation of thyroid cells (Franchini et al, 2022).

IL-6 and TNF-α

A central feature of obesity-related carcinogenesis is chronic low-grade inflammation, a state driven by functional and structural remodeling of adipose tissue. In healthy individuals, adipose tissue acts as a metabolically active endocrine organ that helps maintain energy balance through the controlled release of adipokines. However, as adipocytes undergo hypertrophy in the context of obesity, adipose tissue becomes infiltrated by macrophages and other immune cells, shifting from an anti-inflammatory to a pro-inflammatory phenotype (Kawai, Autieri, & Scalia, 2021; Haase et al, 2014). This transition leads to sustained overproduction of cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) [the level of serum IL-6 (SMD = 1.04, 95% CI: 0.40-1.67, p = 0.001) and the level of serum TNF-α (SMD =1.31, 95% CI: 0.35-2.28, p = 0.008) in TC are significantly higher than those in control], which are known to influence cell proliferation, apoptosis resistance, and extracellular matrix remodeling (Zheng et al, 2019; Zhao et al, 2020). Such systemic inflammatory activation may not only impair thyroid homeostasis, but also encourage the initiation and progression of malignant lesions within the gland.

Adiponectin and leptin

Another crucial element linking obesity with TC is the dysregulation of adipokines, including leptin and adiponectin. Hyperleptinemia in obesity causes increased mitogenic signaling, enhanced angiogenesis, and reduced apoptosis, processes that have been observed in various tumor models, including those of the thyroid (Celano et al, 2019) Conversely, adiponectin, an adipokine with anti-inflammatory and insulin-sensitizing effects, is markedly reduced in individuals with obesity (Nigro et al, 2021).

Insulin resistance and IGF-1

Metabolic alterations associated with obesity, particularly insulin resistance and compensatory hyperinsulinemia, represent an additional pathway that may promote thyroid tumorigenesis. Insulin, acting through the insulin receptor and the insulin-like growth factor 1 (IGF) system, exerts potent mitogenic effects via activation of MAPK and PI3K/AKT pathways (Artim, Mendrola, & Lemmon, 2012). Overexpression of IGF ligands and their receptors has been widely documented across multiple malignancies, including TC (Vella et al, 2001). This upregulation appears to represent an early event in malignant transformation, supporting uncontrolled proliferation and suppressing apoptosis, and is frequently associated with poorer clinical outcomes (Bowers et al, 2015). A meta-analysis of 42 articles indicated increased risk for TC in patients with insulin resistance (RR = 1.59, 95% CI = 1.12–2.27, p = 0.01) (Yin et al, 2018). Further evidence suggests that insulin and IGF-1 may synergize with TSH, the principal physiological stimulator of thyroid cell growth. Although the mitogenic effect of TSH is minimal in the absence of growth factors, it is markedly amplified in the presence of IGF-1 (Vella & Malaguarnera, 2018).

Estrogens

Adipose tissue is a major site of aromatase activity, leading to increased peripheral conversion of androgens to estrogens (Pazaitou-Panayiotou, Polyzos, & Mantzoros, 2013). As thyroid tissue expresses estrogen receptors, predominantly the proliferative ER-α subtype, an estrogen-rich environment may potentiate growth signals and promote more aggressive tumor behavior (Liu, Xu, Ma, & Chang, 2021). The effects of estrogens on thyroid cells involve crosstalk between several oncogenic pathways, including PI3K/AKT, MAPK, and NF-κB, as well as modulation of oxidative stress responses and angiogenesis (Liu, Xu, Ma, & Chang, 2021). These hormonal dynamics may partially explain the higher prevalence of TC in women and the potential influence of menopausal status and adiposity on disease risk.

Oxidative stress

Oxidative stress, defined as an excess of free radicals and reactive metabolites capable of inducing harmful biological effects, represents another mechanistic link between obesity and TC. Excess adiposity and associated metabolic disturbances increase the production of reactive oxygen species (ROS), while simultaneously impairing antioxidant defense systems (Xing, 2012). Thyroid tissue is uniquely susceptible to oxidative stress due to its physiological reliance on hydrogen peroxide for thyroid hormone synthesis (Karbownik-Lewińska & Kokoszko-Bilska, 2012). In the context of obesity, chronic ROS overproduction may exacerbate DNA damage, promote genomic instability, and stimulate oncogenic signaling, thereby creating an environment conducive to neoplastic transformation (Costa, Scholer-Dahirel, & Mechta-Grigoriou, 2014).

Dietary patterns

Emerging evidence suggests that dietary patterns, beyond their role in promoting caloric imbalance, also modulate inflammatory and metabolic pathways relevant to TC development (Neale, Batterham, & Tapsell, 2016). The Dietary Inflammatory Index (DII) is a literature-derived index that evaluates the relationship between multiple dietary components and inflammation-related biomarkers. Higher DII values indicate a more pro-inflammatory dietary pattern and have been linked to an elevated risk of obesity and other chronic conditions, including TC risk, particularly when combined with other obesity-related metabolic abnormalities (Marx et al, 2021). These findings underscore the multifaceted role of nutritional behavior in shaping both systemic inflammation and the carcinogenic susceptibility of thyroid tissue.

Summary of recent data

The latest meta-analysis, which included 22 studies, showed that obesity is significantly associated with an increased risk of TC (HR = 1.33; 95% CI 1.24−1.43) (Hisan, Myung, & Nguyen, 2025). This risk is significantly higher regardless of the type of study (prospective or retrospective cohort study), gender (male or female), continent (America, Europe, or Asia) and study quality (high or low). Another meta-analysis of 21 studies, including 121,999 patients with TC, showed that the risk of TC increases proportionally to the severity of obesity. Each 5-unit increase in BMI, 5 kg increase in weight, 5 cm increase in waist or hip circumference, and 0.1-unit increase in waist-to-hip ratio were associated with 30%, 5%, 5%, and 14% greater risks of TC, respectively (Schmid, Ricci, Behrens, & Leitzmann, 2015). Studies have shown that obesity is significantly positively correlated to papillary, follicular, and anaplastic TC, whereas the association with medullary TC was not confirmed (Schmid, Ricci, Behrens, & Leitzmann, 2015). Furthermore, a study comparing the effects

of various factors on the development of TC found that obesity was associated with an increase in TC risk comparable to that observed with radiation exposure (13%, 95% CI: 5–21%, four studies; 14% 95% CI: 5–23%, eight studies, respectively) (Sadeghi et al, 2018).

The Effect of Obesity Treatment on The Thyroid Gland

With the global obesity epidemic, the use of bariatric surgery and pharmacological agents acting on the incretin axis have increased. Studies assessing the impact of obesity treatment on thyroid morphology and function, as well as the risk of developing cancers, including TC, have already been published.

Bariatric surgery

De Sousa et al (2023) examined the impact of bariatric surgery (BS) on thyroid function and morphology. The study included 70 patients, of whom 40 patients who underwent BS. The results showed that thyroid volume (TV) decreased after BS, differing significantly from the control group without surgical intervention (−1,5 cm3, p = 0.003). The change in thyroid volume (ΔTV) was independently and positively correlated with ΔHOMA-IR (p = 0.007) and ΔIL6 (p = 0.016). A non-significant reduction in TSH within the BS group (−0.3872 vs. −0.2483, p = 0.128) was observed. The conversion of T4 to T3 increased significantly after BS, as demonstrated by the T3/T4 ratio (+5.16, p = 0.01). In another study including 122 patients, with a BS group of 33 patients, TSH and fT3 levels significantly decreased (p = 0.005 and p = 0.002, respectively) with no significant changes in thyroid function in the control group. Thyroid volume increased significantly in the control group but not in the BS group (p = 0.034 vs. 0.270) (Soyer et al, 2025).

Glucagon-like peptide 1 receptor agonists

Early observational studies had raised concerns regarding a potential increased risk of TC with glucagon-like peptide 1 receptor agonists (GLP-1 RAs) (Bezin et al, 2023). However, more recent evidence has not corroborated these results (Baxter et al, 2025). One study investigated the use of GLP-1 RAs compared with use of dipeptidyl peptidase-4 inhibitors (DPP-4i) among patients with type 2 diabetes mellitus and their association with TC development. The results have shown that use of GLP1-RAs relative to use of DPP-4i was not associated with an increased risk of TC (pooled weighted HR 0.81, 95% CI 0.59-1.12). No increased risk of TC was observed with increasing cumulative dose of GLP1-RAs among GLP1-RAs ever-users. Moreover, a meta-analysis by Nagendra, BG, Sharma and Duttam (2023), including data from 37 randomised controlled trials and 19 real-world studies, found no increased risk of TC (2.04; 0.33–12.61), or other neoplasms (0.95; 0.62–1.45) in participants using semaglutide. In a recent large-scale cohort study comparing GLP-1RAs-treated patients with controls, significant risk reduction over the 5-year follow-up included malignancies in thyroid and endocrine glands (HR 0.7, 95% CI 0.56–0.87) (Levy et al, 2025). However, subgroup analysis by individual GLP-1 RAs types showed that semaglutide was associated with a significantly lower risk of TC, while liraglutide increased that risk (HR = 1.702, 95% CI = 1.029–2.815).

Discussion

The findings of this review highlight the complex and multifactorial relationship between obesity, thyroid function, thyroid morphology, and TC risk. Obesity has evolved into a global public health challenge of unprecedented scale, with its prevalence rising sharply across all age groups. As demonstrated in numerous studies, excess adiposity exerts diverse endocrine, metabolic, immune, and molecular effects that can influence thyroid homeostasis and the development of both benign and malignant thyroid disease.

A consistent body of evidence indicates that obesity is associated with alterations in thyroid function driven primarily by leptin-mediated stimulation of the hypothalamus–pituitary–thyroid axis. Hyperleptinemia in individuals with elevated adiposity induces TRH and TSH secretion, which may lead to persistent TSH elevation and consequent thyroid hypertrophy, hyperplasia, and the formation of focal lesions. Clinical studies support this mechanism, showing that even modest weight gain is associated with measurable increases in TSH, whereas weight loss results in decreased TSH levels and improved thyroid hormone dynamics. These findings underscore the physiological sensitivity of the thyroid to metabolic changes arising from excess adipose tissue.

Beyond functional alterations, accumulating evidence demonstrates a strong association between obesity and structural thyroid abnormalities. Several recent analyses show that overweight and obese individuals exhibit a higher prevalence of thyroid nodules, larger thyroid volumes, and worse cytological outcomes on fine-needle aspiration. Many studies consistently report higher rates of suspicious or malignant

cytology among individuals with BMI ≥ 25 kg/m². These observations suggest that obesity may not only promote the development of nodules but may also contribute to a more aggressive morphological profile, which has significant clinical and diagnostic implications. Currently, clinical guidelines do not recommend routine thyroid ultrasonography for screening in patients with obesity. However, in light of the accumulating evidence, this issue may warrant consideration in selected patient populations.

An increasing number of studies linking obesity to a higher risk of TC emphasize the growing clinical importance of these findings. Recent meta-analyses, including large cohorts from multiple continents, demonstrate a clear positive association between BMI and TC incidence. The risk rises proportionally with increasing adiposity, with a 5-unit increase in BMI associated with a 30% higher risk of TC. Importantly, obesity appears to confer a similar magnitude of risk as well-established factors such as radiation exposure. Notably, the association is strongest for papillary, follicular, and anaplastic thyroid carcinomas, but not for medullary thyroid carcinoma, suggesting tumor-type-specific pathways.

Mechanistically, several biological processes may explain how obesity promotes thyroid carcinogenesis. Chronic low-grade inflammation, characterized by elevated circulating IL-6 and TNF-α, contributes to a pro-tumorigenic microenvironment. Dysregulation of adipokines, including increased leptin and reduced adiponectin, further enhances mitogenic signaling, angiogenesis, and resistance to apoptosis. Hyperinsulinemia and insulin resistance, hallmark features of metabolic dysfunction, synergize with TSH to amplify thyrocyte proliferation. Additionally, increased aromatase activity in adipose tissue raises estrogen levels, potentially driving tumorigenesis in tissues expressing estrogen receptors, including the thyroid. Elevated oxidative stress, to which thyroid tissue is uniquely vulnerable, adds another layer of risk by promoting DNA damage and genomic instability. Finally, dietary patterns characterized by high inflammatory potential may further amplify systemic and local carcinogenic processes.

Recent data on obesity treatment provide important insight into the reversibility of obesity-related thyroid alterations. Bariatric surgery has consistently been shown to reduce thyroid volume, improve thyroid hormone profiles, decrease TSH levels, and alleviate metabolic risk factors. Pharmacological treatments, particularly GLP-1 RAs, have generated interest because of earlier concerns regarding TC risk. However, the current evidence strongly suggests that GLP-1 RAs do not increase TC incidence, with several large analyses showing neutral or even protective effects. Notably, the risk profile may differ between GLP-1 RAs subtypes: semaglutide appears to reduce TC risk, while liraglutide may be associated with a modest increase. These findings highlight the need for further subtype-specific evaluations but overall support the safety of GLP-1–based therapies in patients with or at risk for thyroid disease.

Overall, the evidence presented in this review underscores that the relationship between obesity and thyroid disease is clinically significant. Excess adiposity represents a modifiable risk factor whose influence extends from functional thyroid disturbances to morphological abnormalities and carcinogenic potential. With obesity rates continuing to rise globally, addressing this relationship should be a priority in both endocrinology and public health.

Conclusions

Obesity clearly emerges as an important determinant of both functional and structural thyroid abnormalities. A substantial body of epidemiological data shows that obesity significantly increases the risk of developing TC. Importantly, interventions targeting weight reduction appear capable of reversing or attenuating many obesity-related thyroid alterations. Integrating weight management into the evaluation and treatment of thyroid disorders, alongside continued research into the underlying mechanisms and long-term outcomes of obesity-targeted therapies, will be essential for optimizing care and refining clinical guidelines.

Abbreviations
The following abbreviations are used in this review:

ATC — Anaplastic thyroid carcinoma
BMI — Body mass index
DII — Dietary inflammatory index
DPP-4i — Dipeptidyl peptidase-4 inhibitors
FTC — Follicular thyroid carcinoma
GLP-1 RAs — Glucagon-like peptide-1 receptor agonists
IGF-1 — Insulin-like growth factor-1
IL-6 — Interleukin-6
MTC — Medullary thyroid carcinoma
PTC — Papillary thyroid carcinoma
ROS — Reactive oxygen species
TC — Thyroid cancer
TNF-α — Tumor necrosis factor-alpha
TPOAb — Thyroid peroxidase antibodies
TRH — Thyrotropin-releasing hormone
TSH — Thyroid-stimulating hormone
TV — Thyroid volume

Funding Statement: The article did not receive any funding.
Institutional Review and Board Statement: Not applicable.
Informed Consent Statement: Not applicable.
Data Availability Statement: Not applicable.
Conflict of Interest Statement: No conflicts of interest to declare.

REFERENCES

1. Tung, J. Y. L., Poon, G. W. K., Du, J., & Wong, K. K. Y. (2023). Obesity in children and adolescents: Overview of the diagnosis and management. In *Chronic Diseases and Translational Medicine* (Vol. 9, Issue 2). https://doi.org/10.1002/cdt3.58
2. Blüher, M. (2019). Obesity: global epidemiology and pathogenesis. In *Nature Reviews Endocrinology* (Vol. 15, Issue 5). https://doi.org/10.1038/s41574-019-0176-8
3. Sarma, S., Sockalingam, S., & Dash, S. (2021). Obesity as a multisystem disease: Trends in obesity rates and obesity-related complications. In *Diabetes, Obesity and Metabolism* (Vol. 23, Issue S1). https://doi.org/10.1111/dom.14290
4. Lin, X., & Li, H. (2021). Obesity: Epidemiology, Pathophysiology, and Therapeutics. In *Frontiers in Endocrinology* (Vol. 12). https://doi.org/10.3389/fendo.2021.706978
5. Mahmoud, A. M. (2022). An Overview of Epigenetics in Obesity: The Role of Lifestyle and Therapeutic Interventions. In *International Journal of Molecular Sciences* (Vol. 23, Issue 3). https://doi.org/10.3390/ijms23031341
6. Pati, S., Irfan, W., Jameel, A., Ahmed, S., & Shahid, R. K. (2023). Obesity and Cancer: A Current Overview of Epidemiology, Pathogenesis, Outcomes, and Management. In *Cancers* (Vol. 15, Issue 2). https://doi.org/10.3390/cancers15020485
7. WHO. (2000). (1999: Geneva, Switzerland) & World Health Organization. (2000). Obesity : preventing and managing the global epidemic : report of a WHO consultation. *World Health Organization* (Vol. 894).
8. Salminen, P., Kow, L., Aminian, A., Kaplan, L. M., Nimeri, A., Prager, G., Behrens, E., White, K. P., Shikora, S., & IFSO Experts Panel (2024). IFSO Consensus on Definitions and Clinical Practice Guidelines for Obesity Management-an International Delphi Study. *Obesity surgery*, *34*(1), 30–42. https://doi.org/10.1007/s11695-023-06913-8
9. WHO. (2023). WHO acceleration plan to stop obesity. *World Health Organization*.
10. WHO. (2023) Health service delivery framework for prevention and management of obesity. *World Health Organization*.
11. Fitch, A. K., & Bays, H. E. (2022). Obesity definition, diagnosis, bias, standard operating procedures (SOPs), and telehealth: An Obesity Medicine Association (OMA) Clinical Practice Statement (CPS) 2022. *Obesity Pillars*, *1*. https://doi.org/10.1016/j.obpill.2021.100004

12. WHO (2025, May 7). Obesity and overweight. Retrieved from https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
13. Santini, F., Marzullo, P., Rotondi, M., Ceccarini, G., Pagano, L., Ippolito, S., Chiovato, L., & Biondi, B. (2014). Mechanisms in endocrinology: the crosstalk between thyroid gland and adipose tissue: signal integration in health and disease. *European journal of endocrinology*, *171*(4), R137-R152.
14. Biondi, B. (2024). Subclinical Hypothyroidism in Patients with Obesity and Metabolic Syndrome: A Narrative Review. In *Nutrients* (Vol. 16, Issue 1). https://doi.org/10.3390/nu16010087
15. Bjergved, L., Jørgensen, T., Perrild, H., Laurberg, P., Krejbjerg, A., Ovesen, L., Rasmussen, L. B., & Knudsen, N. (2014). Thyroid function and body weight: A community-based longitudinal study. *PLoS ONE*, *9*(4). https://doi.org/10.1371/journal.pone.0093515
16. Guan, B., Chen, Y. Y., Yang, J., Yang, W., & Wang, C. (2017). Effect of Bariatric Surgery on Thyroid Function in Obese Patients: a Systematic Review and Meta-Analysis. In *Obesity Surgery* (Vol. 27, Issue 12). https://doi.org/10.1007/s11695-017-2965-2
17. Baranowska-Bik, A., & Bik, W. (2020). The Association of Obesity with Autoimmune Thyroiditis and Thyroid Function-Possible Mechanisms of Bilateral Interaction. In *International Journal of Endocrinology* (Vol. 2020). https://doi.org/10.1155/2020/8894792
18. Szczepanek-Parulska, E., Zybek-Kocik, A., Woliński, K., Czarnocka, B., & Ruchała, M. (2016). Does TSH Trigger the Anti-thyroid Autoimmune Processes? Observation on a Large Cohort of Naive Patients with Thyroid Hemiagenesis. *Archivum Immunologiae et Therapiae Experimentalis*, *64*(4). https://doi.org/10.1007/s00005-016-0393-y
19. Wu, Z., Xi, Z., Xiao, Y., Zhao, X., Li, J., Feng, N., Hu, L., Zheng, R., Zhang, N., Wang, S., & Huang, T. (2022). TSH-TSHR axis promotes tumor immune evasion. *Journal for ImmunoTherapy of Cancer*, *10*(1). https://doi.org/10.1136/jitc-2021-004049
20. Mastrototaro, L., & Roden, M. (2021). Insulin resistance and insulin sensitizing agents. In *Metabolism: Clinical and Experimental* (Vol. 125). https://doi.org/10.1016/j.metabol.2021.154892
21. Chen, G., Xu, S., Renko, K., & Derwahl, M. (2012). Metformin inhibits growth of thyroid carcinoma cells, suppresses self-renewal of derived cancer stem cells, and potentiates the effect of chemotherapeutic agents. *Journal of Clinical Endocrinology and Metabolism*, *97*(4). https://doi.org/10.1210/jc.2011-1754
22. Lomtadze, N., Giorgadze, E., Janjgava, S., Kacharava, T., & Taboridze, I. (2023). The Relationship between Insulin Resistance and Thyroid Volume in Georgia. *Endocrine, Metabolic & Immune Disorders - Drug Targets*, *23*(10). https://doi.org/10.2174/1871530323666230220093432
23. Marzullo, P., Minocci, A., Tagliaferri, M. A., Guzzaloni, G., di Blasio, A., de Medici, C., Aimaretti, G., & Liuzzi, A. (2010). Investigations of thyroid hormones and antibodies in obesity: Leptin levels are associated with thyroid autoimmunity independent of bioanthropometric, hormonal, and weight-related determinants. *Journal of Clinical Endocrinology and Metabolism*, *95*(8). https://doi.org/10.1210/jc.2009-2798
24. Song, R. H., Wang, B., Yao, Q. M., Li, Q., Jia, X., & Zhang, J. A. (2019). The Impact of Obesity on Thyroid Autoimmunity and Dysfunction: A Systematic Review and Meta-Analysis. In *Frontiers in Immunology* (Vol. 10). https://doi.org/10.3389/fimmu.2019.02349
25. Pemayun, T. G. D. (2016). Current Diagnosis and Management of Thyroid Nodules. In *Acta medica Indonesiana* (Vol. 48, Issue 3).
26. Demetriou, E., Economides, A., Fokou, M., Lamnisos, D., Paschou, S. A., Papageorgis, P., & Economides, P. A. (2025). Adiposity is associated with a higher number of thyroid nodules and worse fine-needle aspiration outcomes. *European Thyroid Journal*, *14*(1), e240176. Retrieved Dec 7, 2025, from https://doi.org/10.1530/ETJ-24-0176
27. Poller, D. N., Cochand-Priollet, B., & Trimboli, P. (2021). Thyroid FNA terminology: The case for a single unified international system for thyroid FNA reporting. In *Cytopathology* (Vol. 32, Issue 6). https://doi.org/10.1111/cyt.13017
28. Fokou, M., Economides, A., Demetriou, E., Lamnisos, D., Agouridis, A. P., Papageorgis, P., & Economides, P. A. (2025). Adiposity Is Associated with a Higher Risk of Thyroid Malignancy in Patients with Hashimoto's Thyroiditis. *Diagnostics*, *15*(7), 853. https://doi.org/10.3390/diagnostics15070853
29. Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, *68*(6). https://doi.org/10.3322/caac.21492
30. Wirth, S., Syleouni, M. E., Karavasiloglou, N., Rinaldi, S., Korol, D., Wanner, M., & Rohrmann, S. (2021). Incidence and mortality trends of thyroid cancer from 1980 to 2016. *Swiss Medical Weekly*, *151*(43–44). https://doi.org/10.4414/smw.2021.w30029
31. Enewold, L., Zhu, K., Ron, E., Marrogi, A. J., Stojadinovic, A., Peoples, G. E., & Devesa, S. S. (2009). Rising thyroid cancer incidence in the United States by demographic and tumor characteristics, 1980-2005. *Cancer Epidemiology Biomarkers and Prevention*, *18*(3). https://doi.org/10.1158/1055-9965.EPI-08-0960
32. Zhang, J., & Xu, S. (2024). High aggressiveness of papillary thyroid cancer: from clinical evidence to regulatory cellular networks. In *Cell Death Discovery* (Vol. 10, Issue 1). https://doi.org/10.1038/s41420-024-02157-2

33. Shen, J., Yan, M., Chen, L., Ou, D., Yao, J., Feng, N., Zhou, X., Lei, Z., & Xu, D. (2024). Prognosis and influencing factors of follicular thyroid cancer. *Cancer Medicine*, *13*(1). https://doi.org/10.1002/cam4.6727
34. Forma, A., Kłodnicka, K., Pająk, W., Flieger, J., Teresińska, B., Januszewski, J., & Baj, J. (2025). Thyroid Cancer: Epidemiology, Classification, Risk Factors, Diagnostic and Prognostic Markers, and Current Treatment Strategies. In *International Journal of Molecular Sciences* (Vol. 26, Issue 11). https://doi.org/10.3390/ijms26115173
35. Li, Y., Zhang, J., Zhou, H., & Du, Z. (2022). Anticancer effects of natural phytochemicals in anaplastic thyroid cancer (Review). In *Oncology Reports* (Vol. 48, Issue 3). https://doi.org/10.3892/or.2022.8368
36. Yin, D. tao, He, H., Yu, K., Xie, J., Lei, M., Ma, R., Li, H., Wang, Y., & Liu, Z. (2018). The association between thyroid cancer and insulin resistance, metabolic syndrome and its components: A systematic review and meta-analysis. In *International Journal of Surgery* (Vol. 57). https://doi.org/10.1016/j.ijsu.2018.07.013
37. Franchini, F., Palatucci, G., Colao, A., Ungaro, P., Macchia, P. E., & Nettore, I. C. (2022). Obesity and Thyroid Cancer Risk: An Update. In *International Journal of Environmental Research and Public Health* (Vol. 19, Issue 3). https://doi.org/10.3390/ijerph19031116
38. Mirkatouli, N. B., Hirota, S., & Yoshinaga, S. (2023). Thyroid cancer risk after radiation exposure in adults - systematic review and meta-analysis. In *Journal of Radiation Research* (Vol. 64, Issue 6). https://doi.org/10.1093/jrr/rrad073
39. Derwahl, M., & Nicula, D. (2014). Estrogen and its role in thyroid cancer. *Endocrine-Related Cancer*, *21*(5). https://doi.org/10.1530/ERC-14-0053
40. Lee, J. H., Chai, Y. J., & Yi, K. H. (2021). Effect of Cigarette Smoking on Thyroid Cancer: Meta-Analysis. *Endocrinology and Metabolism*, *36*(3). https://doi.org/10.3803/ENM.2021.954
41. Dong, W. W., Zhang, D. L., Wang, Z. H., Lv, C. Z., Zhang, P., & Zhang, H. (2022). Different types of diabetes mellitus and risk of thyroid cancer: A meta-analysis of cohort studies. In *Frontiers in Endocrinology* (Vol. 13). https://doi.org/10.3389/fendo.2022.971213
42. Ma, J., Huang, M., Wang, L., Ye, W., Tong, Y., & Wang, H. (2015). Obesity and risk of thyroid cancer: Evidence from a Meta-Analysis of 21 observational studies. *Medical Science Monitor*, *21*. https://doi.org/10.12659/MSM.892035
43. Zhao, Z. G., Guo, X. G., Ba, C. X., Wang, W., Yang, Y. Y., Wang, J., & Cao, H. Y. (2012). Overweight, obesity and thyroid cancer risk: A meta-analysis of cohort studies. *Journal of International Medical Research*, *40*(6). https://doi.org/10.1177/030006051204000601
44. Rezzónico, J. N., Rezzónico, M., Pusiol, E., Pitoia, F., & Niepomniszcze, H. (2009). Increased prevalence of insulin resistance in patients with differentiated thyroid carcinoma. *Metabolic Syndrome and Related Disorders*, *7*(4). https://doi.org/10.1089/met.2008.0062
45. Nettore, I. C., Rocca, C., Mancino, G., Albano, L., Amelio, D., Grande, F., Puoci, F., Pasqua, T., Desiderio, S., Mazza, R., Terracciano, D., Colao, A., Bèguinot, F., Russo, G. L., Dentice, M., Macchia, P. E., Sinicropi, M. S., Angelone, T., & Ungaro, P. (2019). Quercetin and its derivative Q2 modulate chromatin dynamics in adipogenesis and Q2 prevents obesity and metabolic disorders in rats. *Journal of Nutritional Biochemistry*, *69*. https://doi.org/10.1016/j.jnutbio.2019.03.019
46. Kawai, T., Autieri, M. v., & Scalia, R. (2021). Adipose tissue inflammation and metabolic dysfunction in obesity. *American Journal of Physiology - Cell Physiology*, *320*(3). https://doi.org/10.1152/ajpcell.00379.2020
47. Haase, J., Weyer, U., Immig, K., Klöting, N., Blüher, M., Eilers, J., Bechmann, I., & Gericke, M. (2014). Local proliferation of macrophages in adipose tissue during obesity-induced inflammation. *Diabetologia*, *57*(3). https://doi.org/10.1007/s00125-013-3139-y
48. Zheng, R., Chen, G., Li, X., Wei, X., Liu, C., & Derwahl, M. (2019). Effect of IL-6 on proliferation of human thyroid anaplastic cancer stem cells. *International Journal of Clinical and Experimental Pathology*, *12*(11).
49. Zhao, J., Wen, J., Wang, S., Yao, J., Liao, L., & Dong, J. (2020). Association between adipokines and thyroid carcinoma: A meta-analysis of case-control studies. *BMC Cancer*, *20*(1). https://doi.org/10.1186/s12885-020-07299-x
50. Celano, M., Maggisano, V., Lepore, S. M., Sponziello, M., Pecce, V., Verrienti, A., Durante, C., Maranghi, M., Lucia, P., Bulotta, S., Damante, G., & Russo, D. (2019). Expression of Leptin Receptor and Effects of Leptin on Papillary Thyroid Carcinoma Cells. *International Journal of Endocrinology*, *2019*. https://doi.org/10.1155/2019/5031696
51. Nigro, E., Orlandella, F. M., Polito, R., Mariniello, R. M., Monaco, M. L., Mallardo, M., de Stefano, A. E., Iervolino, P. L. C., Salvatore, G., & Daniele, A. (2021). Adiponectin and leptin exert antagonizing effects on proliferation and motility of papillary thyroid cancer cell lines. *Journal of Physiology and Biochemistry*, *77*(2). https://doi.org/10.1007/s13105-021-00789-x
52. Artim, S. C., Mendrola, J. M., & Lemmon, M. A. (2012). Assessing the range of kinase autoinhibition mechanisms in the insulin receptor family. *Biochemical Journal*, *448*(2). https://doi.org/10.1042/BJ20121365
53. Vella, V., Sciacca, L., Pandini, G., Mineo, R., Squatrito, S., Vigneri, R., & Belfiore, A. (2001). The IGF system in thyroid cancer: New concepts. In *Journal of Clinical Pathology - Molecular Pathology* (Vol. 54, Issue 3). https://doi.org/10.1136/mp.54.3.121

54. Bowers, L. W., Rossi, E. L., O'Flanagan, C. H., de Graffenried, L. A., & Hursting, S. D. (2015). The role of the insulin/IGF system in cancer: Lessons learned from clinical trials and the energy balance-cancer link. In *Frontiers in Endocrinology* (Vol. 6, Issue MAY). https://doi.org/10.3389/fendo.2015.00077
55. Vella, V., & Malaguarnera, R. (2018). The emerging role of insulin receptor isoforms in thyroid cancer: Clinical implications and new perspectives. In *International Journal of Molecular Sciences* (Vol. 19, Issue 12). https://doi.org/10.3390/ijms19123814
56. Pazaitou-Panayiotou, K., Polyzos, S. A., & Mantzoros, C. S. (2013). Obesity and thyroid cancer: Epidemiologic associations and underlying mechanisms. In *Obesity Reviews* (Vol. 14, Issue 12). https://doi.org/10.1111/obr.12070
57. Liu, J., Xu, T., Ma, L., & Chang, W. (2021). Signal Pathway of Estrogen and Estrogen Receptor in the Development of Thyroid Cancer. In *Frontiers in Oncology* (Vol. 11). https://doi.org/10.3389/fonc.2021.593479
58. Xing, M. (2012). Oxidative stress: A new risk factor for thyroid cancer. In *Endocrine-Related Cancer* (Vol. 19, Issue 1). https://doi.org/10.1530/ERC-11-0360
59. Karbownik-Lewińska, M., & Kokoszko-Bilska, A. (2012). Oxidative damage to macromolecules in the thyroid - Experimental evidence. In *Thyroid Research* (Vol. 5, Issue 1). https://doi.org/10.1186/1756-6614-5-25
60. Costa, A., Scholer-Dahirel, A., & Mechta-Grigoriou, F. (2014). The role of reactive oxygen species and metabolism on cancer cells and their microenvironment. In *Seminars in Cancer Biology* (Vol. 25). https://doi.org/10.1016/j.semcancer.2013.12.007
61. Neale, E. P., Batterham, M. J., & Tapsell, L. C. (2016). Consumption of a healthy dietary pattern results in significant reductions in C-reactive protein levels in adults: A meta-analysis. In *Nutrition Research* (Vol. 36, Issue 5). https://doi.org/10.1016/j.nutres.2016.02.009
62. Marx, W., Veronese, N., Kelly, J. T., Smith, L., Hockey, M., Collins, S., Trakman, G. L., Hoare, E., Teasdale, S. B., Wade, A., Lane, M., Aslam, H., Davis, J. A., O'neil, A., Shivappa, N., Hebert, J. R., Blekkenhorst, L. C., Berk, M., Segasby, T., & Jacka, F. (2021). The Dietary Inflammatory Index and Human Health: An Umbrella Review of Meta-Analyses of Observational Studies. In *Advances in Nutrition* (Vol. 12, Issue 5). https://doi.org/10.1093/advances/nmab037
63. Hisan, U. K., Myung, S. K., & Nguyen, G. V. (2025). Associations Between Obesity and Risk of Thyroid Cancer: A Meta-Analysis of Cohort Studies. *Nutrition and Cancer*, *77*(2). https://doi.org/10.1080/01635581.2024.2419488
64. Schmid, D., Ricci, C., Behrens, G., & Leitzmann, M. F. (2015). Adiposity and risk of thyroid cancer: A systematic review and meta-analysis. In *Obesity Reviews* (Vol. 16, Issue 12). https://doi.org/10.1111/obr.12321
65. Sadeghi, H., Rafei, M., Bahrami, M., Haghdoost, A., & Shabani, Y. (2018). Attributable risk fraction of four lifestyle risk factors of thyroid cancer: A meta-analysis. *Journal of Public Health (United Kingdom)*, *40*(2). https://doi.org/10.1093/pubmed/fdx088
66. de Sousa, P. A. M., Pereira, J. R. D., Carneiro, J. R. I., de Vasconcelos, A. L., Fortunato, R. S., Carvalho, D. P., & Teixeira, P. de F. dos S. (2023). Impact of Bariatric Surgery on Thyroid Morphology and Thyroid Function. *Obesity Surgery*, *33*(10). https://doi.org/10.1007/s11695-023-06779-w
67. Soyer, A. K., Ertuna, G. N., Çolakoğlu, M. K., Başer, H., Aydın, C., Topaloğlu, O., Ersoy, R., & Çakır, B. (2025). Thyroid Volume Stabilization and Nodule Progression After Bariatric Surgery: Insights from a Retrospective Study. *Obesity Surgery*, *35*(10). https://doi.org/10.1007/s11695-025-08229-1
68. Bezin, J., Gouverneur, A., Penichon, M., Mathieu, C., Garrel, R., Hillaire-Buys, D., Pariente, A., & Faillie, J. L. (2023). GLP-1 Receptor Agonists and the Risk of Thyroid Cancer. *Diabetes Care*, *46*(2). https://doi.org/10.2337/dc22-1148
69. Baxter, S. M., Lund, L. C., Andersen, J. H., Brix, T. H., Hegedüs, L., Hsieh, M. H. C., Su, C. T. T., Cheng, M. C. Y., Chang, Z. C. J., Lai, E. C. C., Hussain, S., Chu, C., Gomes, T., Antoniou, T., Eskander, A., Bouck, Z., Tadrous, M., Bea, S., Choi, E. Y., Shin, J., Y., Modig, K., Talbäck, M., Ljung, R., Gulseth, H. L., Karlstad, Ø., Hicks, B., Pottegård, A. (2025). Glucagon-Like Peptide 1 Receptor Agonists and Risk of Thyroid Cancer: An International Multisite Cohort Study. *Thyroid*, *35*(1). https://doi.org/10.1089/thy.2024.0387
70. Nagendra, L., BG, H., Sharma, M., & Dutta, D. (2023). Semaglutide and cancer: A systematic review and meta-analysis: Semaglutide and cancer. *Diabetes and Metabolic Syndrome: Clinical Research and Reviews*, *17*(9). https://doi.org/10.1016/j.dsx.2023.102834
71. Levy, S., Attia, A., Elshazli, R. M., Abdelmaksoud, A., Tatum, D., Aiash, H., & Toraih, E. A. (2025). Differential Effects of GLP-1 Receptor Agonists on Cancer Risk in Obesity: A Nationwide Analysis of 1.1 Million Patients. *Cancers*, *17*(1). https://doi.org/10.3390/cancers17010078