Narrative Review

Hyperthyroidism, Thyroid cancers, and Osteoprosis

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Abstract

This narrative review explores the intricate relationship between thyroid disorders, both hyperthyroidism and hypothyroidism, and their impact on bone health and fracture risk. Hyperthyroidism, whether overt or subclinical, has been associated with an increased risk of fractures, emphasizing the significance of addressing thyroid dysfunction to prevent fractures. Surgical treatment for hyperthyroidism was found to reduce fracture risk in a nationwide follow-up study, while overt hyperthyroidism was linked to heightened bone turnover, diminished bone density, osteoporosis, and an elevated fracture risk. Additionally, hyperthyroidism's potential to accelerate linear growth and strain on bones further contributes to fracture susceptibility. In older men, lower levels of thyroid-stimulating hormone (TSH) were associated with a higher risk of hip fractures, indicating a specific connection between thyroid function and hip fracture risk. Graves' disease, often leading to prolonged untreated hyperthyroidism, can result in bone density loss and an increased risk of osteoporosis. The impact of thyroid hormones and thyroid autoantibodies on bone mineral density in premenopausal women with Graves' disease was also explored, revealing a clinically relevant influence of thyroid function on bone modulation. Furthermore, the review discusses the potential protective role of TSH receptor antibodies (TRAb) on bones in patients with Graves' thyrotoxicosis and Graves' orbitopathy. The review concludes by highlighting the importance of monitoring bone health in thyroid disease patients and the need for further research to fully understand these complex interactions.

Keywords: Hyperthyroidism, Thyroid cancers, Osteoprosis

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Introduction

Osteoporosis is a common bone disease characterized by a decrease in bone density and quality, leading to an increased risk of fractures and is most frequently diagnosed in postmenopausal women and in older men [1,2]. According to a meta-analysis, the worldwide prevalence of osteoporosis was documented at 18.3% (with a 95% confidence interval ranging from 16.2% to 20.7%), as reported in reference [3]. Bone density scan-confirmed osteoporosis was found to affect 7.8% of the population under study, with a notable gender disparity, as the prevalence was 2.2% in males and 12.7% in females [4]. A family history of the disease, low body weight, smoking, excessive alcohol consumption, and a lack of physical activity are its risk factors [5,6]. The endocrine system plays a crucial role in regulating bone health. diabetes, thyroid issues, and hormonal imbalances can lead to secondary osteoporosis [7]. Various hormones fluctuations cause osteoprosis. Low testosterone levels in men have been associated with a higher risk of osteoporotic fractures [8] and vitamin D status is linked to bone mineral density and bone turnover [9]. Insulin-like growth factor 1 (IGF-1) plays a significant role in bone health and osteoporosis [10]. The liver releases IGF-1 in response to the stimulation of growth hormone (GH). Both GH and IGF-1 play essential roles in maintaining bone health. A deficiency in either GH or IGF-1 can result in reduced bone density and an elevated risk of developing osteoporosis [11]. When severe hyperthyroidism is left untreated, it can elevate the risk of osteoporosis by affecting bone density and encouraging a high rate of bone turnover, ultimately contributing to bone loss [12]. This review aims to comprehensively explore the intricate relationship between thyroid diseases and osteoporosis, two medical conditions that often intersect and impact each other. Thyroid disorders, including hyperthyroidism and hypothyroidism, can have substantial consequences on bone health due to their influence on bone remodeling processes and hormonal imbalances. While hyperthyroidism is associated with increased bone turnover and the potential for osteoporosis, hypothyroidism can result in reduced bone density. The review will delve into the pathophysiological mechanisms underpinning these connections, the impact of thyroid medications on bone health, and clinical management strategies to mitigate osteoporosis risk in individuals with thyroid diseases. A thorough examination of the latest research findings and clinical guidelines will provide a comprehensive overview of the complex interplay between these conditions and offer insights into effective preventative and treatment approaches.

Osteoporosis pathophysiology

Osteoporosis has a multifaceted pathophysiology. It primarily results from an imbalance in bone remodeling, where the rate of bone resorption exceeds bone formation, resulting in a gradual loss of bone mass and increased susceptibility to fractures [13]. Hormonal changes, especially the decline in estrogen levels in postmenopausal women, play a critical role in accelerating bone loss. Aging is another significant factor, as bone density naturally decreases with age, making older individuals more susceptible to osteoporosis [13,14]. Additionally, genetic predisposition, such as a family history of the condition, can heighten the risk. Lifestyle factors, including inadequate calcium and vitamin D intake, a sedentary lifestyle, and smoking, further compound the issue by negatively impacting bone health and exacerbating the condition [13,14].

Pathways of endocrine secondary osteoporosis

Secondary osteoporosis is a form of osteoporosis that is caused by underlying medical conditions [15]. Conditions such as hyperthyroidism, hypogonadism , and Cushing's syndrome can lead to bone loss and osteoporosis[16]. Diabetes mellitus, particularly type 1, is a common secondary cause of osteoporosis [17]. Dysregulation of the thyroid and parathyroid glands can disrupt the balance of calcium and

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other minerals in bones, contributing to osteoporosis[18].

Thyroid hormones and osteoporosis

Overt hypothyroidism, can negatively affect bone turnover, leading to an increased risk of osteoporosis [19]. This condition impairs bone metabolism, potentially resulting in decreased bone mineral density, a hallmark of osteoporosis [20]. Research suggests that TSH has a role in bone health. TSH may improve bone volume, microstructure, and strength by inhibiting certain processes [21]. Thyroid hormones can influence serum calcium levels. Hyperthyroidism can lead to hypercalcemia, while hypothyroidism can result in hypocalcemia [22]. Thyroid hormones can influence how much calcium is stored in bones. In hyperthyroidism, excessive thyroid hormone levels can affect calcium storage in bones [22]. Studies in rats have shown that thyroid dysfunction, specifically hypothyroidism induced by propylthiouracil, can lead to a slow decline in serum calcium levels over several weeks[23]. This suggests a negative correlation between thyroid dysfunction and calcium levels. Thyroid hormones affect the transcellular transport of calcium in rats[24]. There is also a strong negative correlation between TSH and serum calcium levels in both hyperthyroid and hypothyroid conditions[23,24]. Systemic administration of low levels of TSH has been shown to increase bone volume, improve bone microarchitecture, and enhance bone strength in aged ovariectomized (OVX) rats. This suggests a positive effect of TSH on bone health in these rats [25]. Thyroid autoimmunity, including conditions like Hashimoto's and Graves' disease, is associated with decreased bone mineral density in areas like the spine and hip. This decreased bone density can increase the risk of fractures, even in individuals with normal thyroid function (euthyroid)[26].

Graves' disease, toxic multinodular goiter, and toxic adenoma are the main causes of hyperthyroidism; in regions with poor iodine intake, toxic multinodular goiter is the most frequent cause. Hyperthyroidism can also result from consuming too much iodine from prescription drugs or contrast agents. Early diagnosis is typically observed in clinically apparent cases, which are characterized by suppressed thyroid-stimulating hormone (TSH) and high free thyroxine (FT4) and/or free triiodothyronine (FT3). The cardiovascular system may be negatively impacted by hyperthyroidism, thus treatment for the condition must be started right once to reduce symptoms and avoid long-term consequences. Thankfully, clinical practice now only sometimes encounters severe and persistent hyperthyroidism. Overt hyperthyroidism causes a shorter bone remodeling cycle, higher indicators of both bone resorption and creation, and faster bone turnover, which drastically reduces bone density and raises the risk of brittle fractures.

Hyperthyroidism:

studies have shown that hyperthyroidism, both overt and subclinical, is linked to an increased risk of fractures. Subclinical hyperthyroidism, in particular, has been identified as an independent risk factor for fractures, highlighting the importance of addressing thyroid dysfunction to prevent fractures [27,28]. A nationwide follow-up study involving 16,249 patients revealed that surgical treatment for hyperthyroidism is linked to a reduced fracture risk after diagnosis (Relative Risk = 0.66, 95% Confidence Interval: 0.55-0.78) [29]. On the other hand, overt hyperthyroidism, characterized by excessive thyroid hormone production, is associated with heightened bone turnover, diminished bone density, osteoporosis, and an elevated risk of fractures [30]. Hyperthyroidism can also accelerate linear growth in untreated cases. This can lead to increased strain on bones, potentially making them more susceptible to fractures [31]. A study, involving older men, found that while thyroid hormone levels (TSH and FT4) were not linked to bone loss, lower TSH levels were associated with an increased risk of hip fractures, even within the normal TSH range, suggesting a specific connection between thyroid function and hip

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fracture risk in this demographic [32]. According to a different study by Amato et al., even though the aberrant bone structure persisted, high levels of osteoprotegerin (OPG) in hyperthyroidism normalized after receiving medical treatment [33]. Graves' disease often results in prolonged untreated hyperthyroidism, which can lead to a loss of bone density, increasing the risk of osteoporosis [34]. Another study by Siderova et al. aimed to investigate the impact of thyroid hormones, TSH, TSH-receptor antibodies (TRAb), and glucocorticoid treatment on bone health in women with Graves' thyrotoxicosis and Graves' orbitopathy (GO). The results showed that both groups of patients (with and without GO) had significantly lower bone mineral density (BMD) in the spine and femur and a higher risk of fractures compared to healthy controls. Among hyperthyroid patients, those without orbitopathy had lower spine BMD. The study also found correlations between thyroid hormone levels and BMD, suggesting that hyperthyroidism negatively affects BMD. However, TRAb, often elevated in GO patients, may have a protective effect on bones, but more research is needed to understand this fully. The duration of thyrotoxicosis and cumulative steroid dose were also negatively correlated with BMD [35]. the impact of thyroid hormones and thyroid autoantibodies on bone mineral density (BMD) in premenopausal women with untreated Graves' disease was examined. The research revealed that the thyrotoxic state was associated with significantly lower BMD, which improved during antithyroid drug therapy (ATD). However, after discontinuing ATD, femoral neck BMD declined again, independent of age. Thyrotoxicosis affected calcium homeostasis, and TSH receptor antibodies (TRAb) were found to be a positive predictor for better BMD. The results suggest that thyroid function has a clinically relevant influence on bone health in premenopausal women with Graves' disease and imply a potential direct action of TRAb on bones [36].

Thyroid cancers

In U.S. veterans with thyroid cancer, osteoporosis was found to have a higher prevalence compared to control groups, although there was no notable difference in the occurrence of fractures [37]. TSH suppression is a common practice in treating postoperative differentiated thyroid carcinoma (DTC). However, its link to osteoporosis has been debated. A meta-analysis examined the connection between TSH suppressive therapy and osteoporosis in DTC patients. After searching multiple databases, 15 studies with 36 cohorts were analyzed. The findings revealed a higher prevalence of osteoporosis and osteopenia in postmenopausal women on TSH suppression, while men and premenopausal women showed normal or higher bone density [38]. According to data gathered from observational studies, postmenopausal women who undergo TSH suppression therapy face an increased likelihood of having reduced bone mineral density (BMD). This highlights the importance of monitoring the long-term bone health of survivors of DTC to ensure their skeletal well-being [39].

Hypothyroidism:

Overtreated hypothyroidism with levothyroxine, can negatively affect bone health similar to hyperthyroidism [19].

Conclusion:

In conclusion, this comprehensive narrative review highlights the intricate relationship between thyroid disorders and their significant impact on bone health and fracture risk. Hyperthyroidism, whether overt or subclinical, has been consistently linked to an increased risk of fractures, emphasizing the critical importance of addressing thyroid dysfunction to prevent these potentially debilitating events. The review also sheds light on the potential protective role of TSH receptor antibodies (TRAb) in the context of thyroid diseases and their effects on bone health. However, the mechanisms underlying these associations remain complex and multifaceted, warranting further research to elucidate the precise interactions between thyroid function,

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bone health, and fracture risk. As we strive for a better understanding of these relationships, it becomes increasingly vital to monitor and manage the bone health of individuals with thyroid disorders, offering them a chance for a healthier, fracture-free future.

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Conflicts of interests

No conflict of interest was observed during this study.

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References:

1. Salari N, Ghasemi H, Mohammadi L, Behzadi MH, Rabieenia E, Shohaimi S, Mohammadi M. The global prevalence of osteoporosis in the world: a comprehensive systematic review and meta-analysis. Journal of orthopaedic surgery and research. 2021 Dec;16:1-20.
2. McArthur C, Lee A, Alrob HA, Adachi JD, Giangregorio L, Griffith LE, Morin S, Thabane L, Ioannidis G, Lee J, Leslie WD. An update of the prevalence of osteoporosis, fracture risk factors, and medication use among community-dwelling older adults: results from the Canadian Longitudinal Study on Aging (CLSA). Archives of Osteoporosis. 2022 Dec;17(1):31.
3.
4. Rosen CJ. Endocrine disorders and osteoporosis. Current opinion in rheumatology. 1997 Jul 1;9(4):355-61.
5. Cannarella R, Barbagallo F, Condorelli RA, Aversa A, La Vignera S, Calogero AE. Osteoporosis from an endocrine perspective: the role of hormonal changes in the elderly. Journal of clinical medicine. 2019 Oct 1;8(10):1564.
6.
7. 8.Shigehara K, Izumi K, Kadono Y, Mizokami A. Testosterone and bone health in men: a narrative review. Journal of Clinical Medicine. 2021 Feb 2;10(3):530.
8. Lips P, Van Schoor NM. The effect of vitamin D on bone and osteoporosis. Best practice & research Clinical endocrinology & metabolism. 2011 Aug 1;25(4):585-91.
9. Yuan S, Wan ZH, Cheng SL, Michaëlsson K, Larsson SC. Insulin-like growth factor-1, bone mineral density, and fracture: a Mendelian randomization study. The Journal of Clinical Endocrinology & Metabolism. 2021 Apr 1;106(4):1552-8.
10. Giustina A, Mazziotti G, Canalis E. Growth hormone, insulin-like growth factors, and the skeleton. Endocrine reviews. 2008 Aug 1;29(5):535-59.
11. Delitala AP, Scuteri A, Doria C. Thyroid hormone diseases and osteoporosis. Journal of clinical medicine. 2020 Apr 6;9(4):1034.
12. Föger-Samwald U, Dovjak P, Azizi-Semrad U, Kerschan-Schindl K, Pietschmann P. Osteoporosis: Pathophysiology and therapeutic options. EXCLI journal. 2020;19:1017.
13. Raisz LG. Pathogenesis of osteoporosis: concepts, conflicts, and prospects. The Journal of clinical investigation. 2005 Dec 1;115(12):3318-25.
14. Rosen CJ. The Epidemiology and Pathogenesis of Osteoporosis. [Updated 2020 Jun 21]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279134/
15. 15. Ganesan K, Jandu JS, Anastasopoulou C, et al. Secondary Osteoporosis. [Updated 2023 Mar 2]. In:

[Downloaded from intjmi.com on 2026-11-16]

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470166/

16. Sobh MM, Abdalbary M, Elnagar S, Nagy E, Elshabrawy N, Abdelsalam M, Asadipooya K, El-Husseini A. Secondary osteoporosis and metabolic bone diseases. Journal of Clinical Medicine. 2022 Apr 24;11(9):2382.
17. Ebeling PR, Nguyen HH, Aleksova J, Vincent AJ, Wong P, Milat F. Secondary osteoporosis. Endocrine Reviews. 2022 Apr 1;43(2):240-313.
18. Delitala AP, Scuteri A, Doria C. Thyroid Hormone Diseases and Osteoporosis. J Clin Med. 2020 Apr 6;9(4):1034. doi: 10.3390/jcm9041034.
19. Apostu D, Lucaciu O, Oltean-Dan D, Mureșan AD, Moisescu-Pop C, Maxim A, Benea H. The Influence of Thyroid Pathology on Osteoporosis and Fracture Risk: A Review. Diagnostics (Basel). 2020 Mar 7;10(3):149. doi: 10.3390/diagnostics10030149.
20. Modi A, Sahi N. Effect of thyroid hormones on serum calcium and phosphorous. Int J. Clin. Biochem Res. 2018;5:570-3.
21. Gammage MD, Logan SD. Effects of thyroid dysfunction on serum calcium in the rat. Clinical Science (London, England: 1979). 1986 Sep 1;71(3):271-6.
22. Lorenz S, Eszlinger M, Paschke R, Aust G, Weick M, Führer D, Krohn K. Calcium signaling of thyrocytes is modulated by TSH through calcium binding protein expression. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research. 2010 Mar 1;1803(3):352-60.
23. Sampath TK, Simic P, Sendak R, Draca N, Bowe AE, O'Brien S, Schiavi SC, McPherson JM, Vukicevic S. Thyroid-stimulating hormone restores bone volume, microarchitecture, and strength in aged ovariectomized rats. Journal of Bone and Mineral Research. 2007 Jun;22(6):849-59.
24. Polovina SP, Miljic D, Zivojinovic S, Milic N, Micic D, Brkic VP. The impact of thyroid autoimmunity (TPOAb) on bone density and fracture risk in postmenopausal women. Hormones. 2017 Jan;16:54-61.
25. Daya NR, Fretz A, Martin SS, Lutsey PL, Echouffo-Tcheugui JB, Selvin E, Juraschek SP. Association Between Subclinical Thyroid Dysfunction and Fracture Risk. JAMA network open. 2022 Nov 1;5(11):e2240823-.
26. Vestergaard P, Mosekilde L. Fractures in patients with hyperthyroidism and hypothyroidism: a nationwide follow-up study in 16,249 patients. Thyroid. 2002 May 1;12(5):411-9.
27. Ross DS, Muldr JE. Bone disease with hyperthyroidism and thyroid hormone therapy. Upto Date. 2014.
28. Sarezky MD, Corwin DJ, Harrison VS, Jacobstein C. Hyperthyroidism presenting with pathologic fractures. Pediatrics. 2016 Feb 1;137(2).
29. Waring AC, Harrison S, Fink HA, Samuels MH, Cawthon PM, Zmuda JM, Orwoll ES, Bauer DC, Osteoporotic Fractures in Men (MrOS) Study. A prospective study of thyroid function, bone loss, and fractures in older men: the MrOS study. Journal of Bone and Mineral Research. 2013 Mar;28(3):472-9.
30. Amato G, Mazziotti G, Sorvillo F, Piscopo M, Lalli E, Biondi B, Iorio S, Molinari A, Giustina A, Carella C. High serum osteoprotegerin levels in patients with hyperthyroidism: effect of medical treatment. Bone. 2004 Sep 1;35(3):785-91.
31. Jyotsna VP, Sahoo A, Singh AK, Sreenivas V, Gupta N. Bone mineral density in patients of Graves disease pre-& post-treatment in a predominantly vitamin D deficient population. The Indian journal of

[Downloaded from intjmi.com on 2026-11-16]

medical research. 2012 Jan;135(1):36.

32. Siderova M, Hristozov K, Tsukeva A. TSH-receptor antibodies may prevent bone loss in pre-and postmenopausal women with Graves' disease and Graves' orbitopathy. Archives of Endocrinology and Metabolism. 2018 Mar;62:221-6.
33. Belsing TZ, Tofteng C, Langdahl BL, Charles P, Feldt-Rasmussen U. Can bone loss be reversed by antithyroid drug therapy in premenopausal women with Graves' disease?. Nutrition & Metabolism. 2010 Dec;7(1):1-0.
34. Papaleontiou M, Banerjee M, Reyes-Gastelum D, Hawley ST, Haymart MR. Risk of Osteoporosis and Fractures in Patients with Thyroid Cancer: A Case-Control Study in US Veterans. The Oncologist. 2019 Sep 1;24(9):1166-73.
35. Mirghani HO, Altowigri A. Thyroid-stimulating hormone suppressive therapy and osteoporosis: A review and meta-analysis. Sudan Journal of Medical Sciences. 2022 Jul 24;17(2).
36. Ku EJ, Yoo WS, Lee EK, Ahn HY, Woo SH, Hong JH, Chung HK, Park JW. Effect of TSH suppression therapy on bone mineral density in differentiated thyroid cancer: a systematic review and meta-analysis. The Journal of Clinical Endocrinology & Metabolism. 2021 Dec 1;106(12):3655-67.

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