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REVIEW ARTICLE

Thyroid and Cardiovascular Hemodynamics during Menopause

Rashmi Shrivastava[1], Narsingh Verma[1], Abbas Ali Mahdi[2], Sandeep Bhattacharya[1], Amita Pandey[3]

[1]Department of Physiology, King George's Medical University, Lucknow, UP, India
[2]Vice Chancellor, Era University, Lucknow, UP, India
[3]Department of Obstetrics and Gynecology, King George's Medical University, Lucknow, UP, India

Abstract

Background: Serious concerns about noncommunicable disease (NCD) healthcare services in a lower-middle-income nation like India arise from the prevalence of cardiovascular illnesses and lifestyle risk factors among middle-aged and elderly people. Women often have a lesser awareness of the risk associated with cardiovascular diseases (CVD), and these conditions are frequently underdiagnosed. Menopause-related problems include an elevated risk of cardiovascular disease, and low thyroid hormone levels significantly raise the risk of heart disease.

Objective: The purpose of this study is to examine how menopause affects thyroid dysfunction and how it relates to lipid profiles and cardiovascular issues.

Methods: Based on selective searches for clinical trials, meta-analyses, randomized controlled trials, and systematic reviews with the keywords "menopause, thyroid, and cardiovascular disorder" in PubMed and Google Scholar (articles from 2001 to 2023), this review was conducted.

Results: There is a strong correlation between hypertriglyceridemia and hypothyroidism. Low thyroid stimulating hormone (TSH) and menopausal estrogen insufficiency both raise the risk of cardiovascular disease. Women with higher TSH levels have stiffer arteries than those with lower TSH levels. When the TSH quartiles increased, the average pulse wave velocity (PWV) values increased linearly. Additionally, it was found that the serum triglyceride level is a strong predictor of the TSH level.

Conclusion: Following menopause, there is an increased risk of cardiovascular disease. It is important to treat hyperthyroidism as soon as possible and to take into account the possible link between thyroid abnormalities and cardiovascular disease, as the illness is more common in women. TSH suppression must be avoided in perimenopausal or postmenopausal women taking medication for hypothyroidism.

Keywords: Cardiovascular hemodynamics, Menopause, Thyroid disorder

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Introduction

The Indian Menopause Society defines menopause as the period in a woman's life when she moves from the reproductive to the nonreproductive phases. It is a phenomenon that protects the aging population from reproductive morbidity and mortality. It causes noncommunicable diseases to progress more quickly and paves the way for aging. Menopause, spontaneous or natural: It is acknowledged to have happened following a year of amenorrhea, for which there are no apparent physiological or medical reasons. The nearly total but normal reduction in ovarian hormone release is caused by the ovarian follicles' depletion.[1,2]

Menopausal, Thyroid and Coronary Heart disease

Many risk factors can accumulate throughout menopause, one of which is the increased risk of cardiovascular disease caused by the body's normal lowering of estrogen during perimenopause. Greater clinical and socioeconomic relevance for these problems, which are made worse by additional dangers, accompany higher life expectancies. The main topic of this review paper is the inter-relationship between thyroid dysfunction and cardiovascular disease after menopause as a risk factor. Thyroid disorders are more common in older adults and significantly more common in women than in men. Thyroid conditions, such as hyper- and hypothyroidism, influence the risk of heart disease (Figure 1).[3]

Corresponding author

Rashmi Shrivastava, Department of Physiology, King George's Medical University, Lucknow, UP, India. Email: rashmishrivastava417@kgmcindia.edu

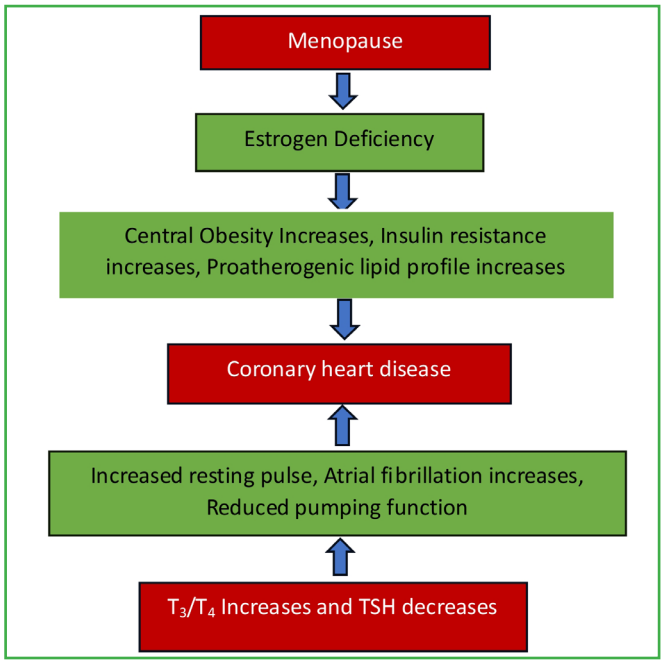

Figure 1: Thyroid conditions influencing the risk of heart disease.

The impact of thyroid hormone on the hemodynamics of the heart- There is a high association between thyroid status and cardiac functions, such as heart rate, cardiac output, and systemic vascular resistance, according to several invasive and noninvasive studies conducted on patients with thyroid disorders. Apart from its established effect of increasing peripheral oxygen consumption and substrate requirements, thyroid hormone also directly increases cardiac contractility, leading to a secondary rise in cardiac contractility. Triiodothyronine reduces the resistance of the systemic circulation by broadening the arterioles of resistance in the peripheral circulation. Vasodilation and relaxation are the immediate results of its action on vascular smooth muscle cells.

The clinical implication of this study is that a large dose of triiodothyronine improves cardiac output and lowers systemic vascular resistance within hours post coronary artery bypass grafting. Thyroid hormone causes an increase in blood volume. The reduction in systemic vascular resistance causes an increase in renin release and the activation of the angiotensin–aldosterone axis, which in turn causes an effective arterial filling capacity to decrease. Consequently, this promotes renal sodium reabsorption, which raises the plasma level and makes it louder. Thyroid hormone also stimulates the formation of erythropoietin. Together, these two processes increase blood volume and preload, which further increases cardiac output (Figure 2).[4]

Methodology

A selective and thorough literature search was conducted in PubMed, Google scholar, and Cochrane for publications from 2001 and 2023 using the keywords "menopause impact on thyroid disorder and cardiovascular hemodynamics." As part of this, clinical studies, meta-analyses, randomized clinical trials, and systematic review articles were reviewed.

Result And Discussion

Relationship between Thyroid Dysfunction and Blood Lipid

Role of Menopausal Impact

There have been significant correlations discovered between hypertriglyceridemia and hypothyroidism. A significant elevated risk of hypertriglyceridemia and hyper-low-density lipoprotein cholesterolemia (H-LDL-C) has been associated with subclinical hypothyroidism. A positive correlation was observed between the risk of low-high density lipoprotein cholesterolemia (L-HDL-C) and hyperthyroidism, whereas a significant negative link was found with the risk of hypercholesterolemia and (H-LDL-C). The correlation between blood lipids and subclinical hyperthyroidism was not found to be significant.

Hypertriglyceridemia was more likely in women who had hypothyroidism than in those who were postmenopausal. Subclinical hypothyroidism was significantly associated with (L-HDL-C) and increased hypertriglyceridemia in premenopausal women. Hyperthyroidism was substantially associated with a lower risk of hypercholesterolemia and (H-LDL-C), in premenopausal women, but a higher risk of (L-HDL-C) in postmenopausal women. Abnormal thyroid function significantly affects blood lipid levels and is closely linked to female menopause.[5]

Heart Disease Risk at Low TSH Levels

A population-based study found that older individuals with low TSH levels (< 0.5 mIU/L) at 2- and 5-year follow-ups were significantly more likely to die from heart disease. At the 2- and 5-year follow-ups, all-cause mortality was higher in this collective with low TSH levels compared to those whose levels were ≥ 0.5 mIU/L. A new meta-analysis found that sub-clinical hyperthyroidism was associated with an increased risk of coronary heart disease. Prolonged suppression of TSH can lead to an increased resting pulse, frequent arrhythmias, such as atrial fibrillation, and poor pump function. Cardiovascular disease risk is higher in patients (male and female) receiving L-thyroxine medication and having suppressed TSH levels.[3]

Role of Thyroid Stimulating Hormone (TSH) on Arterial Stiffness

Women who have elevated TSH levels compared to those with lower TSH levels have stiffer arteries. With rising TSH quartiles, the mean values of pulse wave velocity (PWV) rose linearly. Compared to those whose serum TSH levels were less than 2.5 mIU/mL, those whose PWV values were significantly higher. Upon conducting multivariate analysis, the only significant predictors of PWV found were age, insulin resistance, and TSH levels greater than 2.5 mIU/mL. While thyroid antibodies were not connected to any of the arterial markers, no correlations were observed between the other markers and thyroid hormone levels. A reassessment of the effects on the vasculature on the upper limit of normal TSH in postmenopausal women might be necessary.[6]

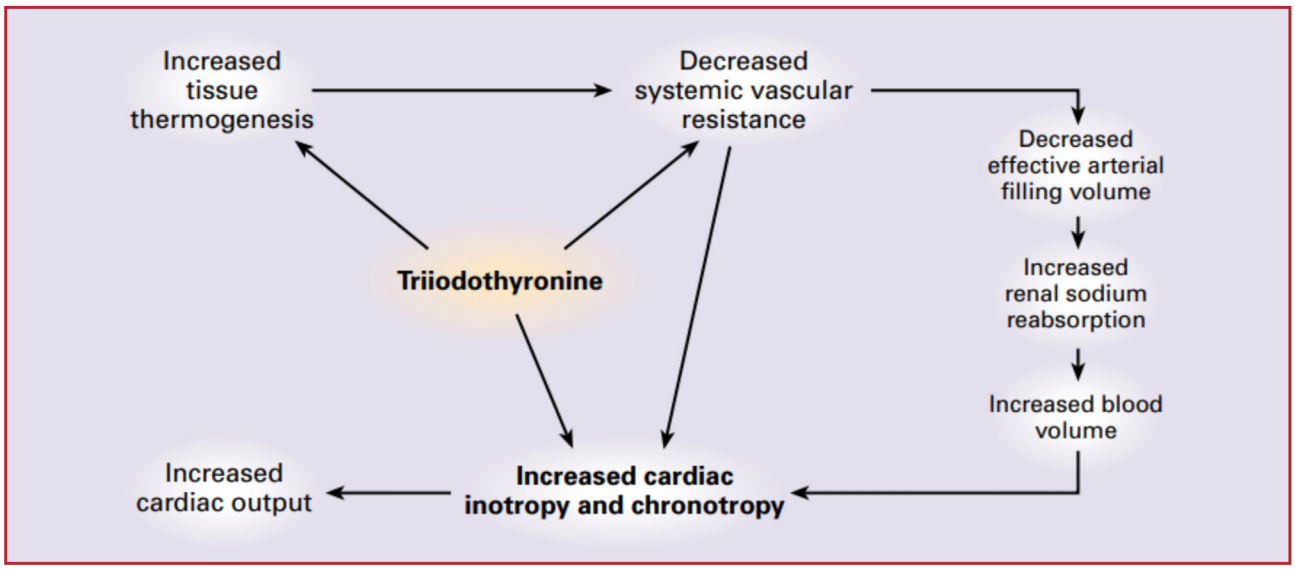

Figure 2: Thyroid hormone also stimulates the formation of erythropoietin, resulting in increased cardiac output.

Role of Thyroid Stimulating Hormone (TSH) on Presence of Coronary Atherosclerosis

Age and TSH were found to be associated with an increased risk of coronary atherosclerosis in euthyroid postmenopausal women. In a study, findings also revealed that serum triglycerides were a significant predictor of serum TSH. Serum TSH and serum triglycerides (TG) were related in multiple linear regression analysis. A higher incidence of coronary atherosclerosis in euthyroid postmenopausal women was linked to rising age and serum TSH in multiple logistic regression analysis. In healthy postmenopausal women, screening and risk assessment for CVD might be beneficial prior to the development of atherosclerosis.[7]

Hyperthyroidism is associated with the Development of Vasospastic Angina

Changes in vasomotor tone are the cause of a functional condition known as vasospastic angina (VA). Results of a study indicated that hyperthyroidism was linked to the onset and outcome of VA. The study's data came from a prospective multicenter registry that included individuals with symptoms that might point to VA. Patients were divided into two groups based on the results of coronary angiography and an ergonovine provocation test: VA and non-VA. 831 patients were categorized as belonging to the VA group out of 1239 patients who had probable VA. Hyperthyroidism was more common in the VA group than in the non-VA group.

The risk of VA was shown to be 3.27 times higher in those with hyperthyroidism, even after controlling for confounding variables. A 4.38-fold increased incidence of VA was linked to hyperthyroidism, particularly in women. Whether hyperthyroidism was present or absent did not affect the overall cause-death rate. The incidence of VA, particularly in women, is independently linked to hyperthyroidism; however, this association did not influence the overall death rate among VA patients. The function of the thyroid in individuals with probable VA has to be understood by clinicians.[8]

Effect of Thyroxin replacement on Endothelial Function and Carotid Artery Intima-media Thickness

A study revealed no correlation between free T4 and serum thyroid-stimulating hormone and the thickness of the intima-media in the carotid arteries or brachial flow-mediated vasodilatation. After a year, the subclinical hypothyroidism control group's flow-mediated vasodilatation significantly decreased (from 17.33 ± 7.88 to 13.1 ± 4.75%, $p = 0.03$), but the L-thyroxine-treated group's flow-mediated vasodilatation did not significantly differ (from 16.81 ± 7.0 to 18.52 ± 7.44%, $p = 0.39$). The mean carotid intima-media thickness did not significantly change following a 12-months course of L-thyroxine administration. Replacement therapy keeps the subclinical hypothyroidism state from progressing while preventing a decrease in flow-mediated vasodilatation. For patients with subclinical hypothyroidism, large prospective multicenter placebo-controlled trials are required to further explore endothelium physiology and identify its role.[9]

The staging of menopause has been explained in the study done by Anklesaria BS (2013).[10]

Conclusion

Menopause raises the risk of cardiovascular diseases, hence screening and evaluating postmenopausal healthy women's risks for CVD might be beneficial before atherosclerosis manifests. Owing to the high incidence of thyroid disease in women, hyperthyroidism, which might increase the risk of the condition, needs to be detected and treated as soon as possible. Thyroid dysfunction is strongly associated with female menopause and has a significant impact on blood lipid levels. Research indicated that serum TG was a significant predictor of serum TSH, and that in postmenopausal euthyroid women, elevated TSH and age were associated with a higher risk of coronary atherosclerosis. TSH suppression should be avoided in postmenopausal and perimenopausal women receiving treatment for hypothyroidism.

Women whose TSH is in the upper reference range have higher arterial stiffness than do those whose TSH is lower. It might be necessary to reevaluate the upper limit of normal TSH in postmenopausal women in light of the effects on the vasculature. Although it has no bearing on the overall death rate among VA patients, hyperthyroidism is independently linked to the development of VA, particularly in women. The vasodilator isoproterenol significantly reduced the amount of radiolabeled phosphate incorporated into the myosin light chains in VSM cells, but T3 had no effect on the phosphorylation of these proteins. Nitric oxide synthesis was absent from primary cultures of vascular endothelial cells exposed to T3, as indicated by cellular cGMP levels and nitrite release, indicating that T3 directly affected the VSM cell.

Replacement therapy prevents a decline in flow-mediated vasodilatation by prolonging the state of subclinical hypothyroidism. Large prospective multicenter placebo-controlled trials are necessary to better understand endothelial physiology in people with subclinical hypothyroidism and explore the effects of L-thyroxine therapy on endothelial function in patients.

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