ORIGINAL ARTICLE

Eastern Journal of Medicine
East J Med 30(2): 275-280, 2025
DOI: 10.5505/ejm.2025.77864

Relationship Between Total Atrial Conduction Time and Epicardial Adipose Tissue In Patients With Subclinical Hypothyroidism

Yemlihan Ceylan[1*], Elif Eker[2]

[1]*Department of Cardiology, Faculty of Medicine, Van Yuzuncu Yil University, Van, Turkey*
[2]*Department of Internal Medicine, Faculty of Medicine, Osmangazi University, Eskisehir, Turkey*

ABSTRACT

Subclinical hypothyroidism (SCH) is characterized by elevated thyroid-stimulating hormone (TSH) levels with normal free thyroxine (fT4) levels. It is associated with increased cardiovascular risk, necessitating regular monitoring of cardiovascular parameters.

This study investigated the relationship between total atrial conduction time (TACT) and epicardial adipose tissue (EAT) in patients diagnosed with SCH, aiming to identify potential cardiovascular risks.

An observational cross-sectional study was conducted at Van Yüzüncü Yıl University from January 2024 to January 2025. Fifty-four patients with SCH (TSH levels 5.0-10 μIU/mL, normal fT4) were compared to fifty-four healthy controls. Echocardiographic measurements, including EAT thickness and TACT, were obtained.

No significant differences were found between groups regarding age, gender, and various laboratory parameters. TSH levels were significantly higher in the patient group 7.39±1.29 μIU/mL compared to controls 2.33±0.93 μIU/mL, p=0.001; EAT 6.74±0.96 mm vs. 4.73±0.41 mm, p=0.001 and TACT 122±8.70 ms vs. 87.8±5.33 ms, p=0.001 were also significantly elevated in SCH patients. A strong positive correlation was observed between EAT and TACT (r=0.895, p=0.001) as well as between TSH and both EAT and TACT (r=0.701, p=0.001; r=0.822, p=0.001).

SCH patients exhibit significantly increased EAT and TACT levels compared to healthy controls, indicating a heightened risk for adverse cardiovascular outcomes. The strong correlation between TSH, EAT, and TACT underscores the importance of monitoring TSH levels and suggests that proactive management of SCH may mitigate cardiovascular risks.

Keywords: Subclinical hypothyroidism, total atrial conduction time, epicardial adipose tissue, cardiovascular risk, echocardiography.

Introduction

Subclinical hypothyroidism (SCH) is an endocrine disease characterized by elevated levels of thyroid-stimulating hormone (TSH), while free thyroxine (fT4) levels are preserved within normal limits. (1) Although SCH is more common in older individuals and women, it can also be seen in the young population. (2) In patients diagnosed with SCH, hormone therapy is recommended if symptoms are or the TSH level is above 10 μIU/mL. In contrast, drug therapy is not recommended in patients without symptoms. (3) SCH is associated with cardiovascular disease and mortality. (4) Therefore, it is essential to regularly monitor individuals diagnosed with SCH and closely monitor cardiovascular risk factors.

Total atrial conduction time (TACT) reflects atrial conduction time and can be measured echocardiographically. Long TACT is associated with arrhythmias, particularly atrial fibrillation. (5,6)

Epicardial adipose tissue (EAT) is a metabolically highly active adipose tissue between myocardial tissue and visceral pericardium. EAT is associated with cardiovascular diseases. EAT has also been shown to be increased in SCH patients. (7)

There are not enough studies investigating the relationship between EAT and TACT in SCH patients. Therefore, investigation of these parameters associated with adverse cardiovascular outcomes may allow early detection of cardiovascular risks in SCH patients, and timely measures may be taken.

This study examined the association between TACT and EAT in patients diagnosed with SCH.

***Corresponding Author:** Dr. Yemlihan Ceylan, Department of Cardiology, Faculty of Medicine, Van Yuzuncu Yil University, Van, Turkey
E-mail: dryceylan@yahoo.com, Telephone number: +90 432 216 47 05 – 6330, Fax number: +90 432 216 47 05
ORCID ID: Yemlihan Ceylan: 0000-0002-0443-1014, **Elif Eker:** 0000-0001-7923-9345
Received: 23.02.2025, **Accepted:** 28.03.2025

Materials and Method

This observational cross-sectional study was designed according to the Strobe guidelines. Between January 2024 and January 2025, patients who were followed up in the Van Yuzuncu Yil University medical faculty endocrinology clinic diagnosed with subclinical hypothyroid and referred to our cardiology outpatient clinic were included. The study was conducted in accordance with the principles stated in the Declaration of Helsinki. The approval of the Van Yüzüncü Yıl University Ethics Committee numbered 16.08.2023/08 was obtained.

Study Population and Protocol: Patients with a diagnosis of subclinical hypothyroidism with serum TSH levels between 5.0-10 μIU/mL and free T4 (fT4) levels within the normal range and without any symptoms were referred to our cardiology outpatient clinic at Van Yüzüncü Yıl University endocrinology outpatient clinic. Fifty-four consecutive patients diagnosed with SCH were included in the study. Fifty-four healthy individuals were matched in terms of age and gender. Individuals with regular thyroid function tests without any chronic disease were selected.

- Patient Recruitment Criteria: - Patients between 18-60 years of age, - consented patients - Exclusion Criteria: - hyperthyroidism, - hypertension, - coronary artery disease, - heart failure (EF<50%) or NYHA 3-4 patients, - diabetes mellitus, - chronic renal failure, - history of stroke, - atrial fibrillation, - severe valvular disease, - patients receiving thyroid hormone therapy or medications that may affect the cardiovascular system (such as beta-blockers, calcium channel blockers, diuretics), - pregnant and lactating patients, - patients with active infections or hospitalization in the last 6 months

Data collection

- EAT thickness was measured as the space between the right ventricular apex and the visceral pericardium at end-systole, as reported in the literature. (8) Figure 1
- TACT was measured from the onset of the p wave to the peak of the velocity a' obtained via tissue Doppler imaging. (9) Figure 2
- Echocardiographic data, EAT thickness, TACT, and laboratory findings were recorded. Transthoracic echocardiograms were performed by an experienced cardiologist unaware of the patient's clinical information. Standard echocardiographic measurements were taken based on the current guidelines (10). PW Doppler transmitral inflow velocities were obtained as the early (E) and late (A) mitral inflow velocities during diastole, and the E/e' ratio was calculated after measuring the early (e') velocity by tissue Doppler imaging.

Statistical Analysis

Sample Size: In the study, Epicardial adipose tissue (EAT) was considered as primarily outcome variable. Standard deviation (σ) for EAT ranged from 0.3 to 1.1. Thus, it was considered as 0.7 in the present study. Effect size was assumed 0.3 and 1.96 of Z value was used for the 0.05 type I error rate. Based on this information and according to the equation of sample size calculation ($n= Z^2 \sigma^2 / d^2$), the minimum sample size was computed as 21.

Descriptive statistics for the continuous variables were presented as Mean ± Standard deviation; while numbers and percentages for categorical variables. Independent t-test was performed to compare the patient and control groups for the studied variables. The Pearson correlation coefficient was utilized to determine the linear relationship between EAT and TACT values. In addition, Regression analysis was performed for EAT and TACT by considering TSH as independent (explanatory) variable. Statistical significance level was considered as 5% and SPSS (ver: 26) statistical package program was used for calculations.

Results

Echocardiographic and laboratory parameters between groups are compared in Table 1. No statistically significant differences were found between of the groups in terms of age, male ratio, smoking, BMI, lipid panel, glucose, hemoglobin, hematocrit, WBC, platelet, LVEF, eGFR, mitral E/A, IVRT, DT, LAVi, fT4 values. TSH values were statistically significant at 7.39±1.29 μIU/mL and 2.33±0.93 μIU/mL in the patient group and control group, respectively (p=0.001). Among echocardiography parameters, mitral lateral E/e' was 8.06±1.26 in the patient group and 7.56±1.38 in the control group, which was statistically significant; p=0.049. EAT and TACT values were significantly higher in the patient group, 6.74±0.96 mm vs 4.73±0.41 mm, p=0.001; 122±8.70 ms vs 87.8±5.33 ms, p=0.001, respectively.

Pearson correlation analysis demonstrated a statistically significant correlation between EAT

Table 1: Descriptive statistics and comparison results for the considered variables

	Patient	Control	p-value
Male, n (%)	12 (22)	11 (20)	0.816
Smoking, n (%)	11 (20)	12 (22)	0.816
	Mean ± SD	Mean ± SD	
Age	42±6.4	41±5.5	0.771
Glucose, mg/dL	87.6±5.2	87.4±4.8	0.818
eGFR, mL/second	98.6±6.17	99.3±6.21	0.525
Hemoglobin, mg/dL	13.4±1.92	13.4±1.62	0.966
Hematocrit, %	40.7±5.47	41.0±4.92	0.754
White blood cell count (WBC), $10^3/mm^3$	8.11±1.62	8.07±1.20	0.896
Platelet count, $10^3/mm^3$	223±44.4	223±41.0	0.946
Body mass index (BMI), kg/m^2	26.3±3.27	25.9±2.94	0.472
LDL cholesterol, mg/dL	113±32.9	107±27.9	0.272
HDL cholesterol, mg/dL	42.7±10.8	46.1±8.30	0.068
Triglyceride, mg/dL	170±88.3	168±80.2	0.890
Epicardial adipose tissue (EAT), mm	6.74±0.96	4.73±0.41	0.001
Ejection fraction (EF), %	62.6±1.93	62.5±1.16	0.857
Mitral inflow E/A	1.20±0.18	1.20±0.09	0.901
Mitral lateral E/e'	8.06±1.26	7.56±1.38	0.049
Mitral septal E/e'	9.30±1.30	8.85±1.50	0.102
Isovolumic relaxation time (IVRT), ms	89.2±7.85	87.6±5.71	0.210
Deceleration time (DT), ms	197±23.0	197±21.9	0.884
Total atrial conduction time (TACT), ms	122±8.70	87.8±5.33	0.001
fT4, ng/dL	1.10±0.15	1.08±0.16	0.669
TSH, μIU/mL	7.39±1.29	2.33±0.93	0.001
LAVi, mL/m^2	29.2±2.33	28.9±1.54	0.447

Abbreviations: eGFR: estimated glomerular filtration rate; E/A: ratio of the early and late velocities E/e': ratio of the early velocities; fT4: free thyroxine; TSH, μIU/mL: thyroid stimulating hormone, micro-international units per milliliter; LAVi: left atrial volume index; SD: Standard Deviation

Table 2: Brief results of Linear regression analysis for EAT and TACT

	Dependent variables: EAT		Dependent variables: TACT	
	Coefficient ± Standard Error	p	Coefficient ± Standard Error	p
Constant	4.203 ± 0.173	0.001	78.180 ± 2.048	0.001
TSH	0.031 ± 0.003	0.001	5.442 ± 0.366	0.001
R2	0.242	0.001	0.457	0.001

and TACT, r=0.895 and p=0.001, and was shown in Figure 3.

Pearson correlation analysis showed a statistically significant correlation of TSH values between EAT and TACT; r=0.701, p=0.001; r=0.822 p=0.001, respectively, and was shown in Figure 4.

Pearson correlation analysis with EAT and TACT according to gender showed no statistically significant relationship: p=0.414 and p=0.590, respectively.

In linear regression analysis, the effect of TSH values on EAT and TACT values was statistically significant, as shown in Table 2.

Discussion

Our study found that the values of EAT, TACT, and mitral lateral E/e' were significantly higher in SCH patients. The high EAT, TACT, and mitral E/e' values are fundamental in showing that SCH

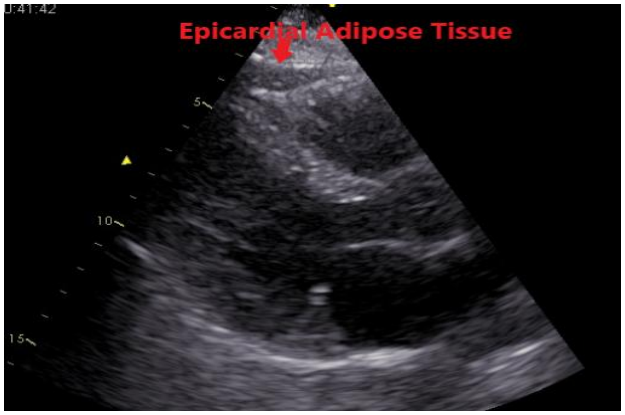

Fig. 1. Epicardial adipose tissue is shown with a red arrow

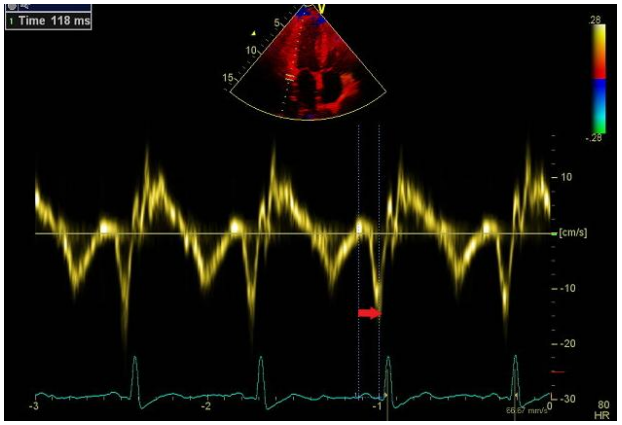

Fig. 2. The total atrial conduction time measurement is shown as a red arrow

patients face the risk of adverse cardiovascular outcomes even without symptoms.

The study by Udovcic et al. (11), which examined the effects of SCH on cardiovascular diseases, showed that the risk of heart failure may increase. Similarly, Nakanishi et al. (12), showed that left atrial reserve and conduction functions in SCH patients were impaired, which may increase the risk of heart failure. The mitral lateral E/e' values, indicators of diastolic function, were higher in SCH patients, which is consistent with the existing literature.

EAT values were significantly higher in SCH patients. Clossa et al. (7) showed in their review that in SCH patients, EAT thickness was increased, which may be associated with cardiovascular risk. Korkmaz et al. (13), showed that EAT increased in patients with SCH, and a positive correlation was found between EAT and TSH. Our study also found a strong correlation between EAT and TSH. These results show the importance of closely monitoring TSH and EAT thickness, which are closely associated with cardiovascular diseases in SCH patients.

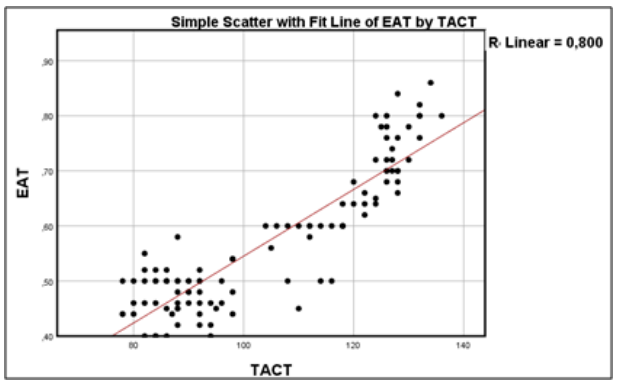

Fig. 3. Pearson correlation analysis between EAT and TACT

TACT time was significantly higher in SCH patients. In the review by Singh et al. (14), SCH was associated with atrial fibrillation. In Irdem et al. (15), diastolic dysfunction, and atrial conduction times were evaluated in pediatric patients with SCH. These values were higher in SCH patients. These results are also compatible with our results. Also, our study found a positive correlation between EAT and TACT. Canpolat et al. (16) reported a positive correlation between EAT and TACT time in patients diagnosed with atrial fibrillation. Ernault et al. (17) showed that EAT increased arrhythmias. Therefore, both EAT and TACT are closely related to arrhythmias. The fact that both values are increased in SCH patients creates a strong basis for the occurrence of arrhythmias and indicates potential targets for preventing arrhythmias.

One of the important results of our study is that there is a significant correlation between TSH values and EAT and TACT. In the review study by Redford et al.(18) reported that high TSH levels may increase cardiovascular risks in SCH patients. Inoue et al. (19) also showed that high TSH levels increased the risk of all-cause mortality. Bielecka-Dabrowa et al. (20), reported in their review that high TSH levels were associated with diastolic dysfunction and increased the risk of heart failure in SCH patients. This positive correlation between TSH levels and EAT and TACT values reveals the importance of close monitoring of TSH levels and initiating hormone therapy at the appropriate time in SCH patients. Indeed, the meta-analysis of Liu et al. (21) showed that left ventricular diastolic and systolic functions could be improved with levothyroxine treatment initiated at the appropriate time in SCH patients.

Study Limitations and Strengths: Our sample size is not satisfactory to generalize our findings to the general population. Large-scale studies help

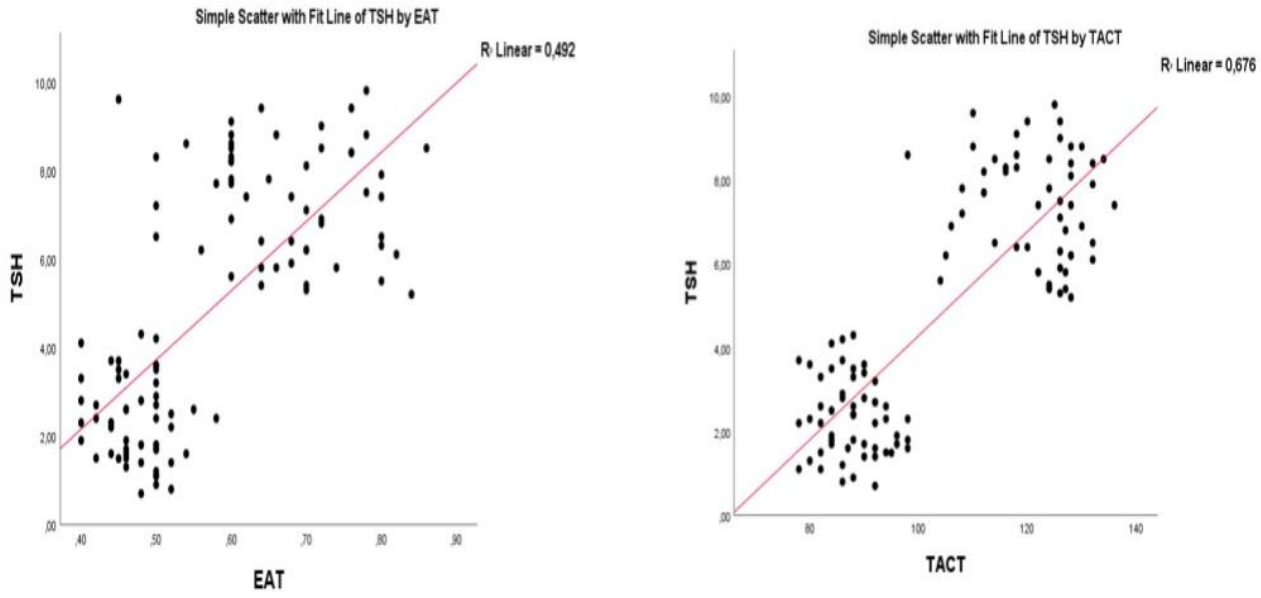

Fig. 4. Pearson correlation analysis of TSH between EAT and TACT

us better understand the effects of SCH on cardiovascular outcomes. TSH levels were measured only once. Monitoring changing TSH levels over time would have allowed us to assess better the changes in EAT, TCAT, and cardiac functions. EAT and TACT values were measured by transthoracic echocardiography. Using different measurement methods or devices may affect the consistency of the results. In our study, patients had no follow-up period. Therefore, we could not observe whether arrhythmic problems or cardiovascular diseases occurred in patients.

The strength of our study was that SCH patients did not have any chronic disease or cardiovascular disease. Therefore, a study design was realized with a very homogeneous population without the possible effects of comorbidities.

This study demonstrates that SCH patients have significantly increased EAT and TACT levels compared to healthy controls, suggesting an increased risk for adverse cardiovascular outcomes. Monitoring EAT and TACT values in SCH patients might help to detect patients at elevated risk for cardiovascular complications. Furthermore, the positive correlation between TSH, EAT, and TACT emphasizes the importance of TSH monitoring in this patient group. These findings suggest that a proactive approach to SCH management should be adopted. Further research is needed to establish the clinical importance of EAT and TACT in this patient group's follow-up and treatment processes.

References

1. Patrizio A, Ferrari SM, Elia G, Ragusa F, Balestri E, Botrini C, et al. Hypothyroidism and metabolic cardiovascular disease. Vol. 15, Frontiers in Endocrinology. Frontiers Media SA; 2024.
2. Wang X, Wang H, Li Q, Wang P, Xing Y, Zhang F, et al. Effect of Levothyroxine Supplementation on the Cardiac Morphology and Function in Patients With Subclinical Hypothyroidism: A Systematic Review and Meta-analysis. Vol. 107, Journal of Clinical Endocrinology and Metabolism. Endocrine Society; 2022. p. 2674–83.
3. Bekkering GE, Agoritsas T, Lytvyn L, Heen AF, Feller M, Moutzouri E, et al. Thyroid hormones treatment for subclinical hypothyroidism: A clinical practice guideline. The BMJ. 2019;365.
4. Tseng FY, Lin WY, Lin CC, Lee LT, Li TC, Sung PK, et al. Subclinical hypothyroidism is associated with increased risk for all-cause and cardiovascular mortality in adults. J Am Coll Cardiol. 2012 Aug 21;60(8):730–7.
5. Müller P, Weijs B, Bemelmans NMAA, Mügge A, Eckardt L, Crijns HJGM, et al. Echocardiography-derived total atrial conduction time (PA-TDI duration): risk stratification and guidance in atrial fibrillation management. Vol. 110, Clinical Research in Cardiology. Springer Science and Business Media Deutschland GmbH; 2021. p. 1734–42.
6. Weijs B, De Vos CB, Tieleman RG, Pisters R, Cheriex EC, Prins MH, et al. Clinical and echocardiographic correlates of intra-atrial

conduction delay. Europace. 2011 Dec;13(12):1681–7.

7. Closs C, Vargas-Uricoechea H, Schwarzstein D, Lobo M, Lagranja E, Godinez-Leiva E, et al. Relationship of Subclinical Hypothyroidism on Epicardial Adipose Tissue: A Systematic Review and Meta-Analysis. Vol. 48, Current Problems in Cardiology. Elsevier Inc.; 2023.
8. Iacobellis G, Ribaudo MC, Assael F, Vecci E, Tiberti C, Zappaterreno A, et al. Echocardiographic Epicardial Adipose Tissue Is Related to Anthropometric and Clinical Parameters of Metabolic Syndrome: A New Indicator of Cardiovascular Risk. Journal of Clinical Endocrinology and Metabolism. 2003 Nov;88(11):5163–8.
9. Müller P, Schiedat F, Bialek A, Bösche L, Ewers A, Kara K, et al. Total atrial conduction time was assessed by tissue Doppler imaging (PA-TDI interval) to predict early recurrence of persistent atrial fibrillation after successful electrical cardioversion. J Cardiovasc Electrophysiol. 2014 Feb;25(2):161–7.
10. Lang RM, Badano LP, Victor MA, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Journal of the American Society of Echocardiography. 2015;28(1):1-39.e14.
11. Udovcic Maja PRHPB. Hypothyroidism and The Heart. Houstonmethodist.org/debakey-journal. 2017;
12. Nakanishi K, Daimon M, Yoshida Y, Sawada N, Hirose K, Iwama K, et al. Subclinical hypothyroidism as an independent determinant of left atrial dysfunction in the general population. 2020; Available from: https://academic.oup.com/endocrinesociety/pages/Author_GuidelinesforAccepted
13. Korkmaz L, Sahin S, Akyuz AR, Ziyrek M, Anaforoglu I, Kose M, et al. Epicardial adipose tissue increased in patients with newly diagnosed subclinical hypothyroidism. Medical Principles and Practice. 2012 Dec;22(1):42–6.
14. Singh H, Shahid MZ, Harrison SL, Lane DA, Lip GYH, Logantha SJRJ. Subclinical thyroid dysfunction and the risk of incident atrial fibrillation: A systematic review and meta-analysis. Vol. 19, PLoS ONE. Public Library of Science; 2024.
15. Irdem A, Aydın Sahin D, Kervancioglu M, Baspinar O, Sucu M, Keskin M, et al. Evaluation of P-Wave Dispersion, Diastolic Function, and Atrial Electromechanical Conduction in Pediatric Patients with Subclinical Hypothyroidism. Echocardiography. 2016 Sep 1;33(9):1397–401.
16. Canpolat U, Aytemir K, Özer N, Oto A. Relationship between the epicardial fat thickness and total atrial conduction time in patients with lone paroxysmal atrial fibrillation. Int J Cardiol. 2015 Apr 15;185:106–8.
17. Ernault AC, de Winter R, Fabrizi B, Bracht JWP, Hau C, van Amersfoorth SCM, et al. MicroRNAs in extracellular vesicles released from epicardial adipose tissue promote arrhythmogenic conduction slowing. Heart Rhythm O2. 2023 Dec 1;4(12):805–14.
18. Redford C, Vaidya B. Subclinical hypothyroidism: Should we treat? Vol. 23, Post Reproductive Health. SAGE Publications Ltd; 2017. p. 55–62.
19. Inoue K, Ritz B, Brent GA, Ebrahimi R, Rhee CM, Leung AM. Association of Subclinical Hypothyroidism and Cardiovascular Disease with Mortality. JAMA Netw Open. 2020;3(2).
20. Bielecka-Dabrowa A, Godoy B, Suzuki T, Banach M, von Haehling S. Subclinical hypothyroidism and the development of heart failure: an overview of risk and effects on cardiac function. Vol. 108, Clinical Research in Cardiology. Dr. Dietrich Steinkopff Verlag GmbH and Co. KG; 2019. p. 225–33.
21. Liu G, Ren M, Du Y, Zhao R, Wu Y, Liu Y, et al. Effect of thyroid hormone replacement treatment on cardiac diastolic function in adult patients with subclinical hypothyroidism: a meta-analysis. Vol. 14, Frontiers in Endocrinology. Frontiers Media SA; 2023.