ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/cardiosci.2021-83346

P Wave and QT Dispersion in Patients with Subclinical Hypothyroidism: Case-control Research

Subklinik Hipotiroidide P Dalga ve QT Dispersiyonunun İncelenmesi: Vaka-kontrol Araştırması

Cennet YILDIZ[a], Ahmet KARAKURT[b]

[a]Clinic of Cardiology, Ekotom Medical Center, İstanbul, TURKEY
[b]Department of Cardiology, Kafkas University Faculty of Medicine, Kars, TURKEY

ABSTRACT Objective: Thyroid hormones have important effects on cardiovascular system. The aim of the present study was to assess QT and P wave dispersion (PWD) in subclinic hypothyroid patients. **Material and Methods:** A total of 125 subjects were enrolled in the study. The study group consisted of 60 subclinical hypothyroid patients, and the control group included 66 age and sex matched individuals. All subjects underwent two-dimensional echocardiographic and electrocardiographic examination. QT dispersion (QTD), corrected QTD (QTDc) and PWD were calculated. **Results:** There were no differences between two groups with respect to age, gender, smoking habit, heart rate, systolic and diastolic blood pressure. Study group had higher values of Max QT, min QT, QTD, max QTc, minQTc, QTDc, P max, P min and PWD and thyroid stimulating hormone (TSH) level compared to control group. Serum TSH levels were positively correlated with max QT, min QT, QTD, max QTc, min QTc, QTDc, P max, P min and PWD intervals. According to multivariate logistic regression analysis, PWD (OR: 1.046, 95% CI: 1.03-1.090, p=0.034) was an independent predictor for the presence of subclinical hypothyroidism. Receiver operating characteristic curve analysis demonstrated that PWD value of 49.5 ms predicted subclinical hypothyroidism with 66.7% sensitivity and 62.1% specificity (AUC: 0.674, 95% CI: 0.581-0.765, p=0.001). **Conclusion:** QTD, QTDc and PWD may be used in clinical practice to evaluate subclinical hypothyroid patients who are at risk of arrhythmias and paroxysmal atrial fibrillation.

Keywords: Hypothyroidism; elektrocardiography; arrhythmias

ÖZET Amaç: Tiroid hormonu kardiyovasküler sistem üzerinde önemli etkilere sahiptir. Bu çalışmanın amacı, subklinik hipotiroidi hastalarında P dalga ve QT dispersiyonunu analiz etmektir. **Gereç ve Yöntemler:** Çalışmaya toplam 125 kişi alındı. Çalışma grubu 60 subklinik hipotiroidi hastası, kontrol grubu ise 66 yaş ve cinsiyete göre eşleştirilmiş bireyden oluştu. Çalışmaya alınan tüm bireylere 2-boyutlu ekokardiyografik inceleme, elektrokardiyogram yapıldı. QT dispersiyonu (QTD), düzeltilmiş QTD (QTDd) ve P dalga disepersiyonu (PDD) ölçüldü. **Bulgular:** Her 2 grup arasında yaş, cinsiyet, sigara içiciliği, sistolik kan basıncı, diyastolik kan basıncı ve kalp hızı bakımından fark bulunmadı. Maksimum QT, minimum QT, QTD, maksimum QTd, minimum QTd, QTDd, P maksimum, P minimum, PDD ve tiroid stimule edici hormon (TSH) çalışma grubunda anlamlı olarak yüksek bulundu. Serum tiroid uyarıcı hormon değeri ile elektrokardiyografik parametreler arasında istatistiksel olarak anlamlı korelasyon saptandı. Multivaryant lojistik regresyon analizine göre PDD subklinik hipotirodi varlığı için bağımsız bir prediktör idi (OR: 1,046, %95 CI: 1,03-1,090, p=0,034). PDD'nin 49,5 ms değeri subklinik hipotiroidiyi %66,7 duyarlılık ve %62,1 özgüllük ile predikte etti (AUC: 0,674, %95 CI: 0,581-0,765, p=0,001). **Sonuç:** QTD, QTDd, PDD subklinik hipotiroidi hastalarında uzamıştır ve bu parametreler aritmi ve paroksizmal atriyal fibrilasyon tahmini için kullanılabilirler.

Anahtar Kelimeler: Hipotiroidi; elektrokardiogram; aritmi

Subclinical hypothyroidism, or mild thyroid failure, is a described as a state in which the thyroid stimulating hormone (TSH) level is increased with normal free T3 and T4 levels. Its prevalence ranges from 4% to 10% in the general population and increases with age.[1] It is mostly asymptomatic, but affected individuals may show symptoms such as those seen in overt hypothyroidism, including tiredness, weight gain, and constipation.[2] Deficiency of thyroid hormones is associated with increased cardiovascular mortality, arrhythmia, autonomic disturbances, and heart failure.[3,4] However, the impact of subclinical hypothyroidism on the cardiovascular autonomic system remains a matter of debate. Several studies have

Correspondence: Cennet YILDIZ
Clinic of Cardiology, Ekotom Medical Center, İstanbul, TURKEY/TÜRKİYE
E-mail: cennet_yildiz@live.com

Peer review under responsibility of Turkiye Klinikleri Cardiovascular Sciences.

Received: 25 Mar 2021 ***Received in revised form:*** 22 May 2021 ***Accepted:*** 24 May 2021 ***Available online:*** 03 Jun 2021

documented a hypofunctional parasympathetic system and increased activity of the sympathetic system by analyzing heart rate variability.[5,6] However, an increase in parasympathetic activity, along with decreased sympathetic activity, has also been reported.[7]

Duration of ventricular depolarization and repolarization are represented on electrocardiogram (ECG) as QT interval. Extension of one or both of these components is associated with QT prolongation. QT dispersion (QTD) is the difference between the shortest and longest QT intervals calculated from a surface ECG. An increase in QTD values is associated with autonomic nervous system abnormalities and decreased parasympathetic tonus in healthy subjects.[8] It has prognostic value in several clinical conditions, such as acute myocardial infarction, heart failure, diabetes mellitus, and stroke.[9-12] An increased QTD has also been reported in systemic lupus erythematosus, rheumatoid arthritis, and ankylosing spondylitis.[13-15] P wave dispersion (PWD) is calculated by subtracting the longest P wave interval from the shortest P wave interval on surface ECG. Increased PWD indicates heterogeneous atrial activation, which favors the generation of atrial arrhythmias. The PWD has a predictive value for atrial fibrillation.[16,17]

Since both PWD and QTD are shown to provide information about autonomic nervous system activity, it is expected that they will become abnormal in various clinical situations. Therefore, the aim of the current study was to investigate these two parameters, which are indirect markers of atrial and ventricular arrhythmias in patients with subclinical hypothyroidism.

MATERIAL AND METHODS

A total of 125 subjects who applied to our clinic between August and December 2020 were included in this case-control study. The study group consisted of 60 subclinical hypothyroid patients, and the control group consisted of 66 age and sex matched individuals. The Kafkas University local ethics committee approval and written informed consent of all participants were obtained prior to the study (approval number: 80576354/223, approval date: 29.05.2020). The study was conducted in accordance with the Helsinki Declaration. Subjects currently taking any medication or those with hypertension, coronary artery disease, rhythm-conduction abnormalities, valvular heart disease, renal/hepatic problems, diabetes mellitus, hyperlipidemia, and chronic diseases were not enrolled in the study.

Body mass index of the study subjects was calculated from self-reported weight and height. Right arm blood pressure (BP) was taken after a five-minute rest. Venous blood samples were drawn from the antecubital vein after an overnight fast. All subjects underwent two-dimensional echocardiographic examination according to the guidelines of the American Society of Echocardiography.[18]

All ECG recordings were performed in relaxed and supine position (Nihon Coden America, Cardiofax S) with a 25 mm/sec paper speed and 1 mV=10 mm calibration. Two cardiologists who were blinded to the patients' data measured P wave and QT intervals manually by using magnifying glass. Measurement of QT interval was done from the beginning of Q wave to the point where T wave returns isoelectric line. If there was an U wave, the nadir between T and U wave was accepted as isoelectric line. Bazzet formula was used to calculate corrected QT interval. For the calculation of P wave duration intersection of the starting and ending points of P wave with isoelectric line was used. PWD was calculated by subtracting the P wave minimum duration from P wave maximum duration. Three consecutive measurements were made for each lead, and averaged value was used for each parameter.

STATISTICAL ANALYSIS

Normality of distribution was assessed by using Kolmogorow-Smirnow test. Parametric and non-parametric data were expressed as mean±SD and median-IQR (IQR1-IQR3), respectively. Comparison between groups was done by using independent samples-t test and Mann-Whitney U test. Categorical data were compared by chi-square test. Correlation between parameters was conducted by Pearson and Spearman correlation analysis. Multivariate logistic regression was made to assess the independent predictors for the presence of subclinical hypothyroidism. Diagnostic values of independent predictors were assessed by receiver operating characteristic

(ROC) curve analysis. A p value of less than 0.05 was considered as significant.

RESULTS

Parameters such as age, gender, smoking habit, systolic blood pressure, diastolic blood pressure and heart rate were not different between two groups. Max QT, min QT, QTD, max QTc, minQTc, QTDc, P max, P min and PWD and TSH level were significantly higher in study group in contrast to control group. Clinical characteristics and electrocardiogram findings of the groups are given in Table 1.

Serum TSH levels were positively correlated with max QT, min QT, QTD, max QTc, min QTc, QTDc, P max, P min and PWD intervals. Correlation of TSH with electrocardiographic parameters is shown in Table 2.

According to multivariate logistic regression analysis, PWD (OR: 1.046, 95% CI: 1.03-1.090, p=0.034) was an independent predictor for the presence of subclinical hypothyroidism. ROC curve analysis demonstrated that PWD value of 49.5 ms predicted subclinical hypothyroidism with 66.7% sensitivity and 62.1% specificity (AUC: 0.674, p=0.001, 95% CI: 0.581-0.766 AUC: 0.675) (Figure 1).

DISCUSSION

There were no differences with respect to free T3 and T4 levels between two groups. Subclinical hypothyroid patients had higher QTD, QTDc, and PWD values than those in the control group. All electrocardiographic parameters had a significantly positive correlation with the TSH level. The only predictor of the presence of subclinical hypothyroidism was PWD

ECG from different leads record the electrical activity of the heart from different angles. Therefore, QTD and PWD were proposed as direct measure-

TABLE 1: Clinical characteristics and electrocardiogram findings of the groups.

	Control group (n=66)	Study group (n=60)	p value
Age (years)	37.56 (31.75-43.00)	36.87 (31.25-41.25)	0.839
Gender (n, %)			0.515
Female	39 (59)	32 (53)	
Male	27 (41)	28 (47)	
Smoking n (%)	10 (15)	9 (15)	0.981
BMI (kg/m^2)	24.555 (23.135-25.797)	24.600 (23.14-25.69)	0.893
SBP (mmHg)	120.00 (100.00-135.00)	120.00 (90.00-130.00)	0.502
DBP (mmHg)	74.50 (69.25-84.00)	75.00 (62.00-84.00)	0.955
HR (bpm)	78.00 (74.00-89.25)	74.00 (69.25-84.00)	0.073
MAX QT (ms)	368.00 (354.75-379.25)	386.50 (355.00-379.00)	<0.001
MIN QT (ms)	332.86±13.382	341.67±12.297	0.039
QTD (ms)	37.42±13.660	45.52±13.351	<0.001
MAX QTc (ms)	386.5 (378.75-395.75)	408.00 (379.00-395.00)	<0.001
MIN QTc (ms)	340.26±13.087	352.28±14.082	<0.001
QTD c (ms)	46.35±14.623	56.90±13.605	0.003
P MAX (ms)	86.00 (84.00-104.00)	98.00 (84.00-104.00)	0.003
P MIN (ms)	53.48±12.045	50.45±13.682	0.003
PWD (ms)	36.41±12.593	48.82±12.861	<0.001
TSH (mU/l)	3.13 (1.862-3.47)	8.95 (6.37-11.20)	<0.001
Free T3 (mU/l)	3.182±0.727	3.365±0.606	0.086
Free T4 (mU/l)	1.275 (1.122-1.427)	1.260 (1.08-1.32)	0.378

BMI: Body mass index; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; HR: Heart rate; Max QT: Maximum QT interval; Max QTc: Maximum corrected QT interval; Min QT: Minimum QT interval; Min QTc: Minimum corrected QT interval; PD: P wave dispersion; P max: Maximum P wave duration; P min: Minimum P wave duration; PWD: P wave dispersion; QTD: QT dispersion; QTDc: Corrected QT dispersion; TSH: Thyroid stimulating hormone; T3: Triiodothyronine; T4: Thyroxine.

TABLE 2: Correlation of thyroid stimulating hormone with electrocardiographic parameters.

	r value	p value
Max QT	0.538**	<0.001
Min QT	0.221*	0.013
QTD	0.383**	<0.001
Max QTc	0.472**	<0.001
Min QTc	0.259**	0.003
QTDc	0.363**	<0.001
P max	0.490**	<0.001
P min	0.174	0.052
PWD	0.430**	<0.001

*Correlations significant at the 0.05 level. **Correlations significant at the 0.01 level. Max QT: Maximum QT interval; Max QTc: Maximum corrected QT interval; Min QT: Minimum QT interval; Min QTc: Minimum corrected QT interval; PD: P wave dispersion; P max: Maximum P wave duration; P min: Minimum P wave duration; PWD: P wave dispersion; QTD: QT dispersion; QTDc: Corrected QT dispersion.

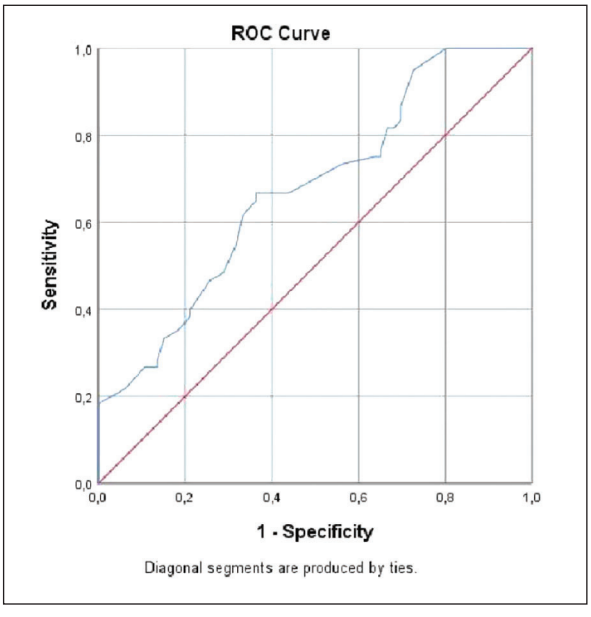

FIGURE 1: ROC analysis of PWD for predicting subclinical hypothyroidisim. PWD: P wave dispersion; ROC: Receiver operating characteristic.

ments of ventricular and atrial repolarization heterogeneity, with large differences indicating an increased risk of arrhythmias and death. Since these parameters provide helpful information about myocardial heterogeneity, increased values may indicate cardiac involvement in subclinic hypothyroid patients.

Since the cardiovascular system is one of the major targets for thyroid hormone action, a slight deficiency of it may affect cardiovascular homeostasis. Hypothyroidism related autonomic nervous dysfunction may be related to elevated thyrotropin-releasing hormone levels, which influence sympathetic activity within the central nervous system.[19] Studies performed on patients with primary hypothyroidism showed that both the QTc interval and the QTD increased in proportion to the level of TSH.[20]

There is a lack of sufficient scientific information on whether subclinical hypothyroidism has an effect on autonomic nervous system activity, and studies on this topic have had controversial results. Galetta et al. measured QTD and heart rate variability (HRV) parameters in subclinical hypothyroid patients. In their study, LF/HF ratio and QTD values were significantly higher than the controls and positively correlated with the serum TSH level.[21] Several other studies have also shown findings indicating higher sympathetic activity with parasympathetic hypofunction.[22-24] It has been suggested that subclinical hypothyroidism is related with increased cardiovascular morbidity and mortality, especially when the serum level of TSH is higher than 10 IU/ml.[25]

Sahin et al. reported that autonomic nervous system activity did not differ between subclinical hypothyroid patients and normal subjects unless the TSH level was higher than 10 mU/l. In this group of patients, there was an increase in sympathetic activity in correlation with the TSH level, which may hint that the high-risk group will likely proceed into overt hypothyroidism.[7] Yet another study found no difference in HRV parameters in subclinic hypothyroid patients compared to their euthyroid counterparts.[26]

Subclinical hypothyroid patients had significantly higher values of QTD, QTDc, which were correlated with TSH levels. According to our analysis, PWD was the only independent predictor of subclinical hypothyroidism. The difference between our study and other studies was that besides measuring QTD and QTDc, we also measured PWD values, and PWD was found to be an independent predictor of the presence of subclinical hypothyroidism. PWD, a marker for atrial remodeling, is an easily obtainable parameter from surface ECG. Increased PWD values indicate prolonged inter-intraatrial conduction time with a disorganized electrical activity and atrial con-

traction.[27] PWD value of ≥40 ms. has been reported to reflect heterogeneous activity in atrium, increased risk of atrial arrhythmias and atrial fibrillation.[28] An increased PWD values should alert physicians about the increased risk of atrial fibrillation.

CONCLUSION

PWD, and QTD are simple and easily obtainable parameters from surface ECG, reflecting variations in atrial and ventricular repolarizations and denoting information about the autonomic nervous system and cardiac functioning. These simple parameters may be used in clinical practice to evaluate subclinical hypothyroid patients who are at risk of arrhythmias and paroxysmal atrial fibrillation.

Some limitations of our study were that it was a single-center study and the sample size was small. Additionally, we did not follow the study group in terms of arrhythmia occurrence, and we did not test the effect of thyroid hormone replacement on electrocardiographic parameters.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Cennet Yıldız, Ahmet Karakurt;* ***Design:*** *Cennet Yıldız, Ahmet Karakurt;* ***Control/Supervision:*** *Cennet Yıldız;* ***Data Collection and/or Processing:*** *Cennet Yıldız;* ***Analysis and/or Interpretation:*** *Cennet Yıldız, Ahmet Karakurt;* ***Literature Review:*** *Cennet Yıldız, Ahmet Karakurt;* ***Writing the Article:*** *Cennet Yıldız;* ***Critical Review:*** *Cennet Yıldız, Ahmet Karakurt;* ***References and Fundings:*** *Cennet Yıldız;* ***Materials:*** *Cennet Yıldız.*

REFERENCES

1. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med. 2000;160(4):526-34. [Crossref] [Pubmed]
2. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2008;29(1):76-131. [Crossref] [Pubmed]
3. Asvold BO, Bjøro T, Platou C, Vatten LJ. Thyroid function and the risk of coronary heart disease: 12-year follow-up of the HUNT study in Norway. Clin Endocrinol (Oxf). 2012;77(6): 911-7. [Crossref] [Pubmed]
4. Foley CM, McAllister RM, Hasser EM. Thyroid status influences baroreflex function and autonomic contributions to arterial pressure and heart rate. Am J Physiol Heart Circ Physiol. 2001;280(5):H2061-8. [Crossref] [Pubmed]
5. Akcakoyun M, Emiroglu Y, Pala S, Kargin R, Guler GB, Esen O, et al. Heart rate recovery and chronotropic incompetence in patients with subclinical hypothyroidism. Pacing Clin Electrophysiol. 2010;33(1):2-5. [Crossref] [Pubmed]
6. Galetta F, Franzoni F, Fallahi P, Rossi M, Carpi A, Rubello D, et al. Heart rate variability and QT dispersion in patients with subclinical hypothyroidism. Biomed Pharmacother. 2006; 60(8):425-30. [Crossref] [Pubmed]
7. Sahin I, Turan N, Kosar F, Taskapan C, Gunen H. Evaluation of autonomic activity in patients with subclinical hypothyroidism. J Endocrinol Invest. 2005;28(3):209-13. [Crossref] [Pubmed]
8. Ishida S, Nakagawa M, Fujino T, Yonemochi H, Saikawa T, Ito M. Circadian variation of QT interval dispersion: correlation with heart rate variability. J Electrocardiol. 1997;30(3):205-10. [Crossref] [Pubmed]
9. Barr CS, Naas A, Freeman M, Lang CC, Struthers AD. QT dispersion and sudden unexpected death in chronic heart failure. Lancet. 1994;343(8893):327-9. [Crossref] [Pubmed]
10. Naas AA, Davidson NC, Thompson C, Cummings F, Ogston SA, Jung RT, et al. QT and QTc dispersion are accurate predictors of cardiac death in newly diagnosed non-insulin dependent diabetes: cohort study. BMJ. 1998; 316(7133):745-6. [Crossref] [Pubmed] [PMC]
11. Schwartz PJ, Wolf S. QT interval prolongation as predictor of sudden death in patients with myocardial infarction. Circulation. 1978;57(6): 1074-7. [Crossref] [Pubmed]
12. Okin PM, Devereux RB, Howard BV, Fabsitz RR, Lee ET, Welty TK. Assessment of QT interval and QT dispersion for prediction of allcause and cardiovascular mortality in American Indians: The Strong Heart Study. Circulation. 2000;101(1):61-6. [Crossref] [Pubmed]
13. Yildirir A, Aksoyek S, Calguneri M, Aytemir K, Kabakci G, Ovunc K, et al. QT dispersion as a predictor of arrhythmic events in patients with ankylosing spondylitis. Rheumatology (Oxford). 2000;39(8):875-9. [Crossref] [Pubmed]
14. Pirildar T, Sekuri C, Utük O, Tezcan UK. QT dispersion in rheumatoid arthritis patients with and without Sjögren's syndrome. Clin Rheumatol. 2003;22(3):225-8. [Crossref] [Pubmed]
15. Yavuz B, Atalar E, Karadag O, Tulumen E, Ozer N, Akdogan A, et al. QT dispersion increases in patients with systemic lupus erythematosus. Clin Rheumatol. 2007;26(3): 376-9. [Crossref] [Pubmed]
16. Dilaveris PE, Gialafos EJ, Sideris SK, Theopistou AM, Andrikopoulos GK, Kyriakidis M, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J. 1998;135(5 Pt 1): 733-8. [Crossref] [Pubmed]

17. Ciaroni S, Cuenoud L, Bloch A. Clinical study to investigate the predictive parameters for the onset of atrial fibrillation in patients with essential hypertension. Am Heart J. 2000; 139(5):814-9. [Crossref] [Pubmed]

18. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Guidelines for Performing a Comprehensive Transthoracic Echocardiographic Examination in Adults: Recommendations from the American Society of Echocardiography. J Am Soc Echo cardiogr. 2019;32(1):1-64. [Crossref] [Pubmed]

19. Polikar R, Burger AG, Scherrer U, Nicod P. The thyroid and the heart. Circulation. 1993; 87(5):1435-41. [Crossref] [Pubmed]

20. Nathaniel C, Caleb L, Azrin MA. QTc prolongation in hypothyroidism. J Am Coll Cardiol. 1994;23:36.

21. Altun A, Altun G, Ozkan B, Kaya M, Ozbay G. The relationship between ventricular repolarization and thyroid stimulating hormone. Ann Noninvasive Electrocardiogr. 1998;3:19.

22. Kahaly GJ. Cardiovascular and atherogenic aspects of subclinical hypothyroidism. Thyroid. 2000;10(8):665-79. [Crossref] [Pubmed]

23. Akcakoyun M, Emiroglu Y, Pala S, Kargin R, Guler GB, Esen O, et al. Heart rate recovery and chronotropic incompetence in patients with subclinical hypothyroidism. Pacing Clin Electrophysiol. 2010;33(1):2-5. [Crossref] [Pubmed]

24. Mahajan AS, Lal R, Dhanwal DK, Jain AK, Chowdhury V. Evaluation of autonomic functions in subclinical hypothyroid and hypothyroid patients. Indian J Endocrinol Metab. 2013;17(3):460-4. [Crossref] [Pubmed] [PMC]

25. Rodondi N, den Elzen WP, Bauer DC, Cappola AR, Razvi S, Walsh JP, et al; Thyroid Studies Collaboration. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA. 2010;304(12):1365-74. [Crossref] [Pubmed] [PMC]

26. de Miranda ÉJFP, Hoshi RA, Bittencourt MS, Goulart AC, Santos IS, Brunoni AR, et al. Relationship between heart rate variability and subclinical thyroid disorders of the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). Braz J Med Biol Res. 2018;51(11): e7704. [Crossref] [Pubmed] [PMC]

27. Pérez-Riera AR, de Abreu LC, Barbosa-Barros R, Grindler J, Fernandes-Cardoso A, Baranchuk A. P-wave dispersion: an update. Indian Pacing Electrophysiol J. 2016;16(4): 126-33. [Crossref] [Pubmed] [PMC]

28. Aytemir K, Ozer N, Atalar E, Sade E, Aksöyek S, Ovünç K, et al. P wave dispersion on 12-lead electrocardiography in patients with paroxysmal atrial fibrillation. Pacing Clin Electrophysiol. 2000;23(7):1109-12. [Crossref] [Pubmed]