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Determination of Cardiovascular Disease Risk with Serum Atherogeneity Index in Thyroid Dysfunction

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Objective: Serum atherogenicity index is a scoring tool that is used to quantitatively assess risk. Serum atherogenicity index aims to prevent deterioration in thyroid dysfunction and predict atherosclerotic risk.

Materials and Methods: A total of 200 individuals (100 hypothyroid, 50 hyperthyroid and 100 control group) were included in the study [a=0.05 ß=0.10 1-ß=0.90 R (Sample Allocation= 2)]. Age, gender, height and weight values of the patients were recorded. Blood glucose, hemogram values, HbA1c levels, renal and liver functions, serum lipid levels were recorded from biochemistry data. Serum atherogenicity indices were calculated as the ratio of plasma triglyceride level to HDL (high density lipoprotein) level. Data were analyzed in SPSS.

Results: Mean TG (triglyceride) and LDL (low density lipoprotein) levels were higher in both hypothyroidism and hyperthyroidism groups compared to the control group (X2=256.367 *p*=0.003; X2=266.976 *p*=0.003). Although the mean HDL level was higher in the hypothyroid and hyperthyroid groups compared to the healthy group, it was not statistically significant alone (X2=88.939 *p*=0.130). TG/HDL was calculated as 3.1 in hypothyroid patients and 3.2 in hyperthyroid patients. When hyperthyroidism and hypothyroidism patients were compared with the control group, atherogenicity index was higher in thyroid dysfunction; the difference was statistically significant (KW=39.49; *p*=0.001). The serum atherogenicity index was considered to be a reliable tool for the assessment of cariovascular risk in thyroid dysfunction.

Conclusion: Coronary artery disease risk was higher in individuals with thyroid dysfunction. The use of serum atherogenicity index for early recognition of cardiovascular risk may be an easily applicable and supportive parameter in clinical practice.

Key Words: *Hypothyroidism, hyperthyroidism, thyroid dysfunction, serum atherogenicity index, cardiovascular disease risk*

Tiroid Fonksiyon Bozukluğunda Serum Aterojenite İndeksi ile Kardiyovasküler Hastalık Riskinin Belirlenmesi

Amaç: Serum aterojenite indeksi kardiyovasküler riski kantitatif olarak değerlendirmeye yarayan bir skorlama aracıdır. Serum atrejenite indeksi ile tiroid fonksiyon bozukluğunda gelişen koroner aterosklerotik riski öngörmek amaçlanmaktadır.

Gereç ve Yöntem: Çalışmaya 100 hipotiroidi, 50 hipertiroidi ve 100 kontrol grubu olmak üzere toplam 200 birey alındı. [a=0,05 ß=0,10 1-ß=0,90 R (Sample Allocation= 2)]. Hastaların yaşı, cinsiyeti, boy, kilo değerleri kaydedildi. Biyokimya verilerinden kan şekeri, hemogram değerleri, HbA1c seviyeleri, böbrek ve karaciğer fonksiyonları, serum lipit düzeyleri kaydedildi. Serum aterojenite indeksleri; plazma trigliserid düzeyinin yüksek yoğunluklu lipoprotein (HDL) düzeyine oranı ile hesaplandı. Veriler SPSS'de (statistical package for the social sciences) analiz edildi.

Bulgular: Ortalama TG (trigliserid) ve LDL (düşük yoğunluklu lipoprotein) düzeyi hem hipotiroidi hem de hipertiroidi grubunda kontrol grubuna göre yüksek bulundu **(**X^2=256.367 *p*=0.003; X^2=266.976 *p*=0.003). Ortalama HDL düzeyi hipotiroidi ve hipertiroidi grubunda sağlıklı gruba göre bulunsa da istatistiksel açıdan tek başına anlamdı değildi (X^2=88.939 *p*=0.130). TG/HDL hipotiroidi hastalarında ortalama 3.1 iken; hipertiroidi hastalarında ortalama 3.2 olarak hesaplandı. Hipertiroidi ve hipotiroidi hastaları kontrol grubu ile karşılaştırıldığında tiroid fonksiyon bozukluğunda aterojenite indeksi yüksek saptandı; fark istatistiksel açıdan anlamlı bulundu (KW=39.49; *p*=0.001). Serum aterojenite indeksinin tiroit fonksiyon bozukluğunda kariyovasküler riski göstermede kullanılabilir güvenilir bir araç olarak değerlendirildi.

Sonuç: Tiroid fonksiyon bozukluğu olan bireylerde koroner arter hastalığı riski daha yüksek saptandı. Kardiyovasküler riskin erken farkedilmesi için serum aterojenite indeksinin kullanılmasının klinik pratikte kolay uygulanabilir ve destekleyici bir parametre olabileceği saptandı.

Anahtar Kelimeler*:* *Hipotiroidi, hipertiroidi, tiroid fonksiyon bozukluğu, serum aterojenite indeksi, kardiyovasküler hastalik riski*

Introduction

Hypothyroidism is when the thyroid gland is underactive or its effect is reduced in the target tissue; hyperthyroidism is when it is overactive or causes excessive extrathyroidal hormone secretion. Thyroid hormones are the main regulators of our metabolism; both high and low levels cause many changes in metabolism, especially in the sympathetic system, neuromuscular system, gastrointestinal system and cardiovascular system (1).

The effects of thyroid dysfunction on the cardiovascular system are mostly through T3 (triiotronin). It causes changes in heart rate, increase in vascular tone, vascular remodeling and changes in vascular structures. In addition, LDL (low-density lipoprotein) disrupts lipid metabolism by altering hepatic LDL receptor function and affecting LDL clearance (2-4). Hypothyroidism predisposes to the development of bradycardia, atherosclerosis with high LDL levels, impaired cardiac nutrition with delayed diastole, and hypertension with irregular angiogenesis and delayed vascular smooth muscle dilatation. Hyperthyroidism, on the other hand, causes arrhythmias with acceleration of cardiac conduction and heart failure with damage to the myocardium and excessive remodeling. Cardiovascular risk is increased in patients with both hypothyroidism and hyperthyroidism (5-8).

Currently accepted risk factors for cardiovascular disease include age, family history, smoking, presence of hypertension and diabetes, hypercholesterolemia, and low HDL (high-density lipoprotein) levels. Cholesterol level measurement is preferred for quantitative evaluation (9). Since ancient times, many non-invasive methods have been tried to be developed to predict coronary risk and to take precautions in these patients and many scoring systems have been established (10). The serum atherogenicity index (Triglyceride/HDL) is a scoring tool used for this purpose and is one of the best laboratory indicators of the presence of coronary atherosclerotic lesions (11).

Materials and Methods

Research and Publication Ethics: This study was approved by Yozgat Bozok University Clinical Research Ethics Committee (2025-255-356) The power analysis of the study was calculated in PASS (power analysis software). In this study, a=0.05 ß=0.10 1-ß=0.90 R (Sample Allocation=2) was taken as the minimum number of patients and the patients were included. Data collection was started after approval from the local ethics committee. A total of 150 patients (50 overt hyperthyroidism, 100 overt hypothyroidism) with thyroid dysfunction for at least one year and 50 healthy controls were included.

Data collection: The data of 100 hypothyroid patients (TSH>4.5 uIU/mL) and 50 hyperthyroid patients (TSH<0.3 uIU/mL) who were over 18 years of age and whose complete file data were available were recorded. Age, gender, laboratory tests (lipid levels, thyroid function, renal function, blood glucose levels, hemogram and C-reactive protein values) and total cholesterol, triglycerides, LDL, HDL cholesterol levels were recorded. The data of patients who declared fasting for at least 12 hours in the morning hours of lipid tests were included. Friedewald Formula was used to calculate the LDL cholesterol value.12 TSH, T4 and T3 tests were performed with the same device and the results were recorded. In anthropometric evaluation, weight and height values were recorded from the system at the time of initial diagnosis. BMI (Body mass index) was calculated as the ratio of weight to height squared. Serum atherogenicity index was calculated as the ratio of plasma triglyceride level to HDL level. Individuals with overt diabetes, known coronary artery disease, individuals receiving antilipidemic treatment, ischemic heart disease, active malignancy, chronic kidney or liver disease, active psychiatric disease, individuals using hormonal and steroid drugs, pregnant women, individuals with a TG over 400, and individuals with a BMI of 30 and over were excluded from the study (12).

Statistical Analysis: When the assumptions could not be fulfilled in SSPS (statistical package for the social sciences), Kruskall-Wallis test was used to compare more than two independent groups, Mann-Whitney U test was used to find the groups that differed as a result of the analysis, and Chi-Square test was used to evaluate the data obtained by counting. The data were expressed as arithmetic mean, standard deviation, median, minimum and maximum value, number and percentage of individuals and the error level was taken as 0.05.

Results

The study included 100 hypothyroid, 50 hyperthyroid and 50 healthy control subjects. Of the 200 individuals included in the study, 42 (21%) were male and 158 (79%) were female. There was no statistical difference between the groups in terms of gender (p=0.052). The minimum and maximum ages of the individuals included in the study were 18 and 75 years, respectively, and the mean age was 49.08 ± 13.86 years. There was no statistically significant difference between the body mass indexes of the individuals in the groups (X^2=10.5; *p*=0.925). There was no statistically significant difference between the mean disease duration of hypothyroid and hyperthyroid patients (*p*=0.096, Table.1).

When blood glucose and HbA1c levels of the patients were compared, there was no statistical difference between the hypothyroid, hyperthyroid and healthy groups. Individuals with HbA1c levels of 6.5 and above were excluded from the study. Thus, the coronary risk caused by diabetes was eliminated and the isolated effect of thyroid dysfunction was more clearly observed. In addition, CRP values recorded to observe the effect of inflammatory thyroid diseases were not statistically different between the groups (*p*=0.570) (Table.2).

Lipid values of euthyroid individuals with a diagnosis of thyroid dysfunction and euthyroid individuals receiving treatment were compared. When hypothyroidism and control group and hyperthyroidism and control group were compared in pairs, LDL and triglyceride values were found to be higher in the hypothyroid and hyperthyroid group compared to the control group; the difference was statistically significant when all groups were compared (X^2=256.367 *p*=0.003; X^2=266.976 *p*=0.003). Although the mean HDL value was also higher in the hypothyroid and hyperthyroid groups compared to the healthy group, the data were not statistically significant (X^2=88.939 *p*=0.130). It was

Table.1. General characteristics and sociodemographic data of the individuals participating in the study

	Hypothyroidism (n= 100)	Hyperthyroidism (n= 50)	Control group (n=50)	Total (n=200)	Analysis Result
Female	86 (%86)	36(%72)	36(%72)	158(%79)	*p*=0.052
Male	14 (%14)	14(%28)	14(%28)	42(%21)	
Age(years)	50.99±10.91	46.12± 12.58	38.56± 6.27	49.08 ±13.86	*p*=0.064
BMI-kg/m^2	24.92 ± 3.67	25.39 ± 3.53	24.54 ± 3.00		*p*=0.925
Duration of illness (mean) (years)	4.9± 3.62	2.1± 1.09			*p*=0.096

(n= number of individuals, % percent; BMI: Body Mass Index; p<0.05 significant)

Table.2. Comparison of laboratory data and serum atherogenicity indices of the groups

	Hypothyroidism	Hyperthyroidism	Control Group	Analysis Result
Fasting glucose (mg/dl)	87 ± 9.65	86 ± 10.32	84 ± 10.32	*p*=0.462
HbA1c (%)	4.9(%) 1.40(%)	4,8(%) 1,16(%)	4,6(%) 0,41(%)	*p*=0.431
TG (mg/dl)	150.48± 83.67	147.12± 73.68	77.20± 26.61	*p*=0.000*(1) *p*=0.000* (2) *p*=0.003*
HDL (mg/dl)	51.12± 12.06	48.20± 9.97	48.12± 8.37	*p*=0.078 1) *p*=0.960 (2) *p*=0.130
LDL (mg/dl)	124.88± 39.15	107.12± 39.41	92.80± 25.17	*p*=0.00* (1) *p*=0.33 (2) *p*=0.003*
C-reactive protein (mg/l)	10.28-20.64	13.59- 30.97	5.3-30.97	*p*=0.570
Serum aterogenite index (TG/HDL)	0.62-10.57 Median: 2.51 Mean: 3.18	1.13-12.47 2.52 3.28	0.82-3.39 1.52 1.66	*p*=0.001*

(TG: Triglyceride; HDLHigh Density Lipoprotein; LDL: Low Density Lipoprotein; CRP: C-reaktif protein;TG/HDL: Serum aterogenite index; p<0,05 significant*; (1): hypotyroidism-control groups; (2): hypertyroidsm-control groups)

observed that dyslipidemia was inevitable in thyroid dysfunction. The serum atherogenicity index, which is easy to calculate in clinical practice, is used as a marker of coronary artery risk. In our study, which we started with the hypothesis that increased coronary artery risk in thyroid dysfunction can be used for early detection of the disease, the index was found to be higher in individuals with hypothyroidism and hyperthyroidism compared to the control group. The data were statistically significant (KW=39.49; *p*=0.001). The serum atherogeity index was evaluated as a reliable tool to be used in thyroid dysfunction to show the cardiovascular risk.

Discussion

No matter how mild thyroid dysfunction is, its effects on the cardiovascular system are considerable. In addition to overt thyroid disorders, changes in the cardiovascular system have been observed in subclinical thyroid dysfunction. Floriani et al. reported that treatment should be initiated to reduce cardiac risk when TSH>10 (thyroid stimulating hormone) and TSH<0.1, even if T4 (thyroxine) and T3 are normal. It has also been emphasized that thyroid functions should be checked in individuals over 60 years of age who are followed up with coronary artery disease and heart failure (13, 14). Similarly, Bayrak et al. planned a retrospective study on individuals with a diagnosis of acute coronary syndrome presenting to the emergency department and evaluated thyroid functions (15). In this study, individuals with both subclinical hypothyroidism and subclinical hyperthyroidism were identified, supporting the presence of cardiac risk even in non-obvious thyroid dysfunctions. Although there are studies supporting the risk of cardiovascular disease in thyroid dysfunction with small experimental data, the physiopathogenesis is not fully understood. Also point out that a new era will be opened especially in the treatment of heart failure with thyroid

hormone when the physiopathogenesis is understood (16-18). Serum atherogenicity index was used to evaluate cardiovascular risk in patients with subclinical hypothyroidism and it was concluded that it is a better parameter than lipid profile (19). A relationship was found between serum atherogenicity index and TSH in hypothyroid patients and it is predicted that atherosclerosis will decrease with euthyroid follow-up (20). In another study, an increase in cardiovascular disease risk was predicted using serum atherogenicity index in hypothyroid patients (21).

In the study by Ulusoy et al. NT-proBNP (natriuretic peptide) level, which is an early marker of cardiac dysfunction, was evaluated in individuals with normal cardiologic examinations but thyroid dysfunction. Elevated NT-proBNP level was defined as an early cardiac risk in these patients (22). Therefore, it is very important to score the cardiovascular risks of patients with thyroid dysfunction quickly and easily in clinical practice and to follow up in cardiology units for both prophylactic treatment and interventional treatment. Öztürk et al. used the TEKHARF scoring system to clinically score the risk of cardiovascular disease in patients with hashimato thyroiditis (23). The serum atherogenicity index, which is easier and faster to apply in clinical practice, is also a good option for patients with thyroid dysfunction. In addition, since it helps us to predict not only cardiologic risk but also deterioration in the vascular system, serum atherogenicity index was associated with the severity of diabetic polyneuropathy in the study by Aciman et al. (24). In another study, insulin resistance and serum atherogenicity index were investigated and no relation was found between the two parameters (25). Therefore, in our study, individuals with endocrinologic syndromes such as obesity and polycystic ovary syndrome, which may cause insulin resistance, were not included in the study. Also demonstrated the reflection of atherosclerosis-induced vascular damage caused by thyroid hormones and cardiac mortality with serum atherogenicity index (26).

It is known that fat metabolism affects thyroid functions in multiple ways. There are studies suggesting that hypothyroidism causes an increase in cholesterol, LDL, TG and adipose tissue and decreases HDL, while hyperthyroidism decreases or does not affect the lipid profile (27-29). Similar to our study, serum atherogenicity index showed an increased cardiovascular risk in the hypothyroid group in an examination performed in 71 hypothyroid patients and 41 healthy groups admitted to the endocrinology outpatient clinic. Similarly, in a study conducted in 50 hypothyroid and 50 healthy groups, an increase in atherogenicity index was found in hypothyroid individuals and it was recommended that severe hypothyroidism should be approached as cardiovascular disease in treatment and follow-up. There are not enough studies on this subject in individuals with hyperthyroidism (30, 31). In our study, serum atherogenicity index was found to be higher in individuals with hyperthyroidism compared to the healthy group and this elevation was found to be statistically significant to the same extent as hypothyroidism ($p<0.05$). This result proves that serum atherogenicity index should not be evaluated only on lipid basis and can be safely used as an independent index to determine cardiovascular risk ($p<0.05$).

Our study has several limitations: It was designed as a retrospective study and did not have an interventional methodology that could correlate with atheroma plaques in the vascular content.

In conclusion, there are a number of studies on the effect of thyroid dysfunction on cardiovascular diseases. However, it is not clear which patients have a higher risk and which individuals should be closely followed up cardiologically or given prophylactic treatment. In our study, it was found that the use of serum atherogenicity index for early recognition of cardiovascular risk in this group of patients may be an easily applicable supportive parameter in clinical practice, but larger-scale studies are needed to be recommended as a risk parameter alone.

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