Negative T wave in chest lead V1: relation to sex and future cardiovascular risk factors

V1 Göğüs derivasyonunda T-dalgası negatifliği ve cinsiyet ve kardiyovasküler risk faktörleri ile ilişkisi

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Objectives: The significance of T-wave negativity in lead V1 in adults and its relationship with cardiovascular risk factors have not been clarified. This study was designed to determine the prevalence of negative T waves in chest lead V1 in an adult cohort.

Study design: The study included 508 adults (278 males, mean age 51.5±9.7 years; 230 females, mean age 51.2±10.0 years) enrolled in the longitudinal Turkish Adult Risk Factor survey from all geographical regions of Turkey, whose prospective data on the prevalence of coronary heart disease and its risk factors were available for comparative assessment of T-wave groups. Associations of negative T waves were sought in relation to age, sex, cardiovascular risk factors, and coronary heart disease.

Results: The prevalence of T-wave negativity in women was significantly higher than that of men (38.3% *vs* 7.2%; p<0.001). No age-related differences were found between the two sexes with respect to the presence or absence of negative T waves (p>0.05). Cardiovascular risk factors and cardiometabolic conditions did not differ among men with respect to the T-wave pattern. However, women presenting negative T waves in lead V1 had significantly lower systolic blood pressure (p=0.007) and HDL-cholesterol (p=0.034) values, and a higher incidence of type 2 diabetes (p=0.048) than women with positive T waves.

Conclusion: No convincing explanation could be offered for the significantly higher female predilection for the presence of negative T-waves in lead V1. Negative T waves in lead V1 were not associated with adverse cardiometabolic risks.

Key words: Blood pressure; coronary disease; electrocardiography; female; risk factors; sex factors.

Amaç: Erişkinlerde V1 derivasyonunda T dalgası negatifliğinin sıklığı ve kardiyovasküler risk faktörleri ile ilişkisi yeterince incelenmemiştir. Bu çalışmada erişkin nüfusa dayalı bir kohortta göğüs V1 derivasyonunda T dalgası negatifliğinin sıklığı araştırıldı.

Çalışma planı: Türk Erişkinlerinde Kalp Hastalığı ve Risk Faktörleri (TEKHARF) çalışmasında izlenmekte olan kohorttan, tüm coğrafik bölgeleri temsil edecek şekilde rastgele seçilen erişkin 508 kişi (278 erkek, ort. yaş 51.5±9.7; 230 kadın, ort. yaş 51.2±10.0) incelendi. Katılımcılarda V1 derivasyonunda T dalgası tipinin karşılaştırmalı değerlendirilebilmesi için koroner kalp hastalığı ve risk faktörleriyle ilgili veriler prospektif olarak elde edilmişti. T dalgası negatifliğinin yaş, cinsiyet, kardiyovasküler risk faktörleri ve koroner kalp hastalığı ile ilişkisi araştırıldı.

Bulgular: Kadınlarda T dalgası negatifliği erkeklere göre anlamlı derecede yüksek bulundu (38.3% ve 7.2%; p<0.001). İki cinsiyet arasında T dalgası negatifliği olup olmaması bakımından yaşla ilgili farklılık görülmedi (p>0.05). Kardiyovasküler risk faktörleri ve kardiyometabolik durumlar erkeklerde T dalgası tipine göre farklılık göstermedi. Bununla birlikte, T dalgası negatifliği olan kadınlarda, T dalgası pozitif olanlara göre sistolik kan basıncı (p=0.007) ve HDL-kolesterol (p=0.034) düzeyleri daha düşük, tip 2 diyabet sıklığı daha yüksek (p=0.048) bulundu.

Sonuç: Kadınlarda T dalgası negatifliğinin erkeklere göre belirgin cinsiyet farkı göstermesinin nedeni açıklanamadı. Bununla birlikte, V1'deki T dalgası negatifliğinin kardiyometabolik risk ile olumsuz bir ilişki içinde olmadığı söylenebilir.

Anahtar sözcükler: Kan basıncı; koroner hastalık; elektrokardiyografi; kadın; risk faktörü; cinsiyet faktörü.

Received: June 29, 2008 *Accepted:* August 29, 2008

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The right precordial T waves in the ECG are negative until the age 12 to 14[1] and usually become upright after the age 16 years, but occasionally negative T waves persist into adulthood and are interpreted as a normal variant designated as the "persistent juvenile T wave". The incidence of inverted T waves in the right precordial leads was, however, reported as no more than 2.7% of 581 subjects with non-specific T-wave changes, making up 2-3 per mille of 67,375 asymptomatic men, aged 20 to 40 years, of the U.S. Air Force.[2] It has been observed that T inversion in lead V1 is much more common in females than males.[3] In studying a Chinese population sample of 5,360 apparently healthy men and women, Wu et al.[4] found that inverted T waves were present in 47% of women, but only in 12% of men. Report on a large recent ECG reference study provided no data on T-wave negativity in lead V1.[5] Thus, there appears to be a great variability in the prevalence of such negative T waves and further information is desirable particularly as to whether a T-wave negativity in V1 has any prognostic cardiovascular significance, a question which has not been clarified to date.

We, therefore, studied the occurrence and, prospectively, the significance of negative T waves in the chest lead V1 in a sample of the longitudinal Turkish Adult Risk Factor Study[6] in which data on cardiovascular disease and its risk factors were available for comparative assessment of T-wave groups.

SUBJECTS AND METHODS

The sample population was recruited from the Turkish Adult Risk Factor Study on the prevalence of cardiac disease and risk factors in a representative sample of adults in Turkey, carried out periodically, almost biennially, since 1990 in 59 communities throughout all geographical regions of the country.[7]

Data were obtained by history of the past years via a questionnaire, physical examination of the cardiovascular system, sampling of blood, and recording of a resting 12-lead electrocardiogram. The ECGs were recorded by a portable 3-channel apparatus with 12 simultaneous leads (Cardiovit AT 3/1, Schiller, Austria) by analog system at a paper speed of 25 mm/sec. Lead V1 was placed in the fourth intercostal space to the immediate right of the sternal border.

Selection of subjects and definition of T waves in V1. We planned to evaluate approximately 500 subjects in relation to an either positive or negative T-wave pattern in lead V1. The evaluator (T.O.), who is experienced in interpreting ECGs, was unaware of clinical data in regard to cardiovascular risk factors of the survey participant. We selected files randomly from different geographical regions of Turkey and evaluated the serial ECGs of participants enrolled between 1990 and 1998, whose biennial follow-up ranged from 5 to 17 years. Subjects with a recruitment age under 35 years were excluded with the purpose of attaining a greater number of elderly subjects so as to have a greater proportion of individuals with risk factors or adverse outcomes. T waves of a voltage of ≤0.2 mV were considered flat. Individuals presenting flat or biphasic T waves in V1, as well as those with negative T waves in V1 through V3 (1 subject) and in V1 to V2 (two subjects) were excluded. Definite technical unreadability of lead V1 was another reason for exclusion.

When lead V1 is registered from a higher intercostal space than the fourth, the pattern of V1 resembles lead aVR presenting a negative P wave, negative T-wave and rSr' or Qr' patterns -also designated as right ventricular inner or outflow tract pattern. To avoid these false negative T waves, such tracings were excluded. Subjects presenting premature beats, an incomplete or complete right bundle branch block were also excluded. For definite consideration of the T wave as either positive or negative, only subjects with consistent findings in this respect in at least two subsequent ECGs were included into the study. Under these conditions, the selected material was considered numerically adequate when a sum of 562 subjects was reached, which represented all regions of Turkey. The ECGs assessed for the T-wave pattern were recorded in the years between 1990 and 1998. Fifty-four subjects (27 males, 27 females) were later eliminated because of missing data on cardiovascular risk factors, leaving a total of 508 subjects (278 males, 230 females) for analysis. These were followed-up for a median of 14 years (80% between 6 to 17 years, 94% between 2 to 17 years).

Measurement of risk factors and definitions. Blood pressure (BP) was measured with an aneroid sphygmomanometer (Erka, Germany) in the sitting position on the right arm and the mean of two recordings 3 min apart was recorded. Waist circumference was measured with the subject standing and wearing only underwear, at the level midway between the lower rib margin and the iliac crest. Physical activity was graded by the participant into four categories of increasing order with the aid of a scheme.[7]

Table 1. Negative and positive T wave distribution in males and females

	Men (n=278)			Women (n=230)			
	n	%	Mean age	n	%	Mean age	*p*⁺
Negative T wave	20	7.2	49.4±14	88	38.3	48.6±8.8*	
Positive T wave	258	92.8	51.7±9.3	142	61.7	52.7±10.4	0.000

*p=0.002 between ages in T-wave groups of women; ⁺For difference in prevalence between sexes.

Hypertension was defined as a BP ≥140 mmHg systolic and/or ≥90 mmHg diastolic, and/or use of antihypertensive medication. Metabolic syndrome (MetS) was identified when three out of the five criteria of the National Cholesterol Education Program ATP-III[8] were met, modified for prediabetes (fasting glucose 100-125 mg/dl, and further for abdominal obesity using the cut point ≥95 cm in men, as recently assessed in the Turkish Adult Risk Factor Study.[9] Diabetes mellitus (DM) was diagnosed with the criteria of the American Diabetes Assocation,[10] namely by self report or when plasma fasting glucose was ≥126 mg/dl or when 2-h postprandial glucose was ≥200 mg/dl.

Diagnosis of nonfatal coronary heart disease (CHD) was based on the presence of angina pectoris, of a history of myocardial infarction with or without accompanying Minnesota codes of the ECG,[11] or on a history of myocardial revascularization. When angina was isolated, typical angina was prerequisite for a diagnosis and, in women, age >45 years. ECG changes of "ischemic type" of greater than minor degree (Codes 1.1-2, 4.1-2, 5.1-2, 7.1) were considered myocardial infarct sequelae or myocardial ischemia, respectively. Diagnosis of CHD did not include isolated chronic heart failure or atrial fibrillation.

Data analysis. Descriptive parameters were shown as mean and standard deviation, or as age-adjusted estimated mean ± standard error and in percentages. Risk variables with which associations of the baseline T-wave pattern were sought belonged to the final examination of the longitudinal study. Pairwise comparisons were made to detect significance between groups of estimated means; two-sided t-tests and Pearson's chi-square test were used to analyze differences between means and proportions of groups. Statistical analyses were performed using SPSS-10 for Windows.

RESULTS

Ratio of negative T waves. The mean and SD values in relation to age and T-wave pattern in lead V1 is presented in Table 1. The proportion of negative T waves in V1 in women was significantly higher than that of men (38.3% *vs* 7.2%; p<0.001). Age distribution at onset of the study was 51.5±9.7 *vs* 51.2±10.0 years in males and females, respectively, and was not significantly different between sexes (p=0.67). The age of subjects presenting negative T waves in V1 did not differ significantly between sexes (p=0.73), nor did the age of subjects with positive T waves in V1 (p=0.29). Age distribution in male subjects was similar in groups presenting negative or positive T waves in V1 (p=0.31). However, a mean difference of about 4 years in age was significantly lower in females presenting negative T waves in V1 (Table 1).

Association of T-wave pattern in V1 with risk factors and cardiometabolic disorders. The following cardiovascular risk variables were analyzed statistically in groups of positive and negative T waves: waist circumference, systolic and diastolic BP, fasting glucose, triglycerides, total cholesterol, HDL-cholesterol, LDL-cholesterol, apolipoproteins A-I,

Table 2. Sex distribution of age-adjusted mean systolic blood pressure and HDL-cholesterol in relation to T-wave pattern in V1

	Negative T-wave		Positive T-wave		
	Mean	SE	Mean	SE	*p*
Systolic blood pressure (mmHg)					
Male (n=278)	130.4	4.8	130.0	1.35	0.93
Female (n=230)	131.0	2.7	140.5	2.16	0.007
HDL-cholesterol (mg/dl)					
Male (n=278)	39.1	2.4	39.3	9.07	0.93
Female (n=230)	45.0	1.3	48.6	1.11	0.034

Table 3. The presence of cardiometabolic risk conditions in female participants in relation to T-wave pattern in lead V1

		Negative T (n=88)		Positive T (n=142)		
	n	n	%	n	%	*p**
Diabetes, type-2						
Absent	178	62	34.8	116	65.2	
Present	52	26	50.0	26	50.0	0.048
Hypertension						
Absent	56	31	55.4	25	44.6	
Present	174	57	32.8	117	67.2	0.002
Metabolic syndrome						
Absent	83	28	33.7	55	66.3	
Present	147	60	40.8	87	59.2	0.304
Coronary heart disease						
Absent	177	68	38.4	109	61.6	
Present	43	18	41.9	25	58.1	0.678

*For difference between presence and absence of disorder.

B and E, fasting insulin, homeostatic model assessment, lipoprotein(a), C-reactive protein, folate, vitamin B_{12}, and sex hormone-binding globulin. These variables did not differ significantly in subjects with a negative or positive T wave in the total, as well as in male and female participants, except that crude systolic BP (130.1±21.9 *vs* 140.4±27.4 mmHg; p=0.004) and HDL-cholesterol (44.8±10.5 *vs* 48.2±12.7 mg/dl; p=0.047) were found to be significantly lower in females presenting negative T waves in lead V1 than women with positive T waves. Since a significant mean difference of four years was found in the female cohorts with negative and positive T waves, these two variables were re-analyzed after age adjustment (Table 2). Women presenting negative T waves in lead V1 had significantly lower age-adjusted BP (p=0.007) and HDL-cholesterol (p=0.034) values than women with positive T waves in V1.

The prevalences of type 2 diabetes mellitus, hypertension, MetS, and CHD were also analyzed by gender in relation to negative and positive T waves. Overall, the T-wave pattern was not significantly associated with diabetes mellitus (p=0.18), MetS (p=0.50), and CHD (p=0.82). The prevalence of hypertension tended to be lower in subjects with negative T waves in V1 compared to those with positive T waves (60.4% *vs* 69.7%; p=0.071). Among men, the incidences of four conditions did not differ significantly in relation to the T-wave pattern. However, women presenting negative T waves in lead V1 had a significantly lower incidence of hypertension and higher incidence of type 2 diabetes than women with positive T waves (Table 3). The frequency of T-wave negativity was 32.8% in hypertensive women and 55.4% in non-hypertensive women (p=0.002). Conversely, negative T waves were present in exactly half of the 52 female diabetic patients compared with 34.8% of 178 non-diabetic women (p=0.048). On the other hand, T-wave negativity was not affected significantly by the presence or absence of MetS and CHD (Table 3).

DISCUSSION

Our findings on middle-aged or elderly subjects demonstrated about five-fold greater prevalence of negative T waves in lead V1 among women than men (38.3% *vs* 7.2%). This significant sex difference confirmed previous findings reported for Caucasian[3] and Chinese[4] populations. It is difficult to explain this fact with the data available. This may be due to a different anatomic positioning of the heart in females presenting negative T waves in lead V1.

Normally, the morphology of the epicardial potential of the anterior right ventricle shows an rS-QRS type with a positive T wave.[12] The positive T wave of the anterior right ventricle may become negative if epicardial potentials are derived from the right ventricular outflow tract. This may be the case if lead V1 is derived from a location higher than the fourth intercostal space. However, such technically suspected cases were excluded from the analyzed sample.

One possibility is that the right ventricular outflow tract pattern observed by epicardial potentials is more pronounced in women with negative T waves. This may be caused by a clockwise rotation of the ventricular septum towards the left or, more possibly, by a counterclockwise rotation of the septum on the sagittal plane (seen from right) resulting in a lower positioning of the right ventricular outflow tract.

However, both possible rotational conditions may only be observed under severe overloading of the heart.[13,14] Why this positioning should occur more frequently in women than men still remains obscure.

As opposed to negative T wave expectation in childhood, a loose relationship was found between positive T waves in V1 and right ventricular hypertrophy in children[15,16] and elevated right ventricular pressure in children under age 12.[17]

Another factor involved in T negativity in V1 might be estrogen activity. Although there was a slight trend to a decreased T-wave voltage with age in Chinese women, this trend was more prominent in men.[4] Likewise, the effect of decreased estrogen hormone might be associated with conversion of T-wave positivity to T-wave negativity with increasing age during menopause. This trend, however, was not evaluated in female participants of our study.

Women presenting negative T waves in V1 showed significantly lower systolic BP and a lower prevalence of hypertension, both of which may be associated with reduced left ventricular strain resulting in the above mentioned rotation of the heart. However, a mean difference of only 10 mmHg is probably not sufficient to deform the heart and to cause an inferior displacement of the right ventricular outflow tract.

In women with negative T waves, furthermore, a significantly higher prevalence of diabetes and lower HDL-cholesterol levels were found. Whether coexistence of epicardial ectopic fat[18] in females with diabetes might contribute to negative T waves in V1 remains only a speculation. Unfortunately, we are unable to offer a plausible explanation for changes in T-wave pattern among women.

We conclude that negative T waves in lead V1 occur far more commonly in women than in men. A variety of cardiovascular risk factors and cardiometabolic conditions are similar among men in relation to the T-wave pattern. In women, negative T waves are associated with lower systolic BP and a higher prevalence of diabetes. The T-wave negativity in lead V1 warrants further investigation in relation to the morphology of the heart.

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