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Effect of implantable cardioverter defibrillator implantation on frontal QRS-T angle

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Abstract. – OBJECTIVE: The frontal plane QRS-T [f(QRS-T)] angle refers to the mean difference between the depolarization and repolarization vectors and can easily be measured by digital electrocardiography (ECG). Pacemaker leads can cause fibrosis of the myocardium adjacent to the electrode-tissue interface. We aimed to evaluate whether a right ventricular implantable cardioverter-defibrillator (ICD) lead modifies the f(QRS-T) angle in patients with systolic heart failure (HF).

PATIENTS AND METHODS: We prospectively analyzed 101 systolic HF patients who underwent single-lead ICD implantation. The f(QRS) angle before and after ICD implantation was compared with the Wilcoxon signed-rank test.

RESULTS: No significant difference in the f(QRS-T) angle was observed before and 6 months after ICD implantation (89.5° ± 97.8° *vs.* 93.0° ± 90.3°, *p*=0.211).

CONCLUSIONS: Histopathological studies showed that the irritating effect of ICD leads may cause fibrosis and scar tissue. However, we found that fibrosis and scar tissue did not affect the f(QRS-T) angle, which suggests that these pathologies may not have clinical significance. Further studies on the f(QRS-T) angle are warranted to understand its clinical significance in ICD-induced local fibrosis.

Key Words:
Vectorcardiography, Frontal QRS-T angle, Implantable cardioverter-defibrillator.

Introduction

Vectorcardiography (VCG), a long-standing method of electrocardiography (ECG) analysis, has been scrutinized following the development of digital ECG[1]. VCG shows the mobility of the heart vectors through the cardiac cycle as loops. The QRS and T loop vectors correspond to depolarization and repolarization, respectively. The spatial QRS-T angle, i.e., the angle between the spatial QRS axis vector and spatial T wave axis, can be measured by VCG. Previous studies[1] have shown that an unusually wide spatial QRS-T angle can be utilized to predict cardiac risk. However, spatial QRS-T angle calculation requires specialized analysis software, hindering its use in daily practice. The frontal plane QRS-T [f(QRS-T)] angle, i.e., the mean difference in depolarization and repolarization vectors, can easily be measured by digital ECG. Zhang et al[2] demonstrated that the f(QRS-T) angle was an appropriate alternative to the spatial QRS-T angle as a clinical marker of cardiac risk. The f(QRS-T) angle is estimated by calculating the absolute difference between the QRS and T axes (obtained using digital ECG).

Heart failure (HF) is a significant cause of morbidity and mortality, affecting millions of patients worldwide[3]. Ventricular tachycardia and ventricular fibrillation, leading to sudden cardiac death (SCD), are responsible for 20-50% of deaths in patients with HF[4]. Implantable cardioverter-defibrillator (ICD) implantation reduces the risk of mortality and SCD in patients with HF[3]. Increasing numbers of ICDs are being implanted worldwide every year.

Artificial material embedded into the right ventricle may lead to a change in vectorial depolarization of the heart. Additionally, fibrosis of the myocardium adjacent to the electrode-tissue interface may be responsible for new reentry circuits, as well as arrhythmogenesis[5]. The effect of ICD on the f(QRS-T) angle has yet to be investigated. Thus, we aimed to evaluate whether right ventricular ICD leads modify the f(QRS-T) angle in patients with HF.

Patients and Methods

This prospective, cross-sectional and observational study was conducted at the Cardiology Department of Ankara City Hospital, Turkey. The Institutional Ethics Committee approved the study, and consent was obtained from all patients for their participation. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

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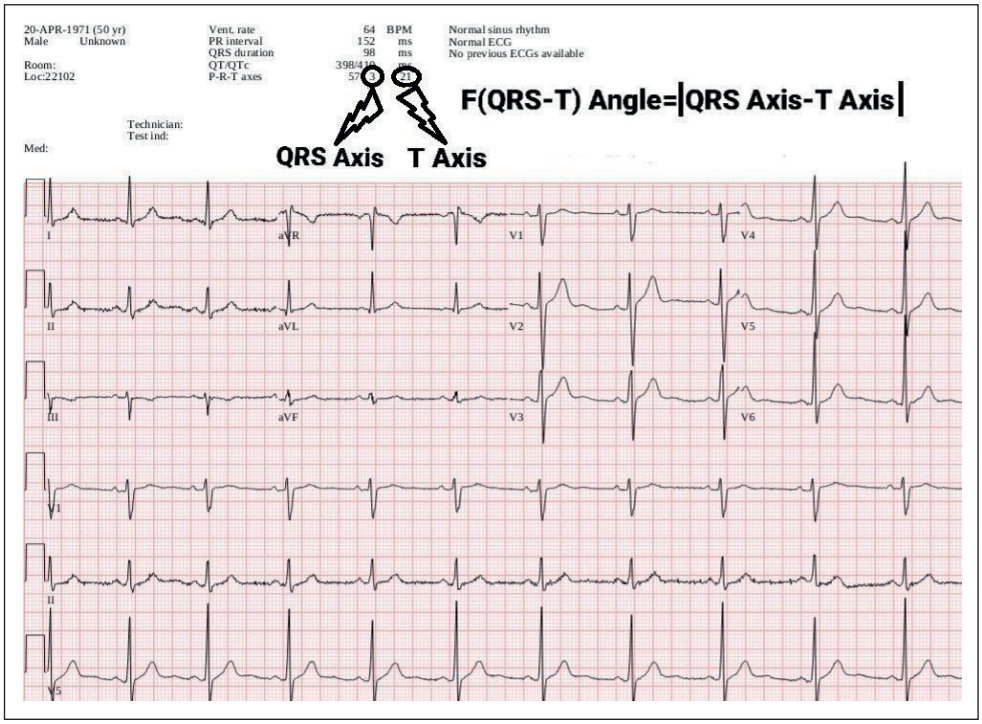

Figure 1. Calculation of the frontal QRS-T angle from the automatic report of surface ECG.

Patient Population

We assessed 166 consecutive patients with systolic HF who underwent single-lead ICD implantation between August 2020 and April 2021. Patients with a history of invasive cardiac procedures (percutaneous coronary, cardiac valvular, or electrophysiologic intervention), as well as patients with atrial fibrillation, a basal conduction defect, severe valvular heart disease, ventricular pace (Vp) $\geq$ 5% or a glomerular filtration rate (GFR) $\leq$ 15 ml/min were excluded. Patients who had been hospitalized with decompensated HF or had a revision medical treatment in the last 6 months were also excluded. We did not include 36 patients based on these exclusion criteria, and 12 other patients declined to participate. Therefore, 118 patients were enrolled in our study and followed over 6 months; 17 patients were lost to follow-up. The f(QRS) angles of 101 patients were calculated just before and 6 months after ICD implantation.

Data Collection

Detailed information on gender, age, medical history, comorbidities, and the results of routine blood laboratory test parameters were collected from the electronic medical records of our hospital.

We defined ischemic cardiomyopathy as chronic left ventricular dysfunction secondary to myocardial infarction, along with established coronary artery disease (CAD) and wall motion abnormalities.

We obtained QRS and T wave axis data from digital ECG (Cardiofax M Model ECG -1250; Nihon Kohden Corporation, Tokyo, Japan) records. The f(QRS-T) angle was calculated as the absolute difference between the QRS and T axes, which can easily be obtained from digital ECG. Figure 1 illustrates the f(QRS-T) angle estimated from an automatically generated surface ECG record. If the difference exceeded 180°, the f(QRS-T) angle was calculated as 360° minus the absolute difference between the f(QRS-T) and T axes[1]. The f(QRS-T) angle before ICD implantation was subtracted from the f(QRS-T) angle calculated 6 months thereafter and defined as the Δf(QRS-T) axis.

All patients underwent a transthoracic echocardiogram performed by two cardiologists blinded to the clinical status of the patients, using the Affiniti 50 echocardiography device (Philips, Bothell, WA, USA). The left ventricular posterior wall thickness (PWT), interventricular septal thickness (IVST), left ventricular end-diastolic diameter (LVEDD), and ascending aorta diameter were measured in the parasternal long-axis view. The left ventricular ejection fraction (LVEF) of

Table I. Demographic and clinical data of study population.

Age, year	58.64 ± 10.95
Gender, male, n (%)	87 (86.1)
Comorbidities, n (%)	
DM	39 (38,6)
HT	74 (73.3)
Stroke/TIA	4 (4)
Ischemic CMP	77 (76.2)
Laboratory findings	
FBG, mg/dL	103 ± 45
Creatinine, mg/dL	1.02 ± 0.32
HDL-C mg/L	36 ± 9
LDL-C mg/L	79 ± 49
WBC, 10^3/uL	8.27 ± 1.97
Hb, g/dL	14.04 ± 1.64
Echocardiographic findings	
LVEDD, cm	5.92 ± 0.66
LVEF, %	26.0 ± 8.0
IVST, cm	1.0 ± 0.3
Drugs, n (%)	
ASA	74 (73.3)
Beta-blocker	94 (93.1)
ACE inhibitor	76 (75.2)
MRA	68 (67.3)
Statin	56 (55.4)

ACE: angiotensin-converting enzyme, ASA: acetylsalicylic acid, CMP: cardiomyopathy, DM: diabetes mellitus, FBG: fasting blood glucose, F(QRS-T) angle: frontal(QRS-T) angle, Hb: hemoglobin, HDL-C: high-density lipoprotein cholesterol, HT: hypertension, IVST: interventricular septal thickness, LDL-C: low-density lipoprotein cholesterol, LVEDD: left ventricular end-diastolic diameter, LVEF: left ventricular ejection fraction, MRA: mineralocorticoid receptor antagonists, TIA: transient ischemic attack, WBC: white blood cell.

the patients was calculated using the Simpson's biplane method.

Single-lead ICDs (single-coil Df4 6935M-62; Medtronic, Minneapolis, MN, USA) were implanted in patients with LVEF ≤ 35% who had primary prevention indication. Two experienced cardiologists implanted all of the ICDs via the left subclavian vein.

Statistical Analysis

All data were analyzed using SPSS software (version 22.0; SPSS Inc., IBM, Armonk, NY, USA). Continuous data are summarized as mean ± standard deviation (SD) or median and interquartile range (IR) as appropriate, and categorical variables are described as numbers or percentages. The f(QRS) angle before and after ICD implantation was compared using the Wilcoxon signed-rank test. We analyzed the Δf(QRS-T) angle according to gender, HF etiology, and ICD shock therapy using the Mann-Whitney U test.

Results

Data from 101 HF patients who underwent single-lead ICD were analyzed. The demographic and clinical data of the participants are presented in Table I. The mean age of the study group was 58.64 ± 10.95 years; 87% were male, 77% had an ischemic etiology, and 9 (8.9%) had undergone shock therapy. We determined no significant difference between the f(QRS-T) angle before and 6 months after ICD implantation (Figures 2, 3). There were no differences in Δf(QRS-T) angle according to gender, HF etiology, or shock therapy status (Table II).

Discussion

The results of our study indicated that there was no statistical difference between the f(QRS-T) angle before and 6 months after ICD implantation.

A narrow planar QRS-T angle (< 45°) has been defined previously in healthy cases. Some experts detected planar QRS-T angles of 45-60° in a small proportion of professional athletes, hypertensive patients, and patients with ischemic heart disease, and defined these cases as abnormal[6]. A wide QRS-T angle indicates electrical heterogeneity caused by depolarization and repolarization discordance. Many scholars[7,8] highlight the importance of spatial and frontal QRS-T angles. Kors et al[7] reported a statistically significant hazard ratio of 5.6 for SCD in patients with an abnormal spatial QRS-T angle. Aro et al[8] demonstrated that a wide f(QRS-T) angle (> 100°) in middle-aged patients in the general population was associated with a more than two-fold higher risk of arrhythmic death. It has been shown that the more easily calculated f(QRS-T) angle can be utilized instead of the spatial QRS-T angle. Pavri et al[6] reported that an f(QRS-T) angle of > 90° was a significant independent predictor of a composite endpoint of death, appropriate ICD shock, and resuscitated cardiac arrest in dilated cardiomyopathy patients. Recently, a wider f(QRS-T) angle was associated with poor outcomes in patients with ST-segment elevation myocardial infarction[9]. Additionally, the f(QRS-T) angle predicted SYNTAX scores in non-ST-segment elevation myocardial infarction patients[10]. Although it is not clear which factors are most influential, increased left ventricular mass, bundle-branch block, pacing, and ischemia have all been associated with a widen

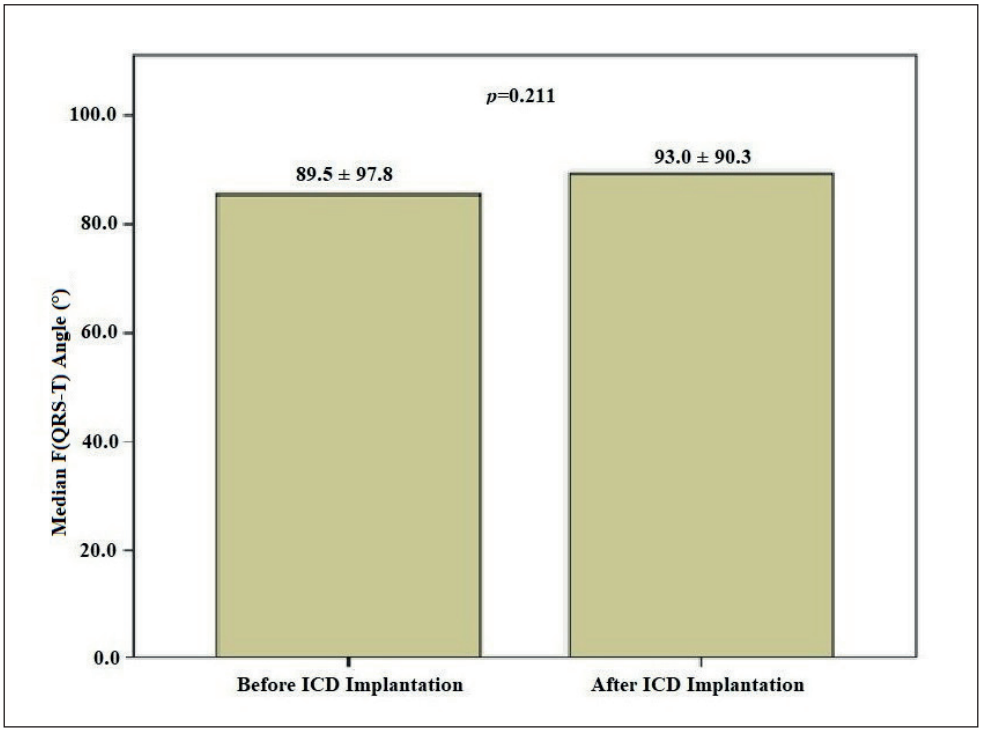

Figure 2. The frontal (QRS-T) angle before and after single lead implantable cardioverter-defibrillator implantation.

QRS-T angle (> 90°)[6]. Mechanical trauma, inflammatory reactions, fibrosis, necrosis, and scar tissue induced by ICD leads may also affect the f(QRS-T) angle. However, this was not seen in our study. Subtle histological changes induced by ICD leads may be undetected by analyses based on the f(QRS-T) angle, which may not be sufficiently sensitive to detect fibrosis and scar tissue in the right ventricle.

The basal mean ± SD ejection fraction of our study patients was 26.0 ± 8.0%, and the median ± IR of (QRS-T) angle was 89.5° ± 97.8°. Unfortunately, there is no clear cut-off value for an abnormal f(QRS-T) angle. It varies with age, sex, inspiration, expiration, and even body mass index[1,11]. For this reason, further studies must be conducted on the f(QRS-T) angle.

It is well known that pacemaker leads induce inflammation. The first response to tissue damage is the development of thrombus, followed by activation of the complement and fibrinolytic systems. Fluid, protein, and blood cell entry into tissue contiguous to the lead leads to an acute inflammatory response mediated by neutrophils, macrophages, foreign body giant cells, and fibroblasts. This is followed by granulation tissue that progresses into fibrous connective scarring tissue[5]. Li et al[12] reported that massive adhesions and fibrosis usually occur along the pacemaker/ICD lead route. This process may lead to a difference in the frontal angle between depolarization and repolarization of the heart. No statistical difference between the f(QRS-T) angle measured before and 6 months after ICD implantation was observed in this study; however, differences in this angle may take longer than 6 months to manifest. The duration of the inflammatory process ending in fibrosis is highly variable across studies. In animal models, the healing process takes between 28 and 90 days, while it can take 2 years or more in humans after implantation of an atrial-septal occlusion device or left atrial appendage occluders[13].

Singer et al[14] reported that use of an ICD lead system and multiple defibrillations result in pathologic changes affecting < 2% of the total myocardial mass. In patients with left ventricular dysfunction and a large left ventricular mass, right ventricular irritation by an ICD lead may not have a significant effect on the f(QRS-T) angle. On the other hand, VVI pacemaker leads with a Vp < 5% in patients with normal left ventricular structure and function may change the f(QRS-T) angle. Additionally, histological changes may be more prominent in patients with a higher Vp ratio, and f(QRS-T) may change in a time-dependent manner.

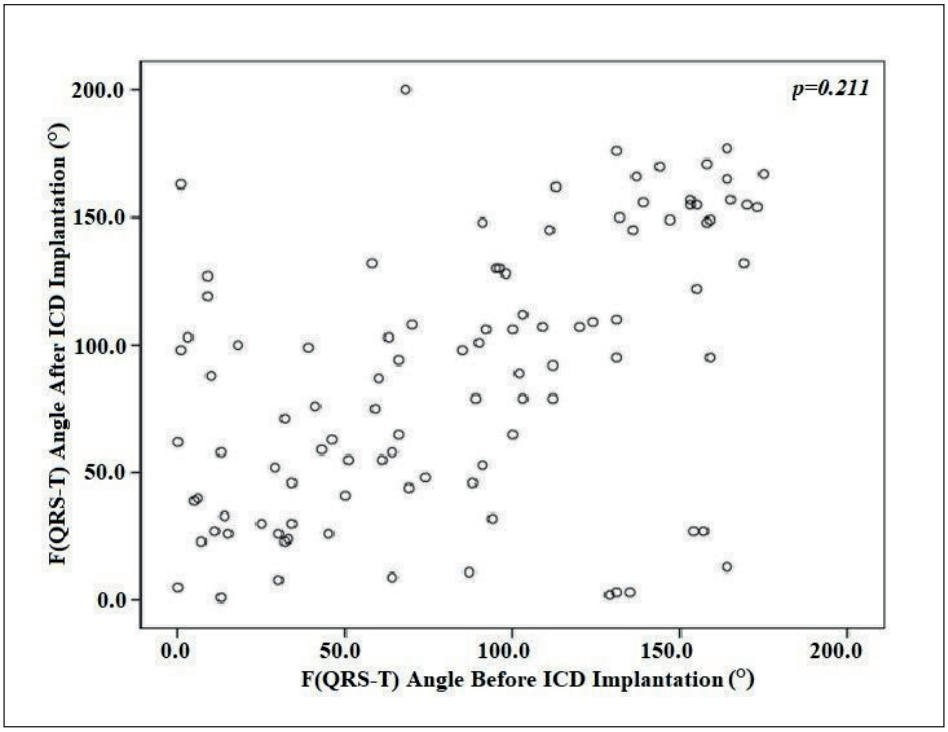

Figure 3. Scatter plot graphic of frontal (QRS-T) angle before and after single lead implantable cardioverter-defibrillator implantation.

ICD lead related fibrosis in the right ventricle may be more frequent in patients who have had shock therapy. A postmortem study[5] reported that interstitial fibrosis varied by lead and acute cell injury was only present in patients who had recently been shocked. In an animal study, Barker-Voelz et al[15] showed that necrosis was concentrated at the distal electrode, where the shocks were delivered. We found no difference in Δf(QRS-T) angle between the patients who had shock therapy and those who did not (Table II). However, only nine (8.9%) patients in our cohort received ICD shock therapy, limiting our ability to determine the effect of ICD shock therapy on Δf(QRS-T) angle. Van Vleet et al[16] reported endocardial fibrosis due to ICD lead implantation in canine hearts without shocks. An inflammatory reaction and endocardial fibrosis in the right ventricle due to an ICD lead can occur independent of shock therapy. Therefore, the absence of any change in the Δf(QRS-T) angle in our patients after ICD shock therapy suggests that ICD shock has no effect on the Δf(QRS-T) angle, rather than indicating a lack of statistical power in this study to detect significant change.

In a study of ICD patients who underwent preimplant cardiac magnetic resonance imaging, the QRS-T angle was wider in patients with an ischemic scar than in those with no evident scar[17]. Similarly, we hypothesized that changes in the right ventricle due to the ICD lead might affect the f(QRS-T) angle. However, since leads with steroid-coated tips were used in our study, inflammatory changes might have been suppressed. Earlier animal studies comparing histological findings between steroid-eluting and non-steroid pacemaker ventricular electrodes reported less connective tissue formation and fewer inflammatory cells in the peri-electrode fibrous connective tissue in steroid-eluting electrodes[18]. However, a human postmortem study showed only marginal differences between the histological findings for steroid-elut-

Table II. ΔF(QRS-T) Angle According to Gender, Heart Failure Etiology and ICD Shock Therapy.

Variables	ΔF(QRS-T) Axis (°)	p-value
Female	22.0 ± 54.8	0.178
Male	4.0 ± 46.8	
Ischemic	4.5 ± 45.8	0.965
Non-ischemic	7.5 ± 55.3	
Shock (-)	4.5 ± 47.3	0.461
Shock (+)	-5.5 ± 64.3	

ICD: Implantable cardioverter-defibrillator; F(QRS-T) Angle: Frontal (QRS-T) Angle; ΔF(QRS-T) = F(QRS-T) (After ICD) - F(QRS-T) (Before ICD).

ing and the non-steroid-eluting pacemaker ventricular electrodes[19]. The effect of ICD leads on the f(QRS-T) angle thus remains unknown.

There were some limitations to our study. First, it was a single-center study with a limited number of patients. Second, we were not able to measure changes in tissue level after ICD implantation *via* histological or imaging methods.

Conclusions

Histopathological studies showed that the irritating effect of ICD leads may lead to fibrosis and scar tissue. However, fibrosis and scar tissue did not affect the f(QRS-T) angle, which suggests that these pathologies may not have clinical significance. Further studies on the f(QRS-T) angle are warranted to understand its clinical significance for ICD-induced local fibrosis.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Authors' Contribution

FB conceived and designed the work, contributed to data acquisition, analyzed and interpreted the data. KGB drafted the manuscript and revised the manuscript critically for important intellectual content.

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Data Availability Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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