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Original Article

The relationships between the repolarization and depolarization markers of sudden cardiac death in smokers

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Abstract

Introduction: The risk of sudden cardiac death (SCD) and atrial fibrillation (AF) increases in smokers. This study aimed to determine the relationships between the repolarization and depolarization predictors of SCD in routine electrocardiography (ECG) in smokers.

Methods: Between January and August 2019, 98 healthy patients with smoking history for more than five years were included in the study group by simple random sampling. The control group consisted of 122 non-smokers. Following routine physical examinations and blood tests, P wave dispersion in the right precordial leads (PWdR) and the left precordial leads (PWdL), T peak-end interval in the right precordial leads (Tp-eR) and the left precordial leads (Tp-eL), QRS dispersion in the right precordial leads (dQRSR) and the left precordial leads (dQRSL), and QRS duration values in the right precordial leads (QRSR) and the left precordial leads (QRSL) were calculated in routine 12-lead ECG + right precordial leads in the both study and control groups.

Results: There was a statistically significant moderate positive correlation between dQRSRxTp-eR/QRSR-value and smoking time in the study group. Also, there was a statistically significant weak negative correlation between dQRSLxTp-eL/QRSL-value and smoking time in the study group (R=0.52, and $P<0.01$, R=0.41 and $P<0.01$, respectively). There was a significant difference between correlation ratio of dQRSRxTp-eR/QRS-value and smoking time and dQRSLxTp-eL/QRSL-value and smoking time in the study group (Z=5.73, p<0.01).

Conclusion: In the current smokers, dQRSRxTp-eR/QRSR and dQRSLxTp-eL/QRSL values were significantly higher than in the control group.

Introduction

Smoking is a major risk factor for atherosclerosis.[1] Although smoking studies on cardiovascular mortality and morbidity are numerous, smoking studies on ventricular arrhythmogenesis are very limited.[2,3] It is estimated that approximately 40-50% of all cardiovascular deaths are sudden cardiac deaths (SCDs), and about 80% of these are due to ventricular tachyarrhythmias.[4] SCD is defined as an unexpected condition thought to be due to ventricular arrhythmias,[5] and most of cardiac arrests occur without warning symptoms and are usually fatal within 1 hour.[6] Determined or suspected risk factors for SCD include age, obesity, diabetes, physical inactivity, dietary factors, hypertension, high serum cholesterol, elevated resting heart rate, and family history of SCD.[7-9]

Recently, there has been an increasing number of publications suggesting that smoking can also lead to arrhythmias without underlying structural heart disease. In the literature, the increased risk of SCD in smokers ranges from 50% to 55%.[10]

PWD is accepted as a risk factor of atrial fibrillation (AF) with or without a systemic disease.[11] PWD is defined as the difference between the longest P wave and the shortest P wave in the superficial ECG. In patients with AF, it is well known that increased P-wave duration and PWD reflect the prolongation of intra- and interatrial conduction time and non-homogeneous spread of sinus impulses.[12] The risk of AF in smokers was found to be significantly higher in a study group of 11047 current smokers compared to the control group at a 10-year follow-up (9.5% vs. 7.8%).[13]

Tp-e interval is electrocardiographic repolarization, and QRS dispersion is depolarization predictor of SCD.[14] The time between the peak and the end of the T wave (Tp-e interval) is accepted as an index of transmural dispersion of ventricular repolarization.[15] Tp-e/QT and Tp-e/QTc ratios are also used as electrocardiographic indexes of ventricular arrhythmogenesis.[16] Although many studies are showing that the Tp-e interval is prolonged in routine standard 12-lead ECG, including smokers, and the risk of SCD is increased, the change in right and left precordial leads has not been examined separately.

dQRS can be calculated by subtracting the minimum QRS from the maximum QRS duration. Increased QRS duration and dispersion showed a better risk of increased

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risk of ventricular arrhythmia in the early stages of myocardial infarction than the dispersion of the corrected QT interval.[17]

Furthermore, there are very few studies on dQRS in the literatures.[18] Besides, dQRS in smokers has not yet been studied. Although dQRSxTp-e/QRS is a new marker of SCD,[19] including depolarization and repolarization markers, no study in the literature evaluates it. Our study aimed to investigate the effect of smoking on P wave dispersion, Tp-e interval, Tp-e/QT, Tp-e/QTc ratios, and dQRS and Tp-e X dQRS/QRS ratio in smokers, separately in the right and left precordial leads with comparing age and sex-matched control group.

Materials and Methods

Study population

Between January and August 2019, 98 healthy smoker subjects (79 males, 80.61% and 19 females, 19.39%) presented to the outpatient cardiology clinic with atypical angina and no pathology detected in their history, physical and blood examinations, were included in the study. The mean age of this group was51.62 ± 12.67 years. The control group consisted of 122 non-smoker subjects (98 males, 80.32% and 24 females, 19.68%) with a healthy history, physical and blood examinations. It was planned to have a total of minimum 200 subjects in the study and control groups, and subjects were included in the study by simple randomized selection. The mean age of the control group was 52.13 ± 11.53 years. The exclusion criteria were having any systemic disease such as diabetes mellitus or hypertension, impaired liver or kidney function test, diastolic dysfunction, structural or significant valvular heart disease, electrolyte imbalance in routine blood examination, anemia or thyroid dysfunction, a disease that may affect the heart, a history of coronary arterial disease or any anti-ischemic treatment, the presence of a cardiac pacemaker, large right and left chambers in the heart, left ventricular ejection fraction under 60%, taking any cardiac treatment affecting the predictors of AF and SCD, being an ex-smoker, the patients whose tricuspid insufficiency is not enough to calculate sPAP and those who have more than the mild degree of tricuspid insufficiency,, previous diagnosis of chronic obstructive pulmonary disease (COPD) and receiving bronchodilator therapy, being unable to perform RFT, and diagnosis of cancer. Informed consent was obtained from each subject. They are questioned in terms of demographic information other diseases, and smoking habits. Following a full physical examination, including three times blood pressure measurement after five minutes of rest, the both study and control groups were taken to ECG, respiratory function test (RFT), transthoracic echocardiography (TTE), and pulse oximetry. The patients whose blood pressure was above three measurements average 140/90 mmHg were excluded from the study. In addition, patients with any of the three measurements of pulmonary function tests were obstructive were excluded.

Electrocardiography

ECG with the right precordial leads ($V_{1-6}R$) and the standard 12-lead were performed at the supine position with a speed of 25 mm/s of paper and 10 mm/mV amplitude by using standard ECG system (Cardiofax V model 9320, Nihon Kohden, Tokyo, Japan). ECG recordings had10 sec length, therefore depending on the heart rate, there were 4-6 beats per lead. The same cardiologist who was blinded to the patient's status, measured each ECG recording manually by the use of a magnifying glass (TorQ, 150 mm Digital Caliper LCD). The RR intervals, P wave duration, QT intervals, and T peak-end intervals and QRS duration of the ECG recordings were measured manually with an accuracy of 0.01 mm.

According to Boston Scientific ECG Screening Tools, in addition to left precordial leads, right ventricular precordial leads were taken by the vertical mirror image of the left ventricular precordial leads and displacement of left and right extremity electrodes.[20] V_1R was defined as left fourth intercostal space of sternum side (1 cm), V_2R as right fourth intercostal space of sternum side (1 cm), and V_4R as right fifth intercostal space and right midclavicular line intersection. The midpoint of V_4R -V_2R line was used as V_3R. The intersection point of right front axillary line and fifth intercostal space was used as V_4R and the right middle axillary line intersection point was used as V_6R. The time from the peak of an R wave to the peak point of the other R wave called RR interval. This measurement was calculated between at least three precordial leads and at least three consecutive R waves for P wave duration, QRS duration, and QT and Tp-e interval in both left and right precordial leads (V_{2-5} precordial right and left leads).

The end of the QT interval was determined from the onset of the QRS wave to the point where the T wave returned to the isoelectric line. This measurement was calculated at least three leads in both left and right precordial leads (V_{2-5} precordial right and left leads) and three consecutive QRS waves in one lead for QT interval. QTc was calculated using Bazett's formula. Arithmetic averages of measurements were used for analysis.

T peak-end interval was determined from the peak to baseline of T wave in the V_2-$_5R$ and $V_{2-5}L$ leads. Tp-e intervals were calculated by multiplying the obtained value in milliseconds by 40. If the U wave was present, the nadir between the T wave and U wave defined as T wave end. cTp-e intervals were calculated by using the Bazett's formula. Arithmetic averages of measurements were used for analysis.

P wave duration was determined from the onset of the P wave to the point where the P wave returned to the isoelectric line. P wave dispersion was calculated by subtracting the shortest P wave duration from the longest P wave duration. The data of ECG with papers at a speed of 25 mm/sc-amplitude of 10 mm/mV, measured in mm

with the digital caliper, were calculated as millisecond multiplied by 40. This measurement was calculated at least both in three right and left precordial leads (V_{2-5} precordial right and left leads) and three consecutive P-QRST cycles in one lead for P wave duration.

QRS duration was termed, as the point where the S wave finished from the onset of the Q wave. dQRS was calculated by subtracting the shortest QRS duration from the longest QRS duration. The data of ECG with papers at a speed of 25 mm/sc-amplitude of 10 mm/mV, measured in mm with the digital caliper, were calculated as millisecond multiplied by 40. This measurement was calculated at least both in three right and left precordial leads (V_{2-5} precordial right and left leads) and three consecutive QRS waves in one lead for QRS duration.

dQRSxTp-e/QRS value was calculated by simply inserting dQRS, Tp-e interval, and QRS duration in the formula.

Respiratory function test

After five minutes of rest, both the study and control groups were taken to the RFT in a sitting position. Following deep inspiration, the subject was asked to perform the full expiration vigorously to the spirometer. The same procedure was performed three times successively. The values obtained from these three measurements were determined using averages. Subjects who could not perform enough expiration were excluded from the study.

Pulse oximetry

Peripheral oxygen saturation (POS) of the subjects was measured by pulse oximetry. After five minutes of rest, the subjects were in the supine position and the measurements were taken under normal weather conditions. During a one-minute pulse oximetry measurement, the most common value was recorded in the display. POS was determined as %.

Transthoracic echocardiography

All subjects underwent two-dimensional echocardiography examination. We obtained standard parasternal long-axis, midventricular short-axis, long apical axis, apical 2- and 4-chamber images with the Phillips HD11XE, 2012 Netherland. Continuous wave Doppler of the Tricuspid Valve Regurgitation (TR) tracing was used to measure the pressure difference between the right ventricle and right atrium. In the Bernoulli formula ($P = 4X\ [TRmax]^2$), the value obtained by the continuous wave replacing over TR and the pressure difference between the right ventricle and the right atrium was calculated. The value obtained from the Bernoulli formula is traditionally calculated by the addition of right atrial pressure (RAP) to calculate sPAP. However, the latest ESC (European Society of Cardiology) guidelines recommend the use of the TR max without additional RAP.[21] We used the Vmax value obtained from TR by simply inserting it into the formula of Bernoulli.

Statistical analysis

Continuous variables were expressed as a mean±standard deviation. Normality of the data was assessed Kolmogorov–Smirnov test. Categorical variables were expressed as percentages. Student *t* test and the chi-square test were used for the comparison of continuous and categorical variables. To compare the values of the different two groups t-test calculator for independent two means and to compare the different values of the same group, T-test calculator for dependent means was used. To compare the proportions Z test calculator for two population proportions were used. The Pearson correlation test was used to examine the correlation between variables. $P< 0.05$ was considered to be significant. Statistical analysis was performed using a commercially available statistical package SPSS version 20.0 (IBM Co., Armonk, NY, USA).

Results

The smoking duration of the study group was 21.29 ± 12.39 packages/year. There were no statistically significant differences between the study group and the control group in terms of socio-demographic properties and basal clinic findings (Table 1).

PWdL and PWdR, PDR, Tp-eR and Tp-eL intervals, dQRSR and dQRSL, QTR and QTL durations, QRSR, and QRSL durations, basal HR, and sPAP values in the study group were significantly higher than in the control group. POS values of the study group were significantly lower than in the control group. There was no difference between the study and control groups in terms of PDL, $FEV_{1,}$ and FVC values (Table 2).

dQRSRxTp-eR/QRSR, dQRSLxTp-eL/QRSL, Tp-eR/QTR, Tp-eR/QTcR, Tp-eL/QTL, and Tp-eL/QTcL ratios, cTp-eR, cTp-eL, QTR and QTL intervals, dQRScR and dQRScL, QRScR and QRScL durations were significantly higher in the study group than in the control group. Furthermore, there is no statistically significant difference between the study group and the control group in terms of FEV_1/FVC ratios (Table 3).

In the study group, there was a strong positive correlation between dQRSR time and smoking time (packages/year). Besides, there were moderate positive correlations between smoking time and dQRSRxTp-e/QRSR, dQRSLxTp-eL/QRSL, dQRSL, Tp-eR, Tp-eL values. There were moderate positive correlations between sPAP, Tp-eR, and dQRSR values. In addition, there were weak positive and statistically significant correlations between smoking times and QTR, QTL, sPAP, dQRSLxTp-eL/QRSL, PWdR, PWdL, and basal HR values. There were statistically significant weak positive correlations between sPAP and Tp-eL and dQRSL values. There were statistically significant weak positive correlations between POS and dQRSR, dQRSL, and Tp-eR values. Furthermore, there was a significant weak negative correlation between POS and Tp-eL values. There were statistically significant moderate negative correlations FEV_1 and Tp-eR and

Table 1. The socio-demographic properties and basal clinic findings of the study and control groups

Variables	Study group	Control group	T or Z-value	*P* value
Age, years	51.62 ± 12.67	52.13± 11.53	T=-0.31	0.758
Males, %	80.61	80.32	Z=0.05	0.963
Females, %	19.39	19.68	Z=0.05	0.963
BMI, kg/m^2	24.82±1.95	25.04±1.84	T=0.85	0.396
Basal HR, beat/min	83.27±12.94	82.99±12.01	T=0.16	0.861
Blood pressure, mm Hg	121.72±10.95	120.01±11.73	T=1.10	0.264
LV mass, gram	174.16±21.84	172.73±20.81	T=0.49	0.623
Glucose, mg/dL	93.83±7.92	91.62±10.15	T=1.76	0.078
TSH, mU/L	2.15±0.73	2.21±0.66	T=0.63	0.523
Total Cholesterol, mg/dL	179.37±31.63	177.92±35.34	T=0.31	0.754
Triglyceride, mg/dL	135.44±22.15	133.69±19.37	T=0.62	0.537
HDL, mg/dL	39.18±12.63	41.72±11.37	T=-1.56	0.112
LDL, mg/dL	142.69±20.52	139.46±22.73	T=1.09	0.274
Sodium, mEq/L	140.16±1.07	140.02±1.72	T=0.70	0.481
Calcium, mg/dL	9.36±0.44	9.41±0.53	T=0.74	0.456
Potassium, mEq/l	3.77±0.28	3.84±0.33	T=1.67	0.098
Magnesium, mg/dL	2.21±0.36	2.19±0.33	T=0.42	0.663
Creatinin, mg/dL	0.93±0.18	0.95±0.13	T=0.95	0.342

Abbreviations: BMI; body mass index, HR; heart rate, LV; left ventricle, TSH; thyroid stimulating hormone, HDL; high-density lipoprotein, LDL; low-density lipoprotein.

Table 2. The comparison of ECG findings of the study and the control groups

Variable	Study group	Control group	T-value	*P* value
PWdR, ms	37.44±11.52	21.83±8.93	11,32	<0.001
PWdL, ms	32.62. ±8.42	24.62±8.59	6,92	<0.001
Tp-eR, ms	88.72±10.33	78.27±9.35	7,86	<0.001
Tp-eL, ms	90.57±12.72	76.11±8.36	10,12	<0.001
dQRSR, ms	34.63±7.93	26.26±8.36	7,55	<0.001
dQRSL, ms	32.69±6.36	23.71±5.82	10,91	<0.001
QTR, ms	362.83±33.92	352.84±33.52	2,18	0.024
QTL, ms	364.52±29.73	354.84±27.26	2,51	0.013
QRSR, ms	94.94±11.72	82.83±10.63	8,02	<0.001
QRSL, ms	93.744±10.92	81.84±11.73	7,71	<0.001
FEV_1, L	2.55±0.72	2.61±0.69	0,62	0.513
FVC, L	3.45±0.69	3.43±0.77	0,2	0,843
POS, %	95.73±1.79	97.99±0.83	-12,39	<0.001
sPAP, mm Hg	35.16±7.52	21.14±4.01	17,7	<0.001
HR, beat/min	84.93±13.5	80.87±12.73	2,28	0.025

Abbreviations: PWdR; P wave dispersion in the right precordial leads, PWdL; P wave dispersion in the left precordial leads, Tp-eR; T peak-end interval in the right precordial leads, Tp-eL; T peak-end interval in the left precordial leads, dQRSR; QRS dispersion in the right precordial leads, dQRSL; QRS dispersion in the left precordial leads, QTR; QT interval in the right precordial leads, QTL; QT interval in the left precordial leads, QRSR; QRS duration in the right precordial leads, QRSL; QRS duration in the left precordial leads, FEV_1; forced expiratory volume in 1 second, FVC; forced vital capacity, POS; peripheral oxygen saturation, sPAP; systolic pulmonary arterial pressure, HR; heart rate.

dQRSR values. Also, there statistically significant weak negative correlation between FEV_1 and dQRSL and Tp-eL values (Figure 1-2, Table 4).

In the control group, there were statistically significant weak positive correlations between sPAP and dQRSR, PWdR, PWdL, Tp-eR, and dQRSL values. Also, there was a significant weak negative correlation between Tp-eL and sPAP values. There was a statistically significant weak negative correlation between POS, Tp-eR, and dQRSR values. Furthermore, there were significant weak negative correlations between POS and dQRSL and Tp-eL values. There were statistically significant weak positive correlations between FEV1 and dQRSR, dQRSL, and Tp-eR values. Besides, there was a statistically significant weak negative correlation between FEV1 and Tp-eL values (Table 5).

Discussion

As can be seen in our study, the relationship between depolarization markers and duration of smoking appears

Table 3: The comparison of ratios and corrected values of the study and control groups

Variable	Study group	Control group	T-value	*P* value
dQRSRxTp-eR/QRSR	35.36±11.33	25.12±9.45	7,3	<0.001
dQRSLxTp-eL/QRSL	30.58±9.37	20.63±7.49	8,75	<0.001
Tp-eR/QTR	0.24±0.03	0.19±0.01	17,26	<0.001
Tp-eR/QTcR	0.22±0.03	0.16±0.01	20,71	<0.001
Tp-eL/QTL	0.23±0.03	0.20±0.02	8,86	<0.001
Tp-eL/QTcL	0.21±0.03	0.17±0.01	13,8	<0.001
cTp-eR	107.68±15.82	87.52±13.63	10,14	<0.001
cTp-eL	110.83±13.74	88.21±7.85	15,33	<0.001
QTcR	431.68±30.48	418.38±31.73	3,14	<0.001
QTcL	417.58±28.47	404.52±26.71	3,5	<0.001
dQRScR	43.83±11.73	33.59±10.58	6,79	<0.001
dQRScL	41.49±10.59	23.38±6.16	15,84	<0.001
QRScR	115.72±17.49	94.72±12.73	10,29	<0.001
QRScL	119.73±18.58	90.73±11.38	14,23	<0.001
FEV_1/FVC	81.03±9.52	82.58±5.23	-1,53	0.124

Abbreviations: Tp-eR; T peak-end interval in the right precordial leads, Tp-eL; T peak-end interval in the left precordial leads, dQRSR; QRS dispersion in the right precordial leads, dQRSL; QRS dispersion in the left precordial leads, QTR; QT interval in the right precordial leads, QTL; QT interval in the left precordial leads, QRSR; QRS duration in the right precordial leads, QRSL; QRS duration in the left precordial leads, FEV1; forced expiratory volume in 1 second, FVC; forced vital capacity, cTp-eR; corrected T peak-end interval in the right precordial leads, cTp-eL; corrected T peak-end interval in the left precordial leads, QTcR; Corrected QT interval in the right precordial leads, QTcL; corrected qt interval in the left precordial leads, dQRScR; corrected QRS dispersion in the right precordial leads, dQRScL; corrected QRS dispersion in the left precordial leads, QRScR; corrected QRS duration in the right precordial leads, QRScL; corrected QRS duration in the left precordial leads.

Table 4. The correlation table of the study group

Variable 1	Variable 2	R-value	*P* value	Correlation
Smoking time	dQRSR	0.78	<0.001	Strong positive
Smoking time	dQRSL	0.61	<0.001	Moderate positive
Smoking time	Tp-eR	0.61	<0.001	Moderate positive
Smoking time	Tp-eL	0.73	<0.001	Moderate positive
Smoking time	QTR	0.44	<0.001	Weak positive
Smoking time	QTL	0.38	<0.001	Weak positive
Smoking time	sPAP	0.49	<0.001	Weak positive
Smoking time	dQRSRxTp-e/QRSR	0.61	<0.001	Moderate positive
Smoking time	dQRSLxTp-eL/QRSL	0.71	<0.001	Moderate positive
Smoking time	PWdR	0.44	<0.001	Weak positive
Smoking time	PWdL	0.38	<0.001	Weak positive
Smoking time	HR	0.33	<0.001	Weak positive
SPAP	Tp-eR	0.56	<0.001	Moderate positive
sPAP	Tp-eL	0.46	<0.001	Weak positive
sPAP	dQRSR	0.62	<0.001	Moderate positive
sPAP	dQRSL	0.49	<0.001	Weak positive
POS	dQRSR	-0.39	<0.001	Weak negative
POS	dQRSL	-0.31	<0.001	Weak negative
POS	Tp-eR	-0.30	<0.001	Weak negative
POS	Tp-eL	-0.21	0.035	Weak negative
FEV_1	dQRSR	-0.53	<0.001	Moderate negative
FEV_1	dQRSL	-0.39	<0.001	Weak negative
FEV_1	Tp-eR	-0.50	<0.001	Moderate negative
FEV_1	Tp-eL	-0.43	<0.001	Weak negative

Abbreviations: PWdR; P wave dispersion in the right precordial leads, PWdL; P wave dispersion in the left precordial leads, Tp-eR; T peak-end interval in the right precordial leads, Tp-eL; T peak-end interval in the left precordial leads, dQRSR; QRS dispersion in the right precordial leads, dQRSL; QRS dispersion in the left precordial leads, QTR; QT interval in the right precordial leads, QTL; QT interval in the left precordial leads, QRSR; QRS duration in the right precordial leads, QRSL; QRS duration in the left precordial leads, FEV_1; forced expiratory volume in 1 second, FVC; forced vital capacity, POS; peripheral oxygen saturation, sPAP; systolic pulmonary arterial pressure, HR; heart rate.

Table 5. The correlation table of the control group

Variable 1	Variable 2	R-value	*P* value	Correlation
sPAP	dQRSR	0.35	<0.001	Weak positive
sPAP	dQRSL	0.26	<0.001	Weak positive
sPAP	Tp-eR	0.30	<0.001	Weak positive
sPAP	Tp-eL	0.23	0.014	Weak positive
sPAP	PWdR	0.38	<0.001	Weak positive
sPAP	PWdL	0.28	<0.001	Weak positive
POS	dQRSR	-0.31	<0.001	Weak negative
POS	dQRSL	-0.22	0.019	Weak negative
POS	Tp-eR	-0.26	<0.001	Weak negative
POS	Tp-eL	-0.20	0.025	Weak negative
FEV_1	dQRSR	-0.33	<0.001	Weak negative
FEV_1	dQRSL	-0.26	<0.001	Weak negative
FEV_1	Tp-eR	-0.30	<0.001	Weak negative
FEV_1	Tp-eL	-0.20	0.025	Weak negative

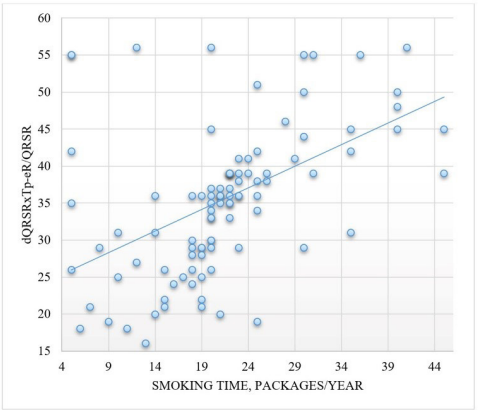
Abbreviations: PWdR; P wave dispersion in the right precordial leads, PWdL; P wave dispersion in the left precordial leads, Tp-eR; T peak-end interval in the right precordial leads, Tp-eL; T peak-end interval in the left precordial leads, dQRSR; QRS dispersion in the right precordial leads, dQRSL; QRS dispersion in the left precordial leads, QTR; QT interval in the right precordial leads, QTL; QT interval in the left precordial leads, QRSR; QRS duration in the right precordial leads, QRSL; QRS duration in the left precordial leads, FEV_1; forced expiratory volume in 1 second, FVC; forced vital capacity, POS; peripheral oxygen saturation, sPAP; systolic pulmonary arterial pressure, HR; heart rate.

to be stronger than the relationship between repolarization markers and the duration of smoking. And again, the type of effect of the heart's right chambers more than the left cavities stands out.

In our study, we found that smoking increases both the risk of AF and the risk of SCD. The AF risk increases in both the right atrium and the left atrium. SCD risk increases in both the right ventricle and the left ventricle. There was a statistically significant weak correlation between smoking time and PWd. This was the same for both the right and left atrium. The strongest correlation was between smoking duration and dQRSR, one of the predictors of SCD. The correlation between smoking duration and dQRSL was found to be moderately positive. The correlation between Tp-eR and TpeL and smoking duration was also found to be moderately positive.

Smoking is a risk factor for AF formation.[22-24] Although smoking is closely associated with AF or malignant ventricular arrhythmias, the underlying mechanism and the association of mechanism with these arrhythmias have not been fully elucidated. In our study, the four chambers of the heart are affected as far as it was seen. The risks of AF from the right and left atrium and the risk of malignant ventricular arrhythmia from the right and left ventricle are significantly higher in smokers compared to controls.

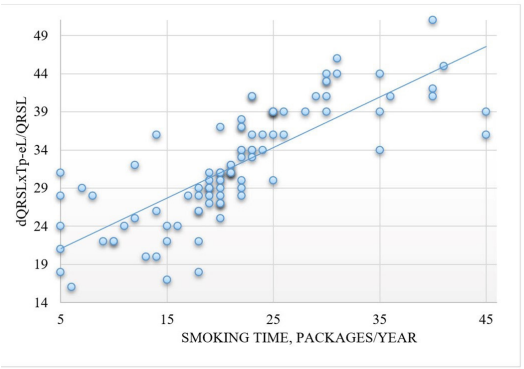
So far, many studies have been conducted to establish that smoking is a predetermined risk factor for cardiovascular diseases such as coronary heart disease and stroke, but



Abbr: dQRSR; QRS dispersion in the Right Precordial Leads, Tp-eR; T peak-end interval in the Right Precordial Leads, QRSR; QRS duration in the Right Precordial Leads

R-value:0.51, p<0.01, Moderate Positive

Figure 1. The Figure of correlation between smoking time and dQRSxTp-eR/QRSR



SL; QRS dispersion in the Left Precordial Leads, Tp-eL; T peak-end interval in the

dial Leads, QRSL; QRS duration in the Left Precordial Leads

i1, p<0.01, Moderate Positive

Figure 2. The figure of correlation of smoking time and dQRSLxTp-eL/QRSL

few studies on tobacco and SCD. Only a few studies are describing the relationship between smoking and SCD in particular.[24,25]

SCD usually occurs due to cardiac arrhythmias, and most SCD occurs without warning symptoms, or within 1 hour after the onset of symptoms, and are generally fatal. Cardiovascular deaths are the leading causes of death in the world. 40-50% of cardiovascular deaths are as SCD, and 80% of these SCDs are due to malignant ventricular arrhythmias.[4]

While malignant ventricular arrhythmias are held responsible for SCD, one of the underlying mechanisms of fatal ventricular arrhythmias is increased sympathetic activity or decreased vagal tone.[26]

The risk of SCD in smokers was 3-fold higher than those who had never smoked and was 38% higher than those who quit smoking. The risk of SCD appears to be two times higher in former smokers than in non-smokers.[27] The number of cigarettes smoked daily, and the duration of smoking was linearly related to the risk of SCD among smokers.[10]

Smoking can cause ventricular fibrillation and SCD by altering ventricular repolarization or depolarization and stimulating sympathetic nervous system activity.[28] The increase in the number of cigarettes smoked per day increases the risk of SCD, and the decrease in the risk of SCD among older smokers compared to existing smokers may explain the underlying biological relationship and their relationship with specific biological mechanisms. It has been proven that all kinds of arrhythmias can occur in smokers, including AF and malignant ventricular arrhythmias.[29,30] This may be related both to the direct increase of sympathetic activity by smoking and to the chronic diseases it might cause.[31] The relationship between smoking and AF may be due to the higher prevalence of cardiovascular risk factors in smokers.[13] Altered ventricular recovery time dispersion indices can lead to ventricular and atrial arrhythmias.[32] Abnormal ventricular repolarization values on ECG may explain the increased risk of cardiovascular events in long-term intensive smokers.[28]

Inter and intra-atrial electromechanical delays were significantly higher in smokers than non-smokers. There was a strong correlation between the smoking amount and interatrial electromechanical delay and a significant correlation between PWD and interatrial electromechanical delay.[33] PWd, as a predictor of AF,[11] myocardial repolarization predictors such as Tp-e interval as well as depolarization markers such as QRS duration and QRS dispersion are used to explain the mechanisms of arrhythmogenesis for malignant ventricular arrhythmias.[14] In addition, Tp-e / QT, Tp-e / QTc and QRSd x Tp-e / QRS, QRSd x Tp-e / QRS x QT ratios can also be used as SCD predictors.[19,34] Chronic smoking is associated with long-term Tp-e interval, high Tp-e / QT ratio, and Tp-e / QTc ratio.[28] No study in the literature evaluates the dQRSxTp-e/QRS ratio, which is a new marker of SCD consisting of repolarization and depolarization markers.

Primary diseases in which P wave dispersion increases are obesity, insulin resistance, slow coronary flow, fibromyalgia, paroxysmal AF, COPD, hypertension, and diastolic dysfunction. The primary diseases with increased Tp-e interval and Tp-e/QT and Tp-e/QTc ratios are arrhythmogenic right ventricular dysplasia, slow coronary flow, HIV infection, subclinical hypothyroidism, mitral valve prolapse, aortic stenosis, hypertrophic cardiomyopathy. Tp-e interval and Tp-e/QT and Tp-e/QTc ratios were examined in standard 12-lead ECG, and it has been found increased in smokers, a significant positive correlation was found between smoking level.[19] Besides, Tp-e and QTc interval, and Tp-e/QT and Tp-e/QTc ratios were increased after varenicline administration in smokers[35], but they were not examined separately in the right and left precordial leads.

dQRS is one of the depolarization markers of SCD.[13] Increases in dQRS in the early stages of myocardial infarction were closely related to SCD. The cut-off points for ventricular tachycardia and fibrillation were 23.5 and 24.5 ms, respectively.[17] To date, the effect of smoking on the dQRS interval has not been investigated, and our study first article that is examining dQRSxTp-e/QRS, which is a new marker of SCD.

Limitatıons of the study

The patients could not be monitored with the 24-hour rhythm Holter device. If 24-hour rhythm Holter monitoring could be done and the relationship of these markers with ventricular arrhythmias, more reliable data could be obtained.

Conclusion

In smokers, PWd, a predictor of AF, Tp-e interval, Tp-e/QT and Tp-e/QTc ratios, QRS duration, QRS dispersion, and dQRSxTp-e/QRS ratio, predictors of SCD, were found to be higher than in the non-smokers. Also, there was

Study Highlights

What is current knowledge?

- Until now, marks of sudden cardiac death have only been studied in the area of repolarization or depolarization. This led to confusing results that were different and difficult to interpret.

What is new here?

- Examination of both repolarization and depolarization areas of sudden cardiac death markers together will lead to clearer and more realistic results. This study, to our knowledge, is the first to examine a marker that simultaneously involves repolarization and depolarization.

the highest positive correlation, statistically significant, between dQRSR and smoking time in the study group. As a result, we found that smoking increased the risk of ventricular arrhythmia in both the right and left ventricles and increased the risk of AF in both the right and left atrium. Furthermore, it can be effective saying to a current smoker how the quantitative risk of AF and SCD is increasing only by ECG with passing smoking time to quit smoking.

Conflict of Interest

The authors declare there is no conflict of interest.

Ethical Approval

All procedures performed in studies involving human participants were following the ethical standards of National Health and Medical Research Council of Turkey and with the 1964 Helsinki declaration and its later comparable ethical standards. Written permission was obtained from Hospital Management. The informed patient consent was obtained from each subject.

Authors' Contribution

All authors have reviewed, approved, and consented to the submission, and they are accountable for all aspects of its accuracy and integrity

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