ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. LXIV, N 1, 5 SECTIO D 2009

[1]Department of Nephrology, [2]Department of Cardiology,
[3]Department of Public Health, Medical University of Lublin

ANDRZEJ J. JAROSZYŃSKI[1], ANNA PAJĄK[2], PIOTR KSIĄŻEK[3],
ANDRZEJ WYSOKIŃSKI[2], ANDRZEJ KSIĄŻEK[1]

Effect of habitual cigarette smoking on QRS-T angle in male subjects

Cigarette smoking has a major impact on the cardiovascular (CV) system, and is associated with an increased risk of sudden cardiac death (SCD) (1). The noninvasive identification of individuals at risk for CV events and especially SCD presents a significant clinical dilemma. It is generally considered, however, that standard ECG has limited utility to predict the risk for SCD in common cardiac diseases such as coronary artery disease and dilated cardiomyopathy (2, 3). Recently, there has been renewed interest in the spatial angle between the three-dimensional vectorcardiographic representation of QRS complex and T-wave loops (QRS-T) to quantify either ventricular repolarization or depolarization. Recent investigations have indicated that QRS-T contains prognostic information, independent of the other ECG characteristics. Several studies have validated the role of the QRS-T as a sensitive, powerful and independent risk stratifier for cardiac events either in the general population (4–6) or in various clinical settings (7–11). The QRS-T is probably especially suited for the prediction of SCD (7). Moreover, QRS-T can be measured easily, and is not affected by observation biases (12).

Despite the influence of cigarette smoking on the cardiovascular system has been studied extensively (1, 13), the influence of smoking on the heterogeneity of ventricular repolarization has not been adequately evaluated. Previous reports have provided conflicting results on the impact of habitual cigarette smoking on ventricular repolarization (14–17). Moreover, even if some studies confirm the negative influence of cigarette smoking on ventricular repolarization (17, 18), no studies have focused on documenting the duration of habitual smoking that possibly induces abnormalities of ventricular repolarization.

The purpose of the study was to estimate the effect of habitual cigarette smoking on ventricular repolarization process expressed as the QRS-T.

METHODS

Study population. The study group consisted of 282 long-term smokers in comparison to age habitual male smokers, aged 30–42 years (mean 36.1±1.6). The study subjects were considered as smokers when they reported a history of regular cigarette smoking of ≥ 15 cigarette daily during at least previous 15 years. All other groups of smokers were not included. The Fagestrom scale score (19) of the studied subjects was 8.7±0.5, ranging from 8 to 12. This scale uses the number of cigarette smoked per day, the duration of smoking, and the intensity of craving for cigarettes. All

smokers had to abstain from cigarette smoking or drink alcohol or caffeine-containing beverages for at least 2 hours before the ECG recordings. One hundred twenty seven male non-smokers took part in the study as a control group; the age range (30–41 years, mean 36.2±1.5) was similar to the group of smokers. The study subjects were considered as non-smokers when they never smoked before the evaluation.

All the studied subjects had normal resting ECG (a sinus rhythm, no evidence of conduction disturbances or pre-excitation, and no structural heart disease as documented by medical history and physical examination. Excluded from the study were subjects with systolic and diastolic blood pressure exceeding 150 and 90 mmHg. Informed consent was obtained from all the study subjects and the studies were approved by members of the local committees of ethics.

Twelve-lead vectorcardiogram (VCG). Surface 12-lead resting ECGs were recorded in an electrically shielded and noise proof room with a computer-based electrocardiograph (Cardioperfect, version 1.1, CardioControl NV, Rijswijk). All 12 leads of each ECGs were recorded simultaneously for 60 sec. ECGs were conducted in while subjects were lying in the supine position and breathing normally after at least 3-min rest.

To derive VCG descriptors, X, Y and Z leads were reconstructed from the 12 leads. The projections of the maximum QRS and T vectors on the frontal (xy), horizontal (xz), and right sagittal (yz) planes were automatically calculated by electrocardiograph. According to previously published trigonometric equations (11, 17), the amplitudes of maximum spatial QRS and T vectors as well as the angular difference between the maximum spatial QRS and T vectors (QRS-T) were calculated from the following formulas:

the amplitude of the maximum spatial T vector (T_{MAX}) = $([Txy^2 + Txz^2 + Tyz^2]/2)^{1/2}$

were: Txy, Txz, Tyz – projection of the maximum T vector on the frontal, horizontal, and right sagittal planes, respectively;

the amplitude of the maximum spatial QRS (QRS_{MAX}) = $([QRSxy^2 + QRSxz^2 + QRSyz^2]/2)^{1/2}$

were: QRSxy, QRSxz, QRSyz – projection of the maximum QRS vector on the frontal, horizontal, and right sagittal planes, respectively;

Cos QRS-T angle = $(QRS_XT_X + QRS_YT_Y + QRS_ZT_Z)/(QRS_{MAX} \times T_{MAX})$

were: QRSx, QRSy, QRSz – projection of the maximum QRS vectors on the X, Y, and Z planes, respectively

Tx, Ty, Tz – projection of the maximum T vectors on the X, Y, and Z planes, respectively.

Mean QT intervals values were adjusted for heart rate according to Fridericia's cubic root formula ($QTc = QT/RR^{1/3}$).

Statistical analysis. Statistical analysis was carried out on an IBM PC using Statistica Version 5. Results were tested for normality. Data are expressed as mean ± SD. The statistical significance of the differences between smokers and non-smokers groups were compared by Student's t test for unpaired data. Linear regression analysis was performed by using the Pearson test. Probability values of less than 0.05 were accepted as significant.

RESULTS

Baseline characteristics of the studied subjects are shown in Table 1. Subjects had smoked an average of 24.7±4.8 (range 15 to 50) cigarettes per day for an average of 19.9±3.1 years (range 15 to 28).

HR was significantly increased in smokers compared with non-smokers ($p<0.001$). Systolic and diastolic blood pressures were not significantly different in groups of smokers and non-smokers. QTc duration showed only a tendency to be higher in smokers in comparison with non-smokers, but did not reach statistical significance ($p=0.089$). The QRS-T was significantly higher in smokers compared with non-smokers ($p=0.007$ and $p<0.001$ respectively).

Table 1. Clinical, electrocardiographic, and vectorcardiographic characteristics of groups of smokers and non-smokers

Parameter	Nonsmokers n=(127)	Smokers (n=282)	p
Age (years)	36.12±1.6	36.2±1.5	0.290
Number of cigarettes/d	-	24.7±4.8	-
Duration of smoking (years)	-	19.9±3.1	-
Systolic blood pressure (mmHg)	122.3±3.1	122.6±4.2	0.512
Diastolic blood pressure (mmHg)	79.4±1.7	80.0±2.1	0.391
Heart rate (bpm)	71.9±3.1	81.9±4.19	<0.001
QTc (ms)	385.3±14.6	389.4±16.0	0.089
QRS-T angle (degree)	19.2±2.9	22.4±3.2	<0.001
QRS-T angle/HR	0.267±0.052	0.273±0.063	0.104

Table 2. Clinical, electrocardiographic, and vectorcardiographic characteristics of two groups of smokers

Parameter	Smokers < 20 years n=(166)	Smokers ≥ 20 years (n=116)	p
Age (years)	35.82±1.24	36.12±1.09	0.070
Number of cigarettes/d	24.9±4.3	25.3±5.1	0.456
Systolic blood pressure (mmHg)	124.4±3.2	124.7±3.6	0.687
Diastolic blood pressure (mmHg)	79.7±1.8	81.2±2.3	0.691
Heart rate (bpm)	80.41±4.19	82.02±4.61	0.046
QTc (ms)	387.1±14.81	387.7±16.33	0.561
Spatial QRS-T angle (degree)	21.76±2.10	23.84±2.42	0.007
Spatial QRS-T angle/HR	0.271±0.038	0.291±0.041	0.004

Either in smokers or nonsmokers the Pearson test showed significant correlations between the HR and QRS-T (r=0.238, p<0.001, and r=0.248, p=0.002 respectively). After the adjustment for HR, QRS-T/HR ratios were not significantly different in smokers compared with non-smokers (Table 1). In the whole group of smokers, no significant correlations were found between QTc as well as QRS-T and the number of years of habitual smoking. However, after the stratification of subjects into subgroups according to the duration of smoking, in a subgroup of 116 subjects smoking ≥ 20 years the QRS-T/HR ratio was higher (p=0.009) in comparison with non-smokers (Table 2). Similarly, significant associations between the number of years of smoking and QRS-T (r=0.274, p=0.003) as well as QRS-T/HR ratio (r=0.249, p=0.012) were found when the cut-off value ≥ 20 years of smoking was assumed. Age as well as the number of cigarettes smoked per day of subjects smoking ≥ 20 years were not significantly different in comparison with subjects smoking < 20 years (Table 2). None relations were found between the number of cigarettes smoked per day and descriptor of ventricular recovery in all the studied subjects as well as in any subgroups of smokers.

DISCUSSION

Our study generated two major findings: (1) cigarette smoking altered QRS-T in male habitual cigarette smokers, however QTc remained unchanged; (2) HR differences between smokers and non-smokers as well as the duration of smoking (≥ 20 years) seem to be important factors altering QRS-T in smokers.

The influence of habitual cigarette smoking on the ventricular repolarization has not been adequately evaluated, and moreover, attainable data are controversial. Some authors have found significance increase of the QT_c interval in smokers (18), others reported no differences (20) in QT_c duration between smokers and non-smokers, whereas Karjalainen et al. (14) found that smoking was associated with shortening of the QT_c interval. Our study demonstrated that QTc duration showed only a tendency to be higher in smokers compared with non-smokers, but did not reach significance. Methodological differences (different formulas applied for the calculation of QT interval correction) as well as other uncontrolled data, such as subjects' age, duration of smoking, the number of cigarettes smoked per day, cigarettes tar and nicotine content, and concomitant diseases could be responsible for the large diversity of results coming from various studies. Further studies are needed to determine the influence of smoking on QT_c duration.

Repolarization abnormalities as shown by spatial QRS-T, have been found to be sensitive predictors of cardiac death in various clinical settings (5–11). Acute cardiac events, such as ventricular fibrillation and SCD, are increased by cigarette smoking, particularly in the presence of preexisting coronary artery disease (1). Our study confirms results of Dilaveris et al. (17) that QRS-T was altered in smokers compared with non-smokers. We need to research further to see if the alterations of QRS-T observed in our study play any clinical role in predicting cardiac events in smokers. It is well known that smokers have an increased sympathetic drive at rest, and higher heart rates (21). QRS-T is correlated with HR either in normal subjects (17) or smokers (17), and such associations were also found also in our study. Taking into consideration that in all the studied subjects, the QRS-T adjusted for the HR showed no significant differences between smokers and non-smokers, the differences in the heterogeneity of ventricular repolarization in the studied subjects were, at least partly, due to HR differences between smokers and non-smokers. Our results are in agreement with Dilaveris et al. (17) who found that QRS-T increase was mainly due to HR differences between smokers and non-smokers.

Our study revealed, however, that in subjects smoking ≥ 20 years the differences in the heterogeneity of ventricular repolarization were not dependent on HR. Moreover, QRS-T corrected for the HR correlated with the duration of smoking. Within our knowledge, the association between the duration of smoking and repolarization parameters, has not been previously reported in the literature. The lack of correlations between duration of smoking and QRS-T in the study of Dilaveris et al. (17) may result from the fact that in the cited paper the authors estimated subjects with duration of smoking shorter nearly four times than in our study. If our results were confirmed in larger groups of smokers it would suggest that approximately 20 years of habitual smoking could be the cut-off value that might lead to ventricular repolarization alteration in different mechanism than increased sympathetic activity. A particular interesting issue, although impossible to clarify at the present stage of study, is the question whether the VCG ventricular repolarization alterations in subjects smoking ≥ 20 years: (1) play any additional clinical role in predicting cardiac events in smokers; (2) are reversible after cessation of smoking; (3) are associated with morphological changes, such as ischemic myocardial damage or subclinical atherosclerosis.

Fauchier et al. (16) have reported significant relation between the number of cigarette smoked per day and duration of QT_c interval. In our study included were only heavy smokers, and it could be responsible for the lack of relations between the number of cigarettes smoked per day and estimated descriptors of ventricular recover time.

In conclusion, habitual cigarette smoking influence ventricular repolarization, expressed as the QRS-T. Duration of smoking (≥ 20 years) and HR differences between smokers and non-smokers seem to be important factors contributing to the higher heterogeneity of ventricular reopolarization in smokers.

Conflict of interest statement. None declared.

REFERENCES

1. Hallstrom A., Cobb L., Ray R.: Smoking as a risk factor for recurrence of sudden cardiac arrest. Am. Heart J., 314, 271, 1986.
2. Ott P., Marcus F.: Electrocardiographic markers of sudden death. Cardiol. Clin., 24, 453, 2006.
3. Engel G., Beckerman J., Froelicher V. et al.: Electrocardiographic arrhythmia risk testing. Curr. Probl. Cardiol., 29, 365, 2004.
4. Yamazaki T., Froelicher V., Myers J. et al.: Spatial QRS-T angle predicts cardiac death in a clinical population. Heart Rhythm, 2, 73, 2005.
5. Kardys I., Kors J., Meer I., Hofman A. et al.: Spatial QRS-T angle predicts cardiac death in a general population. Eur. Heart J., 24, 1357, 2003.
6. Kors J., Rijnbeek P., Herpen G. et al.: Spatial repolarization parameters for predicting cardiac death in the elderly. J. Electrocardiol., 37, 198, 2004.
7. Malik M., Hnatkova K., Batchvarov V.: Post infarction risk stratification using the 3-D angle between QRS complex and T-waves vectors. J. Electrocardiol., 37, 201, 2004.
8. Rautaharju P., Kooperberg C., Larson J. et al.: Electrocardiographic abnormalities that predict coronary heart disease events and mortality in postmenopausal women: the women's health initiative. Circulation, 113, 473, 2006.
9. Rautaharju P., Prineas R., Wood J. et al.: Electrocardiographic predictors of new-onset heart failure in men and in women free of coronary heart disease (from the atherosclerosis in communities) [ARIC] study. Am. J. Cardiol., 100, 1437, 2007.
10. Zhang Z., Prineas R., Case D. et al.: Comparison of the prognostic significance of the electrocardiographic QRS/T angles in predicting incident coronary heart disease and total mortality (from the atherosclerosis risk in communities study). Am. J. Cardiol., 100, 844, 2007.
11. Jaroszynski A., Czekajska-Chechab E., Drelich-Zbroja A. et al.: Spatial QRS-T angle in peritoneal dialysis patients: association with carotid artery atherosclerosis, coronary artery calcification and troponin T. Nephrol. Dial. Transplant., 24, 1003, 2009.
12. Vaidean G., Schroeder E., Whitsel E. et al.: Short-term repeatability of electrocardiographic spatial T-wave axis and QT interval. J. Electrocardiol., 38, 139, 2005.
13. Hinkle L. Jr, Thaler H., Merke D. et al.: The risk factors for arrhythmic death in a sample of men followed for 20 years. Am. J. Epidemiol., 127, 500, 1988.
14. Karjalainen J., Reunanen A., P. et al.: QT interval as a cardiac risk factor in middle aged population. Heart, 77, 543, 1997.
15. Andrŕssy G., Szabo A., Dunai A. et al.: Acute effects of cigarette smoking on the QT interval in healthy smokers. Am. J. Cardiol., 92, 489, 2003.
16. Fauchier L., Maison-Blanche P., Forhan A. et al.: Association between heart rate-corrected QT interval and coronary risk factors in 2,894 healthy subjects (the DESIR Study). Data from an Epidemiological Study on the Insulin Resistance Syndrome. Am. J. Cardiol., 86, 557, 2000.
17. Dilaveris P., Pantazis A., Gialafos E. et al.: The effects of cigarette smoking on the heterogeneity of ventricular repolarization. Am. Heart J., 142, 833, 2001.
18. Ileri M., Yetkin E., Tandogan I. et al.: Effect of habitual smoking on QT interval duration and dispersion. Am. J. Cardiol., 88, 322, 2001.
19. Fagerstrom K.: Measuring degree of physical dependence to tobacco smoke with reference to individualization or treatment. Addict. Behav., 3, 235, 1978.
20. Romero Mestre J., Licea Puig M., Faget Cepero O. et al.: Studies of cardiovascular autonomic function and duration of QTc interval in smokers. Rev. Esp. Cardiol., 49. 259, 1996.

21. Narkiewicz K., Van De Borne P., Hausberg M. et al.: Cigarette smoking increases sympathetic outflow in humans. Circulation, 98, 428, 1998.

SUMMARY

The study was designed to estimate the effect of habitual cigarette smoking on ventricular repolarization process, expressed as the QRS-T angle. 282 healthy male smokers and 127 non--smokers entered the study. The angular differences between the maximum spatial QRS and T vectors (QRS-T) were evaluated in all subjects. QRS-T as well as heart rate (HR) were increased in smokers compared with non-smokers ($p<0.001$ in both cases). Either in smokers or non-smokers correlations between HR and QRS-T were found ($r=0.238$, $p<0.001$, and $r=0.248$, $p=0.002$ respectively). After the adjustment for HR the QRS-T/HR ratio was not significantly different in smokers compared with non-smokers. In the whole group of smokers, no significant correlations were found between either QRS-T or QTc and the number of years of habitual smoking. However, after the stratification of subjects into subgroups according to the duration of smoking, in a subgroup of subjects smoking ≥ 20 years the QRS-T/HR ratio was higher ($p=0.004$) in comparison with non-smokers. Similarly, significant associations between the number of years of smoking and QRS-T ($r=0.294$, $p=0.001$) as well as QRS-T/HR ratio ($r=0.278$, $p=0.009$) were found when the cut-off value ≥ 20 years of smoking was assumed. Habitual cigarette smoking influences ventricular repolarization, expressed as the QRS-T. Duration of smoking (≥ 20 years) and HR differences between smokers and non-smokers seem to be important factors contributing to the higher heterogeneity of ventricular repolarization in smokers.

Wpływ nałogowego palenia papierosów przez mężczyzn na przestrzenny kąt QRS-T

Celem badania była ocena wpływu nałogowego palenia papierosów na proces repolaryzacji komór serca, wyrażony za pomocą przestrzennego kąta QRS-T. Badaniem objęto 282 zdrowych mężczyzn palących oraz 127 niepalących tworzących grupę kontrolną. U wszystkich biorących udział w badaniu określono wartość przestrzennego kąta zawartego miedzy maksymalnymi wektorami zespołu QRS oraz załamka T (QRS-T). Wśród palących kąt QRS-T oraz częstość akcji serca (HR) były wyższe w porównaniu z niepalącymi ($p<0,001$ w obu przypadkach). Zarówno wśród palących jak i niepalących stwierdzono istnienie istotnej zależności między QRS-T oraz HR (odpowiednio $r=0.238$, $p<0.001$ oraz $r=0.248$, $p=0.002$). Po skorygowaniu QRS-T w stosunku do HR uzyskana wartość QRS-T/HR nie różniła się istotnie między obiema badanymi grupami. W całej grupie osób palących nie stwierdzono istotnych zależności między QRS-T jak również QTc oraz czasem trwania palenia. Jednakże w podgrupie osób palących papierosy ≥ 20 lat wskaźnik QRS-T miał większą wartość ($p=0,004$) w porównaniu z grupą osób niepalących. Podobnie w podgrupie osób palących ≥ 20 lat stwierdzono istotną zależność pomiędzy czasem trwania nałogu oraz wartościami QRS-T ($r=0,294$, $p=0,001$) jak również wskaźnika QRS-T/HR ($r=0,278$, $p=0,009$). Nałogowe palenie papierosów zaburza proces repolaryzacji komór serca, wyrażony za pomocą kąta QRS-T. Czas trwania nałogu ≥ 20 lat oraz różnica częstości akcji serca między palącymi oraz niepalącymi stanowią istotne czynniki zwiększonej heterogenności procesu repolaryzacji komór serca u palaczy.