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*Some cardiovascular disease risk factors in men and women  
and QT interval*

Cardiovascular mortality is the reason for the search of indices predicting sudden cardiac death, noticeable and easy to modify at best. One of them is cardiac repolarization time whose prolongation is connected with the increase of cardiovascular risk (3, 7, 11). Repolarization time disorders (recorded as QT interval) can be a prognostic factor of cardiovascular events, which was proved in numerous long-term epidemiological studies (3, 11). Simultaneous study of many indices of sudden cardiac death is more effective in prognostication (1, 13). One of them was the observation of Japanese population carried out for 8.8 years in 3,500 elderly patients, where it was found that prolonged QTc duration is the index of general mortality risk and mortality because of circulatory system diseases and coronary heart disease (7).

Comparison of incidence of repolarization time disorders (on the basis of QT and QTc intervals) in the population of men and women with high and very high cardiovascular disease risk was the aim of the study.

MATERIAL AND METHODS

During the local project for prophylaxis of circulatory system diseases in Lubelszczyzna region the group of high and very high cardiovascular disease risk was isolated on the basis of Polish Cardiological Society criteria from the year 2000. History data and medical examination data were recorded using a questionnaire taking into account cardiovascular disease risk factors (arterial hypertension, diabetes, positive family history, cigarette smoking, overweight, obesity, cardiovascular events). Arterial blood pressure was measured twice at rest, recording the average result. QT duration from resting ECG was measured between the beginning of Q wave and end of T wave (in the place of T wave passage to the isoelectric line). If T wave was overlapped by U wave, the lowest T value was assumed to be the end of T wave. The measurement was made using calipers and magnifying glass (magnification 1x10), in at least 2 leads the average result was recorded. QTc interval was calculated using Bazett's formula. Taking into account QT duration differences in men and women the following QTc was assumed as normal: QTc < 0.45 sec for women (W) and QTc < 0.43 sec for men (M), critical 0.45–0.46 sec (W), 0.43–0.45 sec (M), prolonged QTc > 0.46 sec (W), > 0.45 sec (M) (2). Laboratory studies were made in the hospital laboratory, taking up blood after 12 h of starvation. Lipidogram was determined using bioMerieux kit, glucose level – using enzymatic method with glucose oxidase.

The material was analysed statistically using Statistica 5,0 computer programme. The averages were compared through parametric t-student tests and one factor analysis of variance (ANOVA), cross-tabs, chi-square nonparametric test. 203 people aged from 33 to 75 were examined (average age  $52.18 \pm 7.516$ ), 131 women (W) (64.5%) and 72 men (M) (35.5%).

## RESULTS

Average age of women was  $51.92 \pm 7.88$  and men  $52.65 \pm 6.96$ . Prolonged/critical values occurred more frequently in women (43.5% – 57 W) than in men (15.3% – 11 M). The difference was statistically significant ( $P < 0.05$ ). The percentage of men and women with prolonged QTc was similar (13.0% – 17 women and 13.9% – 10 men) in the studied population (P statistically insignificant).

Under 50 years of age were 81 people (39.9% of the population), 51 women (38.9% W) and 51 men (38.9% M), aged 51–60 were 99 people (48.8% of the population), 65 women (49.6% W) and 34 men (47.2% M), over 60 years of age were 23 people (11.3%), 15 women (11.5% W) and 8 men (11.1% M).

The influence of age on the distribution of repolarization time was evaluated, comparing the duration and incidence of various QT and QTc values in age groups. Statistically significant increase in mean QT values with age was observed in the linear analysis. Mean QT values under 50 years of age were  $0.369 \pm 0.036$  sec, at 51–60 –  $0.376 \pm 0.031$  sec, over 60 –  $0.380 \pm 0.026$  sec ( $P < 0.05$ ). Mean QTc values, however, were the highest in the oldest age groups of women ( $0.429 \pm 0.040$  sec) and men ( $0.442 \pm 0.047$  sec), but the differences between men and women were not statistically significant.

The percentage of prolonged/critical QTc values in women under 50 years of age was 43.1% (22W) and 16.7% in men (5 M), at 51–60 the values were also more frequently observed in women – 40.0% (26 W) than in men – 8.8% (3M), in patients over 60 years of age: in 60.0% of women (9 W) and in 37% of men (3 M). But normal QTc values, especially in younger age groups, occurred in a greater percentage of men than women ( $P < 0.05$ ).

Obesity and overweight occur more frequently in men compared with women, although the differences were not statistically significant. In the studied population BMI from 25 to 29.9 was in 45% women (59 W) and 47.2% men (34 M), BMI > 30 occurred in 24.4% women (32 W) and 30.6% men (22 M). In overweight patients (BMI 25–29.9) prolonged/critical QTc values are in 30.1% of population (28 people), more frequently in women – 44.1% (26 W) than in men – 5.9% (21 M); similarly in obese patients (BMI > 30) prolonged/critical QTc occurs in 24,1% people (13), 37.5% women (12 W) and 4.5% men (1 M). In patients with BMI > 25 about 40 % of women have critical/prolonged QTc values whereas in men the majority of them have normal QTc values ( $P = 0.01$ ). In men there is a connection between BMI and QTc, the higher BMI the higher QTc ( $P < 0.05$ ), however, such a correlation was not observed in women (P statistically insignificant). Thus overweight/obesity increase the differences between men and women.

The studied populations of men and women differed in education levels in a statistically significant way; the number of women with secondary education was the highest – 49.6% (65 W), slightly fewer women had elementary education – 29.8% (39 W) and the fewest women had higher education – 20.6% (27 W). Among men the greatest number were those with elementary education – 44.4% (32 M), fewer men with higher education – 29.2% (21 M) and the fewest with secondary education – 26.4% (19 M). ( $P < 0.05$ ). The comparison of incidence of critical/prolonged QTc values is impossible on account of group size. Critical/prolonged values occurred in 51.3% women (20 W) and in 25.0% men (8 M) with elementary (vocational) education, in 40.0% women (26 W) and 10.5% men (2 M) with secondary education, in 40.7% women (11 W) and 4.8%, men (1 M) with

higher education. However, normal QTc values, regardless of education, occurred in more men than women ( $P < 0.05$ ).

Arterial hypertension (AH) occurred in 52.2% (106 patients). In patients with untreated or badly controlled arterial hypertension prolonged QTc occurred in 18% (16 patients), critical QTc in 16.9% (15 patients) and in patients without AH: critical in 22.8% (26 patients), prolonged in 9.6% (11 patients) ( $P$  statistically insignificant).

In the studied population 31.5% (64 people) smoked cigarettes, among men the percentage of smokers was statistically significantly higher (40.3% – 29 M) compared with women (26.7% – 35 W) ( $P < 0.05$ ). Statistically significant differences were not observed in the incidence of prolonged/critical QTc values in smokers (W: 40% – 14 W), M: 24.1% – 7M). The fact of existing differences between men and women regardless of the influence of the above mentioned factors is confirmed by partial correlation coefficients between sex and QTC levels, when analyzing each of the factors. In each case the correlation is statistically significant ( $P < 0.001$ ).

## DISCUSSION

Robbins' (13) observations comprising 5,888 men and women showed that QTc interval is a good prognostic factor identifying patients with a high cardiovascular disease risk and mortality. In the epidemiological studies Health and Nutrition Examination Survey on 8,561 patients over 40 years of age, QTc was corrected using Fridericia's formula (5). Sex-dependent QT duration differences were taken into account, similarly to our studies; prolonged QT values occurred more frequently in women and in elderly patients. The results of this large study are in accordance with our observations as for the differences between men and women and age impact. In the studied population prolonged and critical QTc values occurred more frequently in women than in men. Also other studies on large populations confirm that repolarization disorders are more frequent in women. The differences between the results in men and women are caused by greater lability of women's nervous system. In the studied population, when comparing repolarization disorders in age groups, the increase in mean QT values with age was observed in the linear analysis; in the oldest age group the highest mean QT values were observed and the highest percentage of patients with prolonged and critical QTc values. If we analyze the incidence of normal QTc values in age groups, the majority of men in younger age groups (80–90%) had normal QTc values.

We studied QT distribution depending on the education level and agreed with many authors that low socio-economic status is a cardiovascular risk factor (2, 9). Studies by Collins (2) on middle-aged men evaluated the influence of career (occupation) on the level of nervous tension, using a questionnaire. According to the authors, higher excitation could be explained by higher exposure to cardiovascular disorders. In our studies nervous tension was not evaluated, however, if QT interval reflects the tension, we should take into consideration the fact that in patients with vocational education are highest percentages of women with critical/prolonged QT.

In patients with obesity and overweight the incidence of prolonged/critical QTc values is more frequent in women than in men. In about 40% of the studied women with  $BMI > 25$  QTc values are prolonged/critical, but in the majority of men QTc values are normal. We observed a higher percentage of patients with normal QTc at higher BMI values in men. Such connections can result from a more frequent occurrence of obesity in men in our population, the majority of them have normal QTc values at  $BMI > 25$ . The fact of existing differences between the values in men and women – regardless of the above mentioned factors – is confirmed by partial correlation coefficients between the sexes and QTc levels, at the control of each of the analyzed factors. In each case the correlation is statistically significant. If we assume QTc to be the index of sudden cardiac death,

our studies can be compared to the observations of POL-MONICA. During 10.7 years of observation on 1,000 people a higher cardiovascular risk was not found in people with overweight expressed as BMI (for BMI 25–29.9 kg/m<sup>2</sup>). Similar data concern other European countries, such as Greece or Italy (8). Changes in ECGs with the increase in obesity were described by Frank who analysed ECGs in 1029 patients. Prolonged QTc values occurred in 28,3% patients with obesity and depended on its level, age sex and blood pressure (5).

Many studies point to the prolongation of QT in arterial hypertension especially in untreated patients (4, 6). In the studies of Leotta et al. (6) a positive correlation of QT and systolic blood pressure in men was found. Untreated or badly treated arterial hypertension results in left-ventricular hypertrophy and becomes a repolarization time prolonging factor. Next, efficient AT treatment, similarly to weight reduction, lead to the decrease in QT values (10, 12). In our population we did not observe a statistically significant correlation of QTc with treated and untreated arterial hypertension. Simultaneous studies of numerous indices of sudden cardiac death are more effective in prognostication (1, 13, 14, 15). Hence further search for sudden cardiac death indices with prognostic value is needed.

### CONCLUSIONS

Repolarization time disorders were greater in women than in men, increased with age and in men also increased with BMI level. No significant correlation was found between arterial hypertension, cigarette smoking, low education level and repolarization time disorders, however, on the basis of studies of other authors it can be assumed that they are greater at the coexistence of these factors.

### REFERENCES

1. Brown D. W. et al.: Impaired fasting glucose, diabetes mellitus, and cardiovascular disease risk factors are associated with prolonged QTc duration. Results from the Third National Health and Nutrition Examination Survey. *J. Cardiovasc. Risk*, 8 (4), 227, 2001.
2. Collins S. M. et al.: Job strain and autonomic indices of cardiovascular disease risk. *Am. J. Ind. Med.*, 48 (3), 182, 2005.
3. Dekker J. M. et al.: ARIC Study. Heart rate-corrected QT interval prolongation predicts risk of coronary heart disease in black and white middle-aged men and women: the ARIC study. *J. Am. Coll. Cardiol.*, 43 (4), 565, 2004.
4. Fazioli F. et al.: Obesity and cardiovascular disease risk factors in Tehran adults: a population-based study. *East Mediterr. Health J.*, 10 (6), 887, 2004.
5. Frank S. et al.: The electrocardiogram in obesity: statistical analysis of 1,029 patients. *J. Am. Coll. Cardiol.*, 7 (2), 295, 1986.
6. Leotta G. et al.: Relationship between QT interval and cardiovascular risk factors in healthy young subjects. *J. Hum. Hypertens.*, 19 (8), 623, 2005.
7. Nakanishi S. et al.: Relation between QT duration and mortality in an elderly Japanese population. *Am. J. Cardiol.*, 93 (9), 1182, 2004.
8. Pająk A. R. et al.: Współczynnik masy ciała a ryzyko zgonu. Badania POL-MONICA w populacji polskiej w średnim wieku. *Kardiologia Pol.*, 62, 101, 2005.
9. Pakalska-Korcala A. et al.: Stres i niskie wsparcie społeczne jako psychospołeczne czynniki ryzyka chorób sercowo-naczyniowych. *Kardiologia Pol.*, 64, 80, 2006.

10. Passino C. et al.: Abnormal ventricular repolarization in hypertensive patients: role of sympatho-vagal imbalance and left ventricular hypertrophy. *Int. J. Cardiol.*, 97 (1), 57, 2004.
11. Piwowska W.: Nagła śmierć sercowa. *Via Medica*, 109 (2), Gdańsk 2005.
12. Pontiroli A. E. et al.: Left ventricular hypertrophy and QT interval in obesity and in hypertension: effects of weight loss and of normalization of blood pressure. *Int. J. Obes. Relat. Metab. Disord.*, 28 (9), 1118, 2004.
13. Robbins J. et al.: The association between the length of the QT interval and mortality in the Cardiovascular Health Study. *Am. J. Med.*, 115 (9), 689, 2003.
14. Risk factors for prolonged QTc among US adults: Third National Health and Nutrition Examination Survey. *Eur. J. Cardiovasc. Prev. Rehabil.*, 12 (4), 363, 2005.
15. Sallés G. F. et al.: Usefulness of QT-interval parameters for cardiovascular risk stratification in type 2 diabetic patients with arterial hypertension. *J. Hum. Hypertens.*, 19 (3), 241, 2005.

### SUMMARY

The aim of the studies was to compare repolarization time disorders on the basis of QTc interval in men (M) and women (W) with high and very high cardiovascular risk. Medical examination, resting ECG, QTc was calculated using Bazett's formula. QTc assumed as normal: <0.45 sec W and QTc <0.43 sec M, critical QTc : 0.45–0.46 sec W, 0.43–0.45 M, prolonged QTc >0.46 sec W, >0.45 sec M. 203 patients were examined, aged 33–65, average age 52.18±7.516, 131 (64.5%) W and 72 (35.5%) M. Average age in women was 51.92±7.85, in men 52.65±6.96. Prolonged/critical QTc values were in 43.5% women (57 W) and in 15.3% men (11 M) (P<0.05). Prolonged QTc occurred in the similar percentage of men and women: in 10 M (13.9%) and 17 W (13%). In the linear analysis the increase in mean QT values with age was observed. In men in younger age groups the majority (about 80–90%) had normal QTc values. (P<0.05). At < 50 years of age prolonged/critical QTc values occurred in 22 W (43.1%) and in 5 M (16.7%), at those aged 51–60 in 26 W (40.0%) and 12 M (52.2%), at > 60 years of age in 9 W (60%) and 12 M (52.2%). In patients with overweight and obesity (BMI>25) the incidence of prolonged/critical QTc values is more frequent in women compared with men. Forty per cent of women have critical/prolonged QTc, in men the majority of QTc values are normal. The differences in values between men and women, regardless of the above mentioned factors, are confirmed by partial correlation coefficients between the sexes and QTc levels, at the control of each of the analyzed factors (P<0.001). Repolarization time disorders were greater in women than in men and also increased with age. In patients with overweight and obesity repolarization disorders occur more frequently in women. No significant correlation was found between arterial hypertension, cigarette smoking, low education level and repolarization time disorders, however, on the basis of studies by other authors it can be assumed that they are greater at the coexistence of these factors.

### Niektóre czynniki ryzyka sercowo-naczyniowego u kobiet i mężczyzn a odstęp QT

Celem pracy jest porównanie zaburzeń repolaryzacji komórek na podstawie oceny odstępu QTc u kobiet (K) i mężczyzn (M) z dużym i bardzo dużym ryzykiem sercowo-naczyniowym. Wykonywano badanie lekarskie, ekg spoczynkowe, obliczano QTc według wzoru Bazetta. Przyjęto QTc za prawidłowe: <0,45 sek K i QTc<0,43 sek M, graniczne: 0,45–0,46 sek K, 0,43–0,45 M, przedłużone QTc >0,46 sek K, QTc>0,45 sek M. Zbadano 203 osoby w wieku od 33 do 65 lat, średnio 52,18±7,516, w tym 131 (64,5%) (K) i 72 (35,5%) (M). Średnia wieku kobiet wynosiła 51,92 ±7,85lat, a mężczyzn

52,65±6,96 lat. Wartości przedłużone/graniczne występowały u 43,5% kobiet (57 K) i u 15,3% mężczyzn (11 M) ( $P<0,05$ ). Natomiast QTc przedłużone występowało w podobnym odsetku u kobiet i mężczyzn: u 17 K (13,0%) i u 10 M (13,9%). Obserwowano w analizie liniowej wzrost średnich wartości QT wraz z wiekiem. Wśród mężczyzn w młodszych grupach wiekowych większość (ok. 80–90%) miała prawidłowe wartości QTc ( $P<0,05$ ). W wieku <50 lat wartości QTc przedłużone/graniczne występowały u 22 K (43,1%), i u 5 M (16,7%), w wieku 51–60 lat u 26 K (40,0% K) i u 12 M (52,2% M), >60 roku życia u 9 K (60% K) i u 12 M (52,2% M). U pacjentów z otyłością i nadwagą ( $BMI>25$ ) rozpowszechnienie przedłużonych/granicznych wartości QTc występuje częściej u kobiet w porównaniu z mężczyznami. Wśród kobiet ok. 40% ma graniczne/przedłużone QTc, natomiast wśród mężczyzn większość ma QTc prawidłowe. Różnice pomiędzy kobietami i mężczyznami niezależnie od oddziaływania wymienionych czynników potwierdzają współczynniki korelacji cząstkowej pomiędzy płcią a poziomem QTc przy kontroli każdego z analizowanych czynników ( $P<0,001$ ). Zaburzenia repolaryzacji były większe wśród kobiet niż wśród mężczyzn, a także zwiększały się z wiekiem. U pacjentów z otyłością i nadwagą zaburzenia repolaryzacji częściej występowały u kobiet. Nie wykazano istotnej zależności nadciśnienia tętniczego, palenia papierosów, niskiego stopnia wykształcenia i zaburzeń repolaryzacji komórek, ale na podstawie badań innych autorów należy sądzić, że są one większe przy współistnieniu tych czynników.