Relation of Sex and ECG on Cardiovascular Mortality Risk in 10 Years Follow Up

G. Muromtseva, A. Deev, S. Shalnova

National Research Centre for Preventive Medicine, Moscow, Russia
Email: gmuromtseva@yahoo.com

Abstract. *Follow up of randomly selected cohort from Moscow population (17821 subjects aged 35-72), baseline examined in 1975-2001 years, was carried out for 20 years on average. We evaluated the effect of the gender on cardiovascular disease mortality (CVD-M) with ECG variables. It is shown that atria fibrillation and left ventricular hypertrophy are more dangerous for females than for males, but on the contrary QQS major and ST-T abnormalities are more dangerous for males. The decrease of the obtained CVD-M RR, detected by ECG variables, with follow up (from 10 to 20 years) is not related to gender.*

Keywords: Standard 12-lead ECG, Relative Mortality Risk, Minnesota Code, Gender Effect

1. Introduction

Cardiovascular disease (CVD) remains the leading cause of mortality in the world [1, 2]. It is well known gender differences in mortality trends in developed countries especially in Russia. The difference between prevalence of ECG abnormalities in men and women was found in many studies [3, 4]. The aim of this analysis is to investigate the gender interaction between ECG variables and CVD mortality (CVD-M).

2. Subject and Methods

Study Population and Follow up
Mortality follow up of randomly selected cohort from Moscow population (17821 subjects aged 35-72, mean age 49.7±8.0 years, 4934 of them were females), baseline examined in 1975-2001 years, was carried out for 20 years on average. There were 9252 deaths from all causes including 4610 cases of CVD. 441 participants have been died due to CVD up to 5 years, 1153 persons – up to 10 years and 4610 persons – up to the end of follow up.

Statistical Analysis
Cox regression model to estimate relative risks (RR) and 95% confidence intervals (CI) for an association between ECG variables with sex- age- interaction and 5 years, 10 years and full CVD-M, with age and sex adjustment was done. 5 years and 20 years CVD-M were used for comparison purposes. We used SAS version 6.12.

ECG-variables
Standard 12-lead ECGs were recorded at baseline in the resting supine position using strictly standardized procedures in single clinical center, in National Centre for Prevention Medicine. ECG data were stored and analyzed by the Minnesota code (1982) by 2 independent ECG-experts. A third one was involved in the work for controversial cases. ECG abnormalities were divided into 6 following groups, including atria fibrillation (AF), left ventricular hypertrophy (LVH), QQS codes (QQSmajor and QQSminor) and ischemic codes (ISCH and ISCHE; see Table 1).

Table 1. Minnesota Codes Categories

Definitions of Minnesota Codes Categories	Description	Minnesota codes
AF (atria fibrillation)	Atria fibrillation or atria flutter	8-3
LVH (left ventricular hypertrophy)	High amplitude of R wave	3-1 or 3-3
QQS major ("definite Myocardial infarction")	Major Q and QS patterns in leads I, II, III, aVL, aVF or in any leads V1-5, V6	1-1-1 through 1-1-7 or 1-2-1 through 1-2-7
QQS minor ("possible Myocardial infarction")	Minor Q and QS patterns in leads I, II, III, aVL, aVF or in any leads V1-5, V6	1-2-8 or 1-3-1 through 1-3-6,
ISCH ("definite ischemia")	ST depression: ST-J and segments depression ≥1,0 mm in leads I, II, III, aVL, aVF or in any leads V1-5, V6 and/or T-wave changes: T wave inversion in lead I, II, III, aVL, V1-6 without LVH	4-1, 4-2, 5-1, 5-2 without 3-1 or 3-3
ISCHE ("possible ischemia")	Minor ST-T changes (borderline ST segment depression and T wave flattening)	4-3, 4-4 and/or 5-3, 5-4

To detect gender specifics of ECG variables on CVD-M we have introduced interactions between gender and ECG variables in a form (sex-1)*ECG variables. As males were coded "1", females – "2", so RR of CVD-M for males this terms were become 0. On this condition those interactions are additional indicators of increment of RR value for females relative to males. We used significant increments: sAF, sLVH, sQQSmajor, sQQSminor, sISCH and sISCHE, as additional to main affects in this analysis.

3. Results and Discussion

The RR of 10 years CVD-M for every of 6 ECG groups of abnormalities were assessed (see Fig. 1). The highest RR of CVD-M was found for AF (RR=4.32; 95% CI 2.88-6.48); ISCH (RR=4.32; 95% CI 3.33-5.61); QQSmajor (RR=3.05; 95% CI 2.24-4.14); the lowest – for LVH (RR=1.89; 95% CI 1.53-2.32).

CVD-M RR of every ECG variables decreased with a follow-up. The RR of AF and QQSmajor at the end of follow-up were approximately equal: 2.5 (95% CI 1.8-3.47) и 2.58 (95% CI 2.11-3.15), respectively (see Fig. 1).

CVD-M RR for "sex" was 0.28 (95% CI 0.21-0.40) in 10 years of follow-up and varied from 0.25 (95% CI 0.15-0.40) in 5 years to 0.31 (95% CI 0.27-0.40) in the end of follow-up.

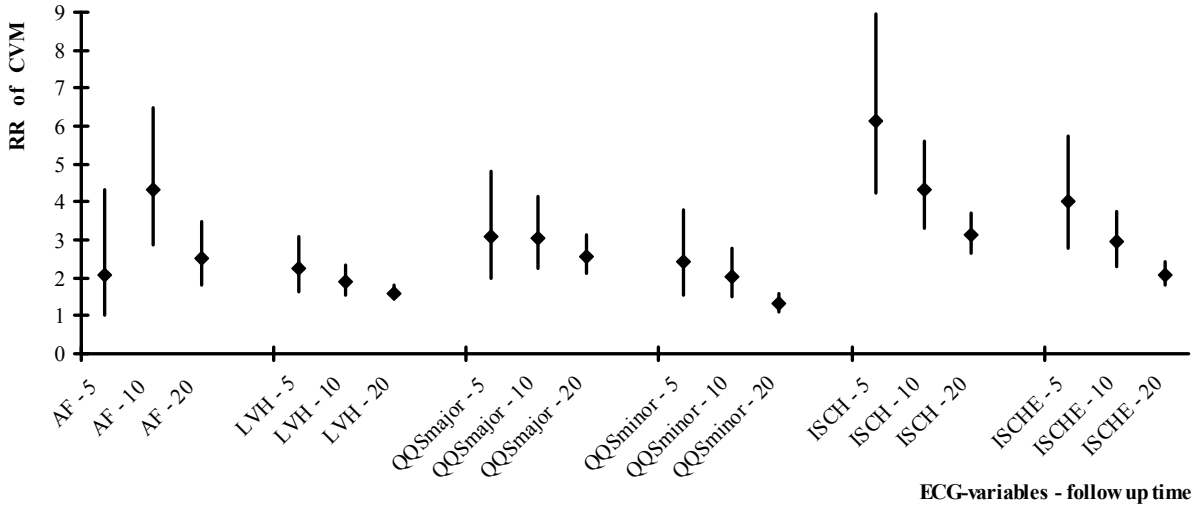

Fig. 1. RR of CVD-M dynamics predicted by 6 ECG variables (AF, LVH, QQSmajor, QQSminor, ISCH and ISCHE) in 5, 10 and 20 years follow up

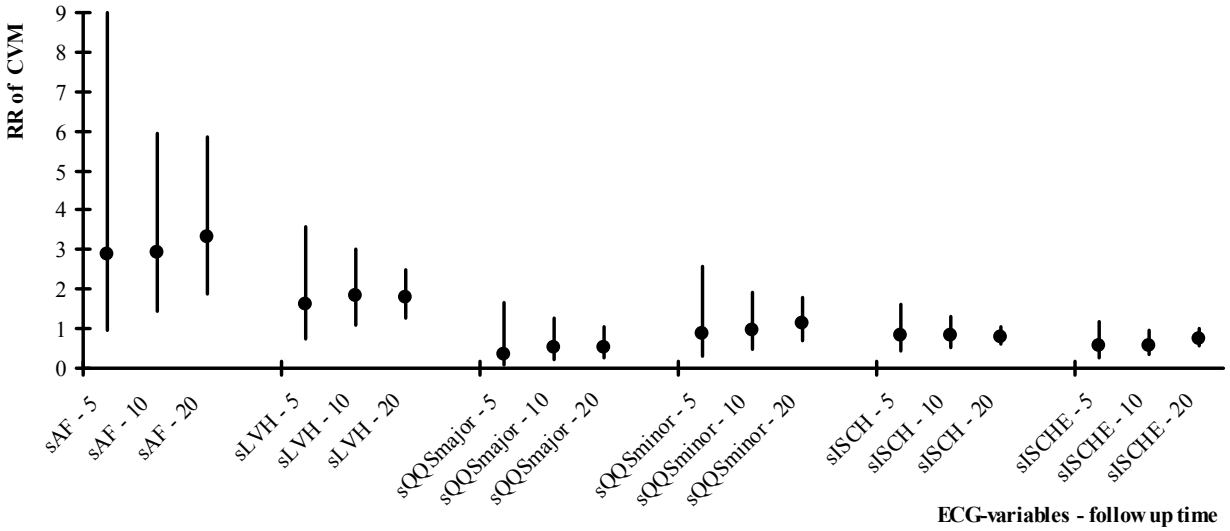

Fig. 2. RR of CVD-M dynamics, predicted by 6 ECG variables (sAF, sLVH, sQQSmajor, sQQSminor, sISCH and sISCHE), in 5, 10 and 20 years follow up

sECG variables analysis are shown on Fig.2 and Table 2. The 10 years RR of sAF detected in females, is about 3 times higher than in males 2.9 (95% CI 1.44-5.94; p=0.003). Also RR of sLVH detected in females is about 1.8 times higher than in men (the 10-years RR=1.82; 95% CI 1.11-3.00; p=0.02). But sQQSmajor, sISCHE and sISCH were more strongly associated with males: 10-years female's risks of CVD-M were 0.51, 0.58 and 0.83 of male's RR, respectively.

As shown in Fig. 2, a decrease of CVD-M RR of sECG variables with a follow-up time was not revealed.

Table 2 demonstrated β-coefficients in regression equation, which were related with impact of every sECG variables in CVD-M RR. The bilateral relations were found: impact of sAF and sLVH on CVD-M RR in females were higher than in males (β-coefficients were positive). Impact of some other interactions was opposite (β-coefficients for them were negative). For sQQSminor the β-coefficient was near zero and CVD-M RR was near "1" (in 10 years of

follow-up RR=0.95; 95% CI 0.47-1.92, Fig. 2). In other words there was not any clear gender predominance for this variable.

Table 2. Impact of sECG variables to prediction of RR of CVD-M

ECG variable	Values of β-coefficient (St.error), p<		
	5-	10-	20 years follow up time
sAF	1.07 (0.58), p<0.06	1.07 (0.36), p<0.003	1.19 (0.29), p<0.0001
sLVH	0.49 (0.40), *	0.60 (0.25), p<0.02	0.58 (0.17), p<0.0006
sQQS major	-1.05 (0.80), *	-0.67 (0.47), *	-0.61 (0.34), p<0.07
sQQS minor	-0.13 (0.55), *	-0.05 (0.36), p<0.02	0.12 (0.23), *
sISCH	-0.17 (0.34), *	-0.19 (0.22), *	-0.24 (0.15), p<0.1
sISCHE	-0.60 (0.40), *	-0.55 (0.25), p<0.03	-0.30 (0.15), p<0.04

* – p>0.05

4. Conclusions

Inclusion of the "Sex" as a significant independent variable in a Cox regression model showed that for females CVD-M RR is 0.25-0.31 RR of males.

There are more detailed gender specific effects for ECG variables on CVD-M. AF and LVH are more dangerous for females than for males, on the contrary QQSmajor and ST-T abnormalities (ISCH and ISCHE) are more dangerous for males in respect of CVD-M.

The decreased association between CVD-M RR and ECG variables with follow up (from 10 to 20-years; see Fig. 1) did not related to gender (see Fig. 2 and Table 2).

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