

Electrocardiographic Risk Markers for Heart Failure in Women vs Men

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ABSTRACT

Heart failure (HF) is one of the leading causes of hospitalization in the Western world. Women have a lower HF hospitalization rate and mortality compared to men. The role of electrocardiography as a risk marker of future HF in women is not well known. We studied association of electrocardiographic (ECG) risk factors for HF hospitalization in women from a large middle-aged general population with a long-term follow-up and compared the risk profile to men. Standard 12-lead ECG markers were analyzed from 10,864 subjects (49% women), and their predictive value for HF hospitalization was analyzed. During the follow-up (30 ± 11 years), a total of 1,743 subjects had HF hospitalization; of these, 861 were women (49%). Several baseline characteristics, such as age, body mass index, blood pressure, and history of prior cardiac disease predicted the occurrence of HF both in women and men ($P < 0.001$ for all). After adjusting for baseline variables, ECG sign of left ventricular hypertrophy (LVH) ($P < 0.001$), and atrial fibrillation ($P < 0.001$) were the only baseline ECG variables that predicted future HF in women. In men, HF was predicted by fast heart rate ($P = 0.008$), T-wave inversions ($P < 0.001$), abnormal Q-waves ($P = 0.002$), and atrial fibrillation ($P < 0.001$). Statistically significant gender interactions in prediction of HF were observed in ECG sign of LVH, inferolateral T-wave inversions, and heart rate. In conclusion, ECG sign of LVH predicts future HF in middle-aged women, and T-wave inversions and elevated heart rate are associated with HF hospitalization in men.

Key words: Heart failure, Gender differences, ECG, Left ventricular hypertrophy

INTRODUCTION

Heart failure (HF) is one of the leading causes of hospitalization in western societies ¹. In contrast to other heart diseases nearly half of all HF patients ^{2,3} and 40-50% of hospitalized HF patients are women ¹. Despite the improvements in medical treatments, the prognosis of patients with HF has remained poor ⁴. Patients hospitalized for HF are experiencing high readmission rates, and though post-discharge survival in women with HF seems to be better than in men ^{2,3,5} they have more comorbidities and worse quality of life ^{2,5}. Even though almost half of the HF patients are women they represent only about 20% of the study population in randomized trials ³. Women are underrepresented in most of the data from randomized clinical trials ^{3,5} with a couple of exceptions ¹. Also, global registry data on electrocardiographic (ECG) findings in patients hospitalized for HF is limited ¹. We have previously reported the predictive value of ECG markers for all-cause mortality and sudden cardiac death from the Finnish middle-aged population ^{6,7}. This study examines ECG risk factors for hospitalization in men vs women for HF.

METHODS

The study population consists of 10,957 subjects between ages 30 and 59 years (48% female, N=5,254) from Social Insurance Institution's Coronary Heart Disease Study which is part of large prospective Mobile Clinic Health Survey carried out between 1966 and 1972 in 4 different geographical areas in Finland. Details of the study population have been described previously ⁸. After excluding 93 subjects with unreadable electrocardiogram, in the study remained 10,864 subjects with electrocardiogram (49% female, N=5,215, mean age 44 ± 9 years, Figure 1).

Records for all hospitalizations in Finland have been collected in a nationwide registry maintained by the National Institute for Health and Welfare since 1969 and diagnoses have been validated by Sund et al. ⁹. Primary endpoint of the study was hospitalization due to HF until the 31st

December 2011. Follow-up period was defined as the time from the initial study visit to the occurrence of hospitalization, death or the end of the follow-up, whichever came first.

Standard resting 12-lead electrocardiograms were recorded at paper speed of 50 mm/s at study baseline. The electrocardiograms were analyzed by 9 trained readers for bundle branch blocks, left ventricular hypertrophy (Sokolow-Lyon criteria: R-wave in V5 or V6 + S wave in V1 \geq 35 mm, whichever greater) (LVH), QRS duration and QTc interval (corrected for heart rate with Bazett's formula). Minnesota coding was used to assess Q-waves (codes 1.1 – 1.3), ST segment abnormalities (codes 4.1 – 4.4) and T-wave items (codes 5.1 – 5.4). Presence of early repolarization \geq 0.1mV with horizontal or descending ST segment and fragmented QRS were assessed as described previously⁶. Early repolarization was classified inferolateral if there were \geq 2 slurred or notched J-point elevations \geq 0.1 mV in inferior (II, III, aVF) or lateral (I, aVL, V4 to V6) leads. ST segment was classified as horizontal or descending if it was under 0.1 mV 100ms after the QRS complex had ended. Fragmented QRS complexes were classified by coronary artery regions as anterior (V1 to V3), inferior or lateral if there were \geq 2 fragmented QRS complexes within the region. Similarly, inferolateral T-wave inversions were classified by coronary artery regions as inferior or lateral if T-wave amplitude was $<$ -0.1mV in \geq 2 contiguous leads in the same region.

Student's t-test was used to compare continuous variables and results are presented as mean \pm standard deviation. Categorical variables were compared between the groups using Pearson Chi-Square test. Interaction between gender and ECG markers was assessed using Cox regression analysis with gender, ECG marker and their interaction term in the same model. If the interaction term was statistically significant, the interaction was further analyzed. Graphical illustration of the interaction was made using the Kaplan-Meier curves. Univariate and multivariate risk ratios were estimated with Cox proportional hazards model. The proportional hazard assumption was verified for each risk marker by plotting Schoenfeld residuals against survival time transformed into natural logarithms. All statistical analyses were performed using Statistical Package for Social Studies 25.0 (SPSS Inc.,

Chicago, IL). All reported P-values are 2-sided and values < 0.05 are considered as statistically significant.

RESULTS

Out of the 10,864 subjects (49% female, N=5,215), a total of 1,743 subjects were hospitalized due to HF during the follow-up time (30 ± 11 years); 17% of women (N=861) and 16% of men (N=882; Figure 1). The average time from recording of electrocardiogram to HF hospitalization was 23.7 ± 11.2 years, and the average yearly incidence rate for HF hospitalizations were similar between genders: 0.69% and 0.75% for women and men, respectively (P=0.639). Men seemed to have slightly increased risk for HF hospitalization (hazard ratio [HR]: 1.2; 95% confidence interval [CI]: 1.1-1.3; P=0.004). Women were older at the time of hospitalization for HF compared to men (75 ± 11 years vs. 70 ± 11 years; P<0.001). The other baseline characteristics of the study population are represented in the Table 1. Gender interaction effects for clinical risk markers of HF hospitalization are represented in Table 2 and unadjusted hazard ratios of clinical risk factors for HF in Table 3.

After hospitalization for HF, 651 women (76%; P<0.001) and 721 men (82%; P<0.001) died during the follow-up, and all-cause mortality was considerably higher than in those without the HF (42% of women and 61% of men, respectively; P<0.001 for both). Cardiac death occurred in 249 women and 330 men hospitalized for HF (29% vs. 37%; P<0.001 for both) whereas only in 10% women (N=444) and 20% men (N=949) without hospitalization died for cardiac cause (P<0.001, for both). After HF diagnosis we did not observe gender difference in all-cause mortality (Figure 2) but the rate of cardiac death increased more rapidly among male patients even though in the end of the follow-up time survival in women was only slightly better compared to men (Figure 3). However, significant gender differences in survival could be seen in sudden cardiac death in which the survival among female patient was significantly better compared to men (Figure 4).

ECG findings in patients with and without HF hospitalization are shown in Table 4. Women with HF hospitalization had increased heart rate compared to men. As expected, women had on average longer QTc duration than men and QTc duration was longer in women with hospitalization for HF than those without hospitalization. However, QTc > 470 ms in women with hospitalization for HF was less common than QTc > 450 ms in hospitalized men. In both genders QTc prolongation was more common finding among HF hospitalized patients (Table 4) but did not remain significant in multivariate analysis (Table 5). Even though ECG marker for LVH was more common among men (Table 4) it did not remain statistically significant in multivariable analysis (Table 5). However, ECG sign for LVH was considerably more prevalent in women with hospitalization for HF than those without (Table 4) and remained statistically significant risk factor for HF hospitalization after adjustments with clinical and demographic variables (Table 5). Inferolateral T-wave inversions were more prevalent in men than in women with hospitalization for HF though not statistically significant. Also, pathological Q-waves and atrial fibrillation/flutter were more common findings in patients hospitalized for HF, especially in men. (Table 4).

Statistically significant gender interaction was observed in ECG sign of LVH, inferolateral T-wave inversions and heart rate (Table 3, Figure 5). ECG evidence of LVH was predictive of HF hospitalization only in women. As opposed to LVH, inferolateral T-wave inversion remained independently predictive of HF hospitalization only in men. (Table 5, Figure 5). Similarly, elevated resting heart rate was associated with outcome only among men. Pathological Q-waves were associated with outcome in both genders but remained independent predictors of HF hospitalization only among men (Table 5). The difference in risk of future hospitalization is represented for each ECG variable by gender and history of ischemic heart disease in Table 6. Prevalence of atrial fibrillation/flutter was very low in this population (Table 4), but it conveyed a significant risk for HF hospitalization in both genders (Table 5).

DISCUSSION

The main findings of the study are that there are some gender related differences that predict future hospitalization for HF in middle-aged subjects. Sokolow-Lyon index of LVH in the ECG predicted HF hospitalization only in women and T-wave inversions only in men. Pathological Q-waves and elevated heart rate increased the risk for HF hospitalization only in men. To our knowledge, there are only few large-scale studies assessing the role of standard 12-lead electrocardiography in predicting the occurrence of HF. Furthermore, most of the studies have predominantly included men in their data collection and analysis ^{3,5}.

ECG sign of LVH, assessed by Sokolow-Lyon index, was the most important risk factor of HF in women but not in men, even though it was more commonly found in men. The prevalence difference between genders may be explained with the higher average BMI of women as we know from the earlier literature that the sensitivity of Sokolow-Lyon criteria is low especially among obese women¹⁰. LVH has been previously associated with higher incidence and earlier development of HF in elderly population ¹¹. In addition, the LIFE study ¹² found that regression in LVH defined by criteria of Cornell decreased the risk of HF and death. LVH has been most commonly associated with undiagnosed and/or poorly controlled hypertension ¹³, and when detected by echocardiographic is more prevalent finding in women than in men among hypertensive patients ¹⁴ suggesting that adequate control of blood pressure may be crucial in prevention of HF especially in women.

After adjustments T-inversions and Q-waves were associated with HF hospitalization only in men, although the prevalence of inferolateral T-wave inversions was quite low in both genders. These kind of ECG abnormalities are quite common among patient with advanced HF and prior myocardial infarction or cardiomyopathy, and as the coronary artery disease is more prevalent cause of HF among men ^{2,3,15,16} it may explain the gender differences. However, when analysing the risk for HF hospitalization taking into account the history of ischemic heart disease, the risk for HF hospitalization did not differ considerably among male subjects with and without ischemic heart

disease. In the present study, atrial fibrillation or flutter in the analysed electrocardiogram was associated with increased risk for HF hospitalization among both genders. However, the prevalence of atrial fibrillation in this study was extremely low. Previously, many studies have shown the adverse effect of atrial fibrillation among HF patients¹⁷, but the evidence to suggest that atrial fibrillation would ultimately cause HF are lacking. After all, almost all the risk factors for HF are interchangeable with atrial fibrillation risk¹⁷. In addition, among men the increased heart rate was among statistically significant risk factors for HF hospitalization which is in line with previous studies¹⁸.

The prevalence of hospitalization for HF during the follow-up time was similar in both genders, as well as the average yearly incidence rate for HF hospitalizations. Higher hospitalization and readmission rates for women have been previously reported in some studies¹⁹ while other studies³¹ have shown higher rates among men. Male gender increased risk for hospitalization which is consistent with some of the previous studies²² but not with all^{23,24}. Women hospitalized for HF had a lower prevalence of cardiac death or all-cause mortality in comparison to men. Taking account that main causes of death of HF patients are sudden cardiac death and progressive pump failure²⁵, one explanation for better survival of women could be the higher prevalence of HF with preserved ejection fraction in women² and the different etiology behind HF in women and men^{2,3}.

However, among hospitalized women the rate of cardiac death during the first 2 decades of the follow-up time was lower compared to men, but the gender difference narrowed considerably towards the end of the follow-up time. We did not notice gender differences in survival of all-cause mortality. Women had considerably better prognosis for sudden cardiac death compared to men. Previous data considering the prognosis of women with HF hospitalization is controversial with most of the studies supporting the greater prognostic value of HF in women^{2,3} while some suggesting the opposite²⁸ and some did not find difference in in-hospital and post-discharge outcomes between the genders²⁹.

One possible limitation in this study is the fact that medication and other treatments for HF have changed dramatically during the long follow-up period and all results might not be completely

transferable to current era. It is also possible that the health behaviour has changed remarkably during the long follow-up period. In addition, we did not have echocardiographic data in this population and thus cannot evaluate proportion of HF with or without systolic or diastolic left ventricular dysfunction. As well, we were not able to use a criteria of a total 12-lead QRS voltage as ECG sign of LVH which has been previously reported in some studies as superior to other ECG criteria for LVH³⁰, and also data of strain changes lacked. Nevertheless, this is to our knowledge the largest general population cohort with extensive follow-up and validated outcome data.

In conclusion, we studied clinical and ECG risk markers for hospitalization due to HF in middle aged general population in Finland. Among patients who had experienced hospitalization for HF, ECG sign of LVH was a significant risk factor for future HF hospitalization in women but not in men, and inferolateral T-wave inversion was a risk factor in men but not in women. Pathological Q-waves and elevated heart rate increased risk for hospitalization only in men. Overall, the present data show that if LVH is observed in a standard 12-lead electrocardiogram in a middle-aged woman, emphasis should be put on adequate treatment of hypertension or diagnosing other possible causes of LVH to prevent future HF.

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FIGURE LEGENDS

Figure 1. Flow chart of the study.

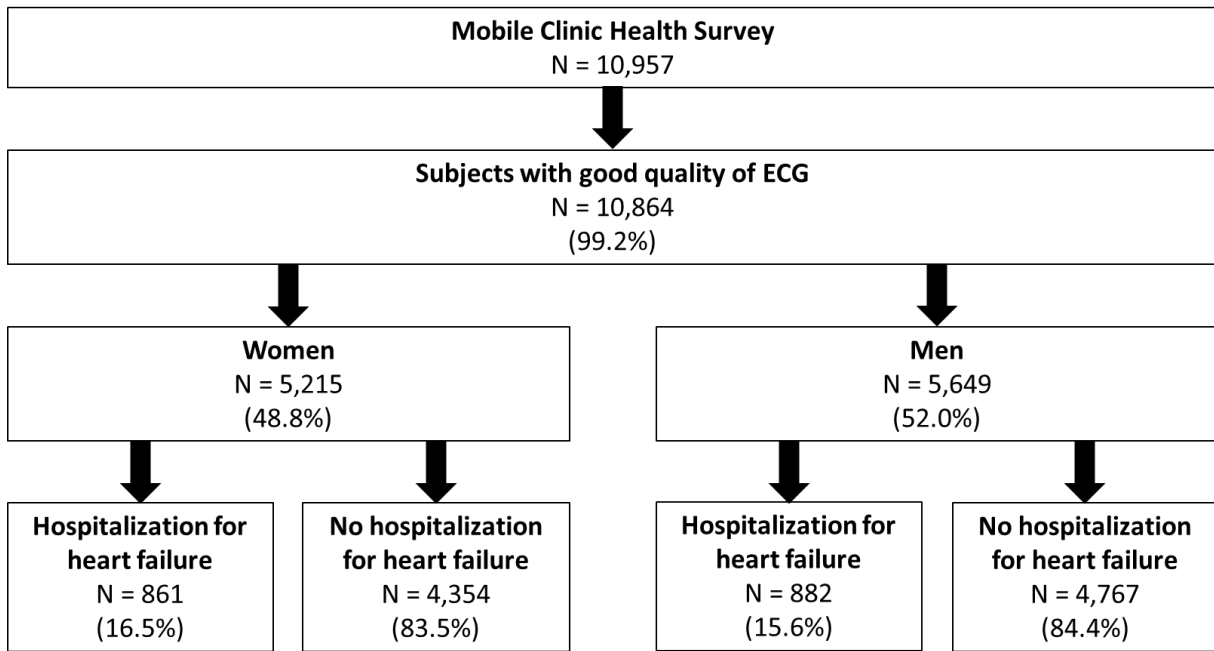


Figure 2. Kaplan-Meier curves of all-cause mortality for men and women after the diagnosis of HF.

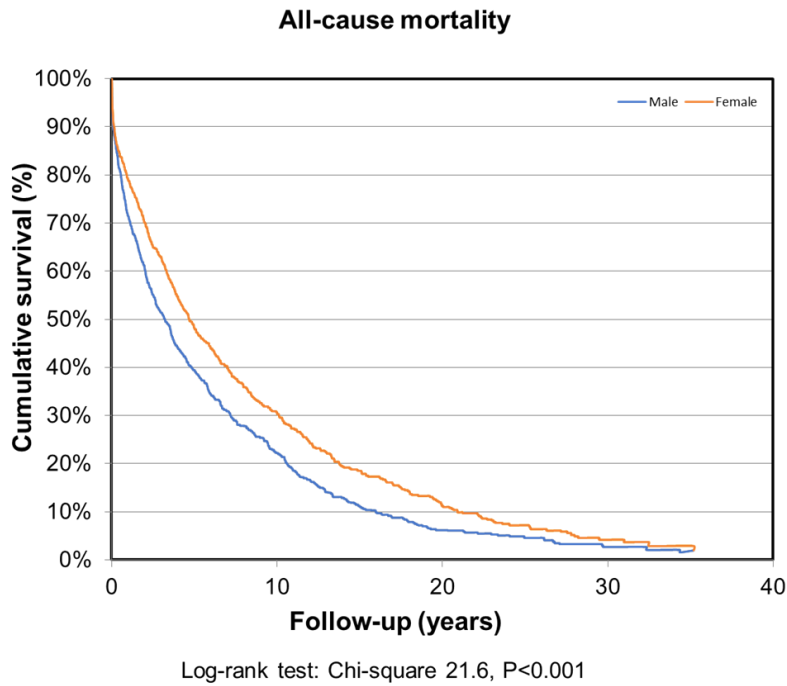


Figure 3. *Kaplan-Meier curves of cardiac mortality for men and women after the diagnosis of HF.*

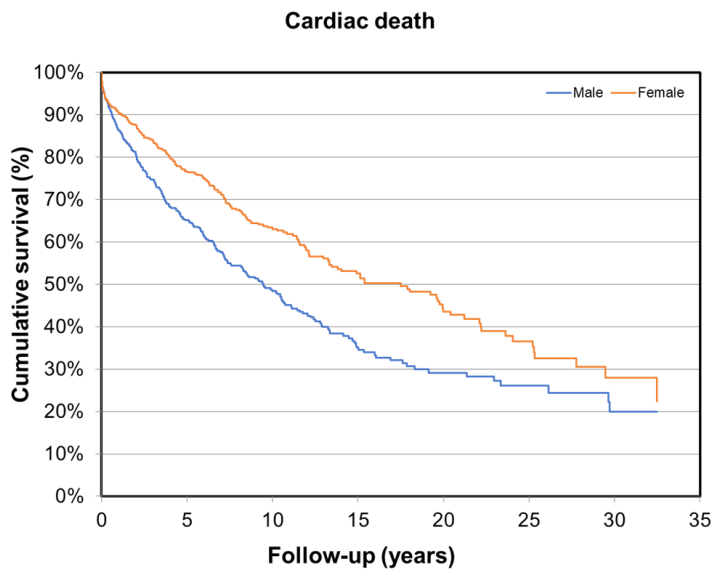


Figure 4. *Kaplan-Meier curves of sudden cardiac death for men and women after the diagnosis of HF.*

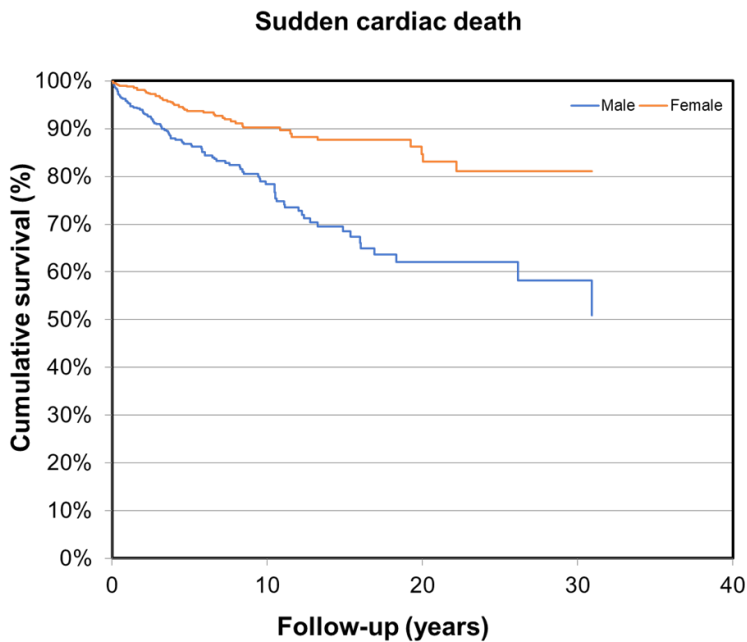


Figure 5. Kaplan-Meier curves for men and women with and without ECG-based LVH and T-wave inversion.

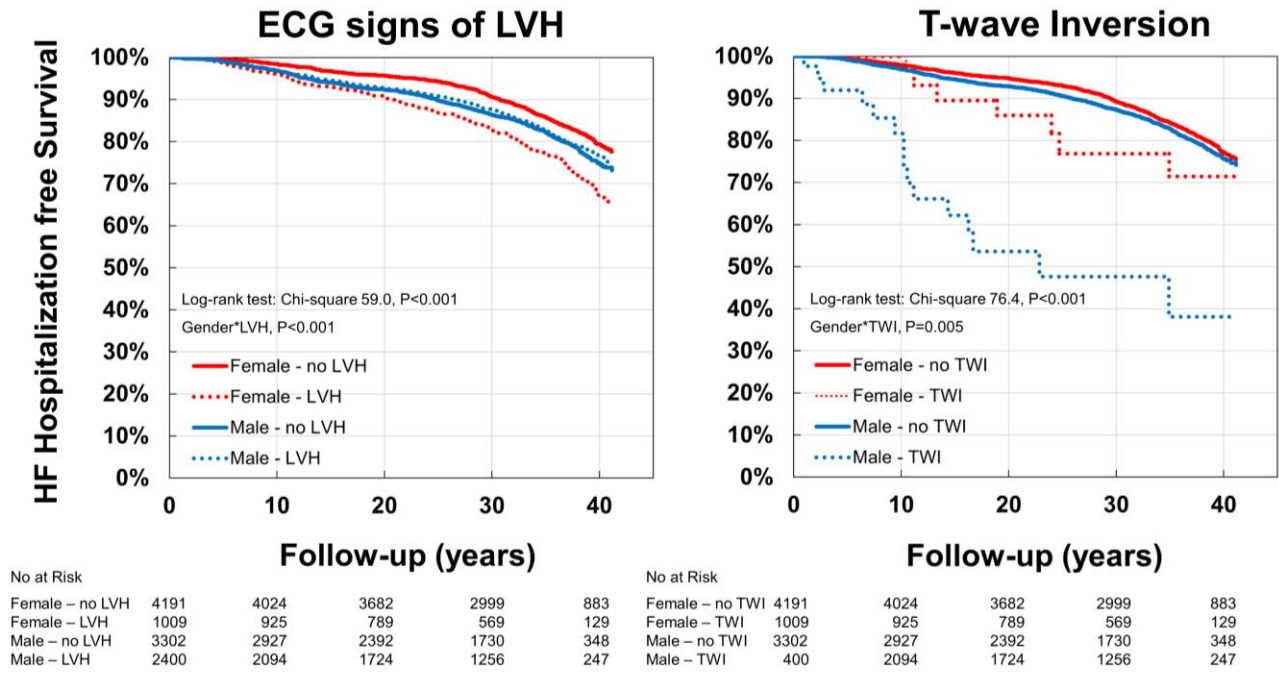


Table 1. Baseline characteristics of HF hospitalized subjects and subjects who were not hospitalized due to HF among men and women.

Variable	Women (N=5,215)			Men (N=5,649)		
	Control N=4,354 (83%)	HF hospitalization N=861 (17%)	P-value	Control N=4,767 (84%)	HF hospitalization N=882 (16%)	P-value
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
Age (years)	43 ± 8	50 ± 7	<0.001	43 ± 8	47 ± 8	<0.001
BMI (kg/m ²)	26 ± 4	28 ± 5	<0.001	25 ± 3	27 ± 4	<0.001
Systolic blood pressure (mmHg)	137 ± 23	146 ± 27	<0.001	138 ± 19	141 ± 22	<0.001
Diastolic blood pressure (mmHg)	83 ± 12	87 ± 13	<0.001	81 ± 12	84 ± 14	<0.001
Follow-up time (years)	33 ± 9	25 ± 11	<0.001	29 ± 12	22 ± 11	<0.001

	N (%)	N (%)	P-value	N (%)	N (%)	P-value
Previous cardiac disease	239 (6%)	121 (14%)	<0.001	381 (8%)	149 (17%)	<0.001
Smoker	575 (13%)	107 (12%)	0.538	2,503 (53%)	494 (56%)	0.053
Medication for hypertension	235 (5%)	97 (11%)	<0.001	86 (2%)	50 (6%)	<0.001

Statistical analyses are made without adjustments using Student's t-test for continuous variables and Pearson Chi-Square test for categorial variables. Significant differences ($P < 0.05$) between subjects with and without hospitalization for HF highlighted in bold. BMI = body mass index; HF = heart failure; SD= standard deviation.

Table 2. Risk of HF hospitalization and gender interactions.

Variable	Women vs. Men		
	Risk	95% CI	P-value
Age (years)	1.0	1.0 – 1.0	0.012
BMI (kg/m ²)	1.0	1.0 – 1.0	0.116
Systolic blood pressure (mmHg)	1.0	1.0 – 1.0	0.010
Diastolic blood pressure (mmHg)	1.0	1.0 – 1.0	0.009
Heart rate (1/min)	1.0	1.0 – 1.0	0.017
Previous cardiac disease	1.3	0.8 – 1.3	0.792
Medication for hypertension	0.5	0.3 – 0.7	<0.001
Smoker	0.7	0.5 – 0.8	0.003
QRS \geq 110 ms	0.9	0.4 – 2.0	0.758
QTc \geq 470/450 ms*	1.0	0.6 – 1.7	0.966

ER	0.6	0.4 – 1.1	0.089
Inferolateral T-inversion	0.3	0.1 – 0.7	0.005
fQRS	1.1	0.8 – 1.3	0.699
LVH	1.9	1.5 – 2.3	<0.001
Pathological Q-waves	0.9	0.4 – 2.1	0.835
Atrial fibrillation/flutter	1.1	0.3 – 3.9	0.895
Left bundle branch block	0.2	0.0 – 1.3	0.082
Right bundle branch block	1.6	0.3 – 8.3	0.540
Cardiac death	1.1	0.9 - 1.3	0.412
Death	1.1	0.8 – 1.3	0.628

**QTc cutoff point 470 ms for women and 450 ms for men. Interactions between gender and ECG markers were assessed using univariate Cox regression analysis. Statistically significant interactions ($P < 0.05$) are highlighted in bold. BMI = body mass index; CI = confidence interval; ECG = electrocardiographic; ER = early repolarization with horizontal or descending ST segment; fQRS = fragmented QRS complex; HF = heart failure; LVH = left ventricular hypertrophy; QTc = heart rate corrected QT time.*

Table 3. *Unadjusted hazard ratios of clinical risk factors resulting to hospitalization for HF during the follow-up.*

Variable	Women (N=5,215)			Men (N=5,649)		
	HR	95% CI	P-value	HR	95% CI	P-value
Age (years)	1.2	1.1 - 1.2	<0.001	1.1	1.1 - 1.1	<0.001
BMI (kg/m ²)	1.1	1.1 - 1.1	<0.001	1.1	1.1 - 1.1	<0.001
Systolic blood pressure (mmHg)	1.0	1.0 - 1.0	<0.001	1.0	1.0 - 1.0	<0.001
Diastolic blood pressure (mmHg)	1.0	1.0 - 1.0	<0.001	1.0	1.0 - 1.0	<0.001
Smoker	1.0	0.8 - 1.2	0.888	1.4	1.2 - 1.6	<0.001
Medication for hypertension	3.2	2.6 - 4.0	<0.001	6.3	4.7 - 8.4	<0.001
Previous cardiac disease	3.8	3.1 - 4.6	<0.001	3.7	3.1 - 4.5	<0.001

Subject is considered as a smoker if she/he smokes cigarettes, cigars or pipe daily. Hazard ratios were analyzed using unadjusted Cox Regression analysis. Significant differences ($P < 0.05$) between subjects with and without hospitalization for HF highlighted in bold. BMI = body mass index; CI = confidence interval; HF = heart failure; HR = hazard ratio.

Table 4. Comparison of ECG variables between HF hospitalized subjects and subjects who were not hospitalized due to HF.

Variable	Women (N=5,215)			Men (N=5,649)		
	Control	HF hospitalization	P-value	Control	HF hospitalization	P-value
	N=4,354 (83%)	N=861 (17%)		N=4,767 (84%)	N=882 (16%)	
	Mean \pm SD	Mean \pm SD		Mean \pm SD	Mean \pm SD	
QRS duration (ms)	82 \pm 10	82 \pm 10	0.223	88 \pm 11	87 \pm 12	0.132
QTc interval (ms)	415 \pm 26	417 \pm 26	0.020	401 \pm 27	405 \pm 26	<0.001
Heart rate (1/min)	79 \pm 16	80 \pm 16	0.195	72 \pm 15	73 \pm 14	0.007

	N (%)	N (%)	P-value	N (%)	N (%)	P-value
QRS \geq 110 ms	35 (0.8%)	7 (0.8%)	0.954	224 (5%)	50 (6%)	0.194
QTc \geq 470/450 ms*	83 (2%)	27 (3%)	0.023	187 (4%)	47 (5%)	0.044
ER	157 (4%)	19 (2%)	0.039	189 (4%)	36 (4%)	0.832
Inferolateral T-inversion	26 (0.6%)	7 (0.8%)	0.368	30 (0.6%)	15 (2%)	0.001
fQRS	644 (15%)	145 (17%)	0.140	997 (21%)	203 (24%)	0.095
Anterior	135 (3%)	27 (4%)	0.376	142 (4%)	32 (5%)	0.214
Inferior	553 (13%)	120 (15%)	0.152	885 (19%)	179 (21%)	0.129
Lateral	30 (0.7%)	7 (1%)	0.339	45 (1%)	8 (1%)	0.978
LVH	788 (18%)	223 (26%)	<0.001	2,046 (42%)	354 (40%)	0.203
Pathological Q-waves	57 (1%)	77 (3%)	0.005	104 (2%)	39 (4%)	<0.001
Atrial fibrillation/flutter	4 (0.1%)	5 (0.6%)	<0.001	6 (0.1%)	8 (0.9%)	<0.001
Left bundle branch block	13 (0.3%)	1 (0.1%)	0.387	15 (0.3%)	5 (0.6%)	0.241

Right bundle branch block	9 (0.2%)	3 (0.3%)	0.531	28 (0.6%)	3 (0.3%)	0.367
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*QTc cutoff point 470ms for women and 450ms for men. Statistical analyses are made without adjustments using Student's t-test for continuous variables and Pearson Chi-Square test for categorical variables. Significant differences ($P < 0.05$) between subjects with and without hospitalization for HF highlighted in bold. ECG = electrocardiographic; ER = early repolarization with horizontal or descending ST segment; fQRS = fragmented QRS complex; HF = heart failure; LVH = left ventricular hypertrophy; QTc = heart rate corrected QTc time; SD = standard deviation.

Table 5. Hazard ratios of ECG variables as predictors of HF hospitalization among men and women.

Variable	Women (N=5,215)						Men (N=5,649)					
	Unadjusted			Adjusted			Unadjusted			Adjusted		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Heart rate (1/min)	1.0	1.0-1.1	0.701	1.0	1.0 -1.1	0.686	1.1	1.1 - 1.1	<0.001	1.1	1.0 - 1.1	0.008
QRS \geq 110 ms	01.0	0.5 - 2.1	0.988	0.7	0.3 - 1.6	0.402	1.1	0.9 - 1.5	0.371	1.3	1.0 - 1.7	0.114
QTc \geq 470/450 ms*	1.9	1.3 - 2.8	0.001	1.2	0.8 - 1.8	0.275	1.8	1.3 - 2.4	<0.001	1.9	1.7 - 2.2	0.095
ER	0.7	0.5 - 1.2	0.187	0.6	0.4 - 0.9	0.025	1.2	0.9 - 1.7	0.274	1.2	0.8 - 2.2	0.397

Inferolateral T-inversion	1.7	0.8 - 3.5	0.179	1.2	0.6 - 2.5	0.679	5.9	3.5 - 9.8	<0.001	2.5	1.5 - 4.3	<0.001
fQRS	1.2	1.0 - 1.4	0.048	1.0	0.8 - 1.1	0.596	1.1	1.0 - 1.3	0.108	1.1	0.9 - 1.3	0.450
Anterior	1.2	0.8 - 1.7	0.412	1.1	0.7 - 1.6	0.654	1.3	0.9 - 1.9	0.109	1.2	0.8 - 1.7	0.404
Inferior	1.2	1.0 - 1.5	0.045	0.9	0.8 - 1.1	0.408	1.1	1.0 - 1.3	0.194	1.1	0.9 - 1.2	0.542
Lateral	1.5	0.7 - 3.2	0.259	1.1	0.5 - 2.5	0.802	1.4	0.7 - 2.7	0.399	1.6	0.8 - 3.2	0.213
LVH	1.8	1.5 - 2.1	<0.001	1.4	1.2 - 1.6	<0.001	0.9	0.8 - 1.1	0.311	1.1	0.9 - 1.2	0.455
Pathological Q-waves	2.2	1.4 - 3.3	<0.001	1.2	0.8 - 1.8	0.531	2.5	1.8 - 3.5	<0.001	1.7	1.2 - 2.3	0.002
Atrial fibrillation/flutter	14.0	5.2 - 37.4	<0.001	6.7	2.4 - 18.2	<0.001	10.8	5.4 - 21.6	<0.001	6.8	3.3 - 13.8	<0.001
Left bundle branch block	0.52	0.07-3.72	0.518	0.2	0.0 - 1.4	0.099	3.4	1.4 - 8.1	0.007	2.4	1.0 - 5.7	0.054
Right bundle branch block	1.56	0.50-4.84	0.444	1.1	0.4 - 3.5	0.856	0.9	0.3 - 2.8	0.915	0.6	0.2 - 1.9	0.383

*QTc cutoff point 470ms for women and 450ms for men. Statistical analysis was performed using Cox regression analysis. Adjustments for age, BMI, smoking, diastolic blood pressure, prior cardiac disease and medication for arterial hypertension. Significant differences ($P<0.05$) between subjects with and without hospitalization for HF highlighted in bold. BMI = body mass index; CI = confidence interval; ECG = electrocardiographic; ER = early repolarization with horizontal or descending ST segment; fQRS = fragmented QRS complex; HF = heart failure; HR = hazard ratio; LVH = left ventricular hypertrophy; QTc = corrected QT time.

Table 6. Hazard ratios of ECG variables as predictors of HF hospitalization by the history of ischemic heart disease.

Variable	Women (N=5,201)						Men (N=5,703)					
	Without MCC N=3,683 (71%)			With MCC N=1,518 (29%)			Without MCC N= 3,629 (64%)			With MCC N=2,074 (36%)		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Heart rate (1/min)												
QRS \geq 110 ms	1.2	0.4 - 3.7	0.783	0.4	0.1 - 1.4	0.152	1.1	0.7 - 1.9	0.608	1.3	0.9 - 1.8	0.151
QTc \geq 470/450 ms*	1.3	0.7 - 2.4	0.413	1.3	0.8 - 2.2	0.348	1.1	0.6 - 2.1	0.657	1.2	0.9 - 1.7	0.276
ER	0.4	0.1 – 1.0	0.046	0.7	0.4 - 1.2	0.218	1.1	0.6 - 1.9	0.843	1.3	0.8 - 1.9	0.278

Inferolateral T-inversion	1.3	0.4 - 4.1	0.638	1.1	0.4 - 3.0	0.821	3.4	1.5 - 7.8	0.004	2.1	1.1 - 4.1	0.027
fQRS	1.0	0.8 - 1.3	0.993	1.0	0.8 - 1.2	0.793	1.1	0.8 - 1.4	0.734	1.1	0.9 - 1.3	0.324
Anterior	1.3	0.7 - 2.4	0.338	1.0	0.6 - 1.6	0.884	1.1	0.6 - 2.0	0.755	1.2	0.8 - 1.9	0.432
Inferior	1.0	0.7 - 1.3	0.940	0.9	0.7 - 1.2	0.484	1.1	0.8 - 1.4	0.675	1.1	0.9 - 1.3	0.452
Lateral	0.9	0.2 - 3.6	0.875	1.4	0.5 - 3.9	0.480	1.5	0.6 - 4.1	0.411	2.5	0.9 - 6.7	0.072
LVH	1.2	1.0 - 1.6	0.113	1.5	1.2 - 1.9	<0.001	1.2	0.9 - 1.5	0.228	1.0	0.8 - 1.2	0.983
Pathological Q-waves	1.7	0.4 - 7.4	0.489	1.2	0.5 - 2.9	0.741	3.2	1.1 - 9.6	0.034	3.4	1.9 - 5.9	<0.001
Atrial fibrillation/flutter	16.5	3.6 - 74.7	<0.001	0.0	0.0 - [0.982	6.2	1.5 - 25.6	0.012	5.3	1.7 - 16.4	0.004
Left bundle branch block	0.5	0.1 - 3.5	0.480	0.0	0.0 - [0.922	1.2	0.2 - 8.3	0.893	3.1	1.1 - 8.2	0.027
Right bundle branch block	1.1	0.2 - 8.1	0.898	0.9	9.2 - 3.5	0.843	0.0	0.0 - [0.930	0.9	0.3 - 2.8	0.862

**QTc cutoff point 470ms for women and 450ms for men. Statistical analysis was performed using Cox regression analysis. Adjustments for age, BMI, smoking, diastolic blood pressure, prior cardiac disease and medication for arterial hypertension. Significant differences ($P<0.05$) between subjects with and without hospitalization for HF highlighted in bold. BMI = body mass index; CI = confidence interval; ECG = electrocardiographic; ER = early repolarization with horizontal or descending ST segment; fQRS = fragmented QRS complex; HF = heart failure; HR = hazard ratio; LVH = left ventricular hypertrophy; MCC = morbus cordis coronarius; QTc = corrected QT time.*
