Short-term and one-year prognosis of diabetic patients with a first-ever myocardial infarction

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Key words*: myocardial infarction; electrocardiogram; diabetes; prognosis; mortality.*

Summary. *Objectives. To clarify the importance of clinical features and changes in the first electrocardiogram in 28-day and 1-year mortality in patients with diabetes.*

Material and methods. Men and women of Kaunas city aged 25–64 years with the first-ever myocardial infarction during 1983–1992 and with the first electrocardiogram were enrolled in the study. Electrocardiograms were coded using the WHO MONICA Project Protocol criteria and the Minnesota Code. The Kaunas Ischemic Heart Disease Register was the source of data; deaths from ischemic heart disease were identified via death register.

Results. Diabetes was diagnosed in 124 patients: 65 (52.4%) men and 59 (47.6%) women. The 28-day (P=0.01) and 1-year mortality rates (P<0.001) were higher in diabetic than in nondiabetic patients with myocardial infarction. Among diabetic patients, who died during 28 days or one year, myocardial infarction was more often complicated by acute heart failure, and changes in ECG were more often detected than among those who were alive. Female gender (RR=30.2, P=0.02) was associated with an increased risk of death from a first-ever myocardial infarction during the first 28 days, while acute heart failure (RR=4.48, P=0.01) and anterior location of Q wave in the first ECG (RR=2.71, P=0.04) increased the risk of death from ischemic heart disease during one year after a first-ever myocardial infarction.

Conclusions. Acute heart failure and Q-wave in derivations of the first electrocardiogram reflecting anterior site of myocardial infarction increased the risk of death from ischemic heart disease during the first year, and female gender – during the first 28 days in diabetic patients with myocardial infarction.

Introduction

The World Health Organization estimates that by 2025, there will be 300 million diabetic patients (5.4% of the world population) (1). Despite many advances in modern medicine, diabetes continues to be associated with increased morbidity and mortality. The leading cause of death in people with diabetes continues to be myocardial infarction (MI) (2). Among patients admitted with MI, the proportion of diabetic patients is at least 10%. The majority of them have type 2 diabetes mellitus. Furthermore, diabetic patients have a substantially higher mortality rate after an acute MI than nondiabetic patients, which has partly been attributed to the development of congestive heart failure (CHF) (3, 5). Patients with diabetes are in general older, more frequently female, less often smokers, and more frequently have pre-existing cardiovascular disease, including increased frequency of previous MI (2, 4).

However, there are only few studies that analyzed prognosis of patients with diabetes after an acute MI in respect to clinical signs, comorbidities, and changes in electrocardiogram (ECG). The present study has been designed to clarify the importance of clinical signs and changes in the first ECG in short- and long-term mortality after MI in patients with diabetes.

Material and methods

A total of 2496 patients (1892 or 76% men and 604 or 24% women) aged 25–64 years with the first-ever acute MI and any recorded ECG and admitted to the all four hospitals of the city of Kaunas during 1983–1992 were enrolled into the study. The criteria of MI and codes of the first ECG were described in details earlier (6). The diagnosis of diabetes mellitus was taken from clinical diagnosis of the event.

Recurrent MI that occurred within the first 28 days after the initial MI was assessed as the same event.

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Deaths from ischemic heart disease (IHD) were identified via death register. Risk of death from IHD was analyzed in the period of 0–365 days, and the risk of recurrent MI was analyzed in the period of 29–365 days after the initial MI. Fatal events have had diagnostic confirmation during life-time, or there was evidence of recent MI or coronary thrombosis or chronic occlusive coronary disease at autopsy, or a past history of CHD, or suggestive symptoms before death in the absence of evidence for a competing cause of death.

The following demographic and clinical features were selected for the analysis: age, gender, symptoms typical for MI, acute heart failure (pulmonary edema, cardiogenic shock), cardiac arrhythmias (atrial flutter and fibrillation, ventricular fibrillation), complete atrioventricular block, history of other diseases (arterial hypertension, stroke, and obesity), changes in the first coded ECG (Q wave, ST segment elevation, ST segment depression, negative T wave).

The investigation conforms to the principles outlined in the Declaration of Helsinki and was approved by the local ethics committee.

Statistical analysis. t-tests were used to analyze the differences between two groups. Cox proportional hazard regression model was used to determine prognostic factors for outcomes after an acute MI – death from IHD and recurrent MI (7). Log-linear models were used to test the differences adjusted for age, complications of MI, comorbidities. A P value <0.05 was regarded as statistically significant.

Results

The first ECG, coded and recorded from symptoms occurrence, was available for 2008 (80%) patients (1552 men and 456 women). Diabetes was diagnosed in 124 patients: 65 (52.4%) men and 59 (47.6%) wom-

Table 1. **Demographic, clinical features and changes in the first electrocardiogram of the patients aged 25–64 years with a first-ever acute myocardial infarction according to the history of diabetes**

Characteristic	Nondiabetic patients N=1884		Diabetic patients N=124		P value
	n	%	n	%	
Age, mean±SD, years	**53.51±0.18**		**57.11±0.58**		**<0.001**
Females	**397**	**21.1**	**59**	**47.6**	**<0.001**
Typical symptoms	1429	75.8	102	82.3	0.11
Complications of MI					
Acute heart failure	**110**	**5.8**	**15**	**12.1**	**0.02**
Atrial flutter or fibrillation	142	7.5	12	9.7	0.49
Ventricular fibrillation	147	7.8	7	5.6	0.27
Atrioventricular block	42	2.2	4	3.2	0.67
Comorbidities					
Arterial hypertension	**392**	**20.8**	**42**	**33.9**	**<0.001**
History of stroke	43	2.3	4	3.2	0.70
Obesity	**182**	**9.7**	**26**	**21.0**	**<0.001**
Death from ischemic heart disease	**838**	**44.5**	**85**	**68.5**	**<0.001**
Death in 28 days after MI	**98**	**5.2**	**15**	**12.1**	**0.01**
Death in 29–365 days	88	4.7	10	8.1	0.17
Death in 1 year after MI	**186**	**9.9**	**25**	**20.2**	**<0.001**
Recurrent MI	608	32.3	42	33.9	0.78
Recurrent MI in one year	155	8.2	13	10.5	0.48
Changes in the first ECG					
Q wave in first ECG	**554**	**29.4**	**49**	**39.5**	**0.03**
Changes without Q wave	**800**	**42.5**	**41**	**33.1**	**0.03**
Q wave in lateral site	**23**	**1.2**	**6**	**4.8**	**0.03**
Changes without Q wave in inferior site	**225**	**11.9**	**8**	**6.5**	**0.02**
ST elevation in the first ECG	**338**	**17.9**	**13**	**10.5**	**0.01**
ST elevation in inferior site	**178**	**9.4**	**5**	**4.0**	**0.01**

ECG – electrocardiogram; MI – myocardial infarction.

en. Demographic and clinical features of 2008 patients by history of diabetes are presented in Table 1. Diabetic patients with a first-ever acute MI were more likely to be older than nondiabetic patients and more often were women (Table 1). Diabetics had a higher incidence of acute heart failure (P=0.02), arterial hypertension (P<0.001), and obesity (P<0.001) than nondiabetic MI patients.

The 28-day (P=0.01) and one-year mortality rates (P<0.001) were significantly higher in diabetic than in nondiabetic MI patients. There was no difference in the rates of recurrent MI between the two groups. Comparing diabetic and nondiabetic patients in respect of changes in the first ECG, the following differences were detected: Q wave (P=0.03) and Q wave in lateral site (P=0.03) was more prevalent among the diabetic patients, whereas changes without Q wave (P=0.03), changes without Q wave in inferior site (P=0.02), ST elevation (P=0.01), and ST elevation in inferior site (P=0.01) were more prevalent among the nondiabetic patients (Table 1).

Diabetic patients were analyzed according to survival status at 28th day and at one year after a first-ever MI (Table 2). There were more women with diabetes who died in one year after MI than survived. In patients who died during 28-day or one-year period, MI was more often complicated by an acute heart failure compared to those who survived (8.3% *vs.* 40.0%, P<0.001, and 6.1% *vs.* 36.0%, P<0.001, respectively). The first ECG without changes was more often recorded among patients with diabetes who survived than among those who died during 28 days (P=0.01). Recurrent MI was more frequent among the patients who died during the one year after their first-ever MI than among those who survived (Table 2).

The only prognostic factor that appeared to be independently associated with 28-day mortality after a first-ever MI in patients with diabetes was female gender (relative risk estimate RR=30.2, P=0.02). Acute heart failure increased the risk of death during one year after a first-ever MI by 4.5-fold (P=0.01). None of all other analyzed clinical signs had any significance on the risk of death in diabetic patients after a first-ever MI during 28-day and one-year period (Table 3).

In order to determine the role of certain ECG changes in the prognosis of MI in diabetic patients, several Cox regression models were constructed. Each model included age, gender, acute heart failure, and one of the analyzed changes of ECG. Results of these models are presented in Table 3. The only sign of ECG,

Table 2. **Demographic, clinical features and changes in the first electrocardiogram of myocardial infarction patients with diabetes aged 25–64 years according to the survival status**

Characteristic	Alive at 28th day N=109		Dead during 28 days N=15		P value	Alive at one year N=99		Dead during one year N=25		P value
	n	%	n	%		n	%	n	%	
Age, mean±SD, years	56.59±0.64		60.93±0.88			56.51±0.67		59.52±1.10		
Females	**48**	**44.0**	**11**	**73.3**	**0.049**	**43**	**43.4**	**16**	**64.0**	**0.09**
Complications of MI										
Acute heart failure	**9**	**8.3**	**6**	**40.0**	**<0.001**	**6**	**6.1**	**9**	**36.0**	**<0.001**
Atrial flutter or fibrillation	11	10.1	1	6.7	0.34	9	9.1	3	12.0	0.83
Ventricular fibrillation	6	5.5	1	6.7	0.76	5	5.1	2	8.0	0.77
Atrioventricular block	2	1.8	2	13.3	0.14	2	2.0	2	8.0	0.27
Comorbidities										
Arterial hypertension	39	35.8	3	20.0	0.12	35	35.4	7	28.0	0.39
History of stroke	4	3.7	–	–	–	4	4.0	–	–	–
Obesity	24	22.0	2	13.3	0.24	21	21.2	5	20.0	0.76
Recurrent MI in 29–365 days	–	–	–	–	–	6	6.1	7	28.0	0.01
Changes in the first ECG										
Q wave in first ECG	43	39.4	6	40.0	0.86	37	37.4	12	48.0	0.41
Q wave in anterior site	24	22.0	5	33.3	0.48	20	20.2	9	36.0	0.15
Changes without Q wave	33	30.3	8	53.3	0.13	32	32.3	9	36.0	0.84
ECG without changes	**32**	**29.4**	**1**	**6.7**	**0.01**	29	29.3	4	16.0	0.10
ST elevation in the ECG	10	9.2	3	20.0	0.38	9	9.1	4	16.0	0.44
ST depression in the ECG	11	10.1	1	6.7	0.34	11	11.1	1	4.0	0.09
Negative T wave	12	11.0	4	26.7	0.21	12	12.1	4	16.0	0.75

ECG – electrocardiogram; MI – myocardial infarction.

Table 3. **Prognostic factors for risk of death from ischemic heart disease during 28 days and one year after a first-ever acute myocardial infarction in patients with diabetes (multivariate Cox proportional hazard regression model)**

Characteristic	Death in 28 days			Death in one year		
	RR	95% CI	P value	RR	95% CI	P value
Age	1.28	0.95–1.72	0.11	1.07	0.96–1.19	0.22
Females	**30.2**	**1.75–523.18**	**0.02**	2.84	0.84–9.54	0.09
Acute heart failure	4.8	0.99–24.85	0.051	**4.48**	**1.51–13.30**	**0.01**
Ventricular fibrillation	–	–	–	3.17	0.30–33.33	0.34
Atrial flutter or fibrillation	0.90	0.05–15.47	0.94	1.77	0.43–7.30	0.43
Arterial hypertension	0.20	0.02–1.90	0.17	0.69	0.23–2.10	0.51
Stroke	–	–	–	–	–	–
Obesity	0.07	0.00–2.18	0.13	0.76	0.15–3.95	0.75
Q wave in the first ECG	1.13	0.30–4.28	0.86	1.82	0.74–4.48	0.20
Changes without Q wave	2.46	0.66–9.23	0.18	0.93	0.35–2.47	0.89
Q wave in anterior site	1.79	0.44–7.25	0.42	**2.71**	**1.04–7.07**	**0.04**
ECG without changes	–	–	–	0.48	0.14–1.65	0.24

CI – confidence interval; ECG – electrocardiogram; RR – relative risk.

which was associated with significantly increased risk of death from IHD during one year after first ever MI, was anterior location of Q wave in the first ECG (RR=2.71, 95% CI 1.04–7.07; P=0.04).

Prognostic factors, which increase the risk of death from IHD during 28 days and one year after first-ever acute MI in nondiabetic patients, were each one year of age, acute heart failure, ventricular fibrillation, atrial flutter or fibrillation, obesity (Table 4). Female gender decreased risk of death during one year by 34%, and stroke increased risk by 3.15-fold. ECG without Q wave decreased risk of death during 28 days in patients without diabetes (P=0.03). In nondiabetic patients like in diabetic ones, Q wave at the anterior site increased risk of death during one year after the first-ever MI (Table 4).

Further, in order to elucidate the true impact of various clinical variables on the prognosis after a first-ever MI during the first year in diabetic patients, stratification according to the presence or absence of

Table 4. **Prognostic factors of risk of death from ischemic heart disease during 28 days and one year after a first-ever acute myocardial infarction in nondiabetic patients (multivariate Cox proportional hazard regression model)**

Characteristic	Death in 28 days			Death in one year		
	RR	95% CI	P value	RR	95% CI	P value
Age	**1.11**	**1.06–1.16**	**<0.001**	**1.07**	**1.05–1.10**	**<0.001**
Females	0.92	0.54–1.58	0.77	**0.66**	**0.44–0.98**	**0.04**
Acute heart failure	**10.0**	**5.86–17.10**	**<0.001**	**5.16**	**3.41–7.82**	**<0.001**
Ventricular fibrillation	**2.83**	**1.49–5.39**	**<0.001**	**1.84**	**1.14–2.98**	**0.01**
Atrial flutter or fibrillation	**1.98**	**1.09–3.58**	**0.02**	**1.54**	**1.27–2.96**	**<0.001**
Arterial hypertension	0.74	0.39–1.43	0.38	0.93	0.63–1.38	0.71
Stroke	1.79	0.60–5.30	0.30	**3.15**	**1.58–6.25**	**<0.001**
Obesity	**3.17**	**1.68–5.98**	**<0.001**	**1.77**	**1.09–2.87**	**0.02**
Q wave in the first ECG	1.21	0.74–1.98	0.44	1.29	0.93–1.78	0.13
Changes without Q wave	**0.55**	**0.33–0.94**	**0.03**	**0.83**	0.60 – 1.14	0.25
Q wave in anterior site	1.21	0.74–1.98	0.44	**1.49**	**1.03–2.16**	**0.04**
ECG without changes	1.06	0.56–1.87	0.86	0.83	0.56–1.22	0.34

CI – confidence interval; ECG – electrocardiogram; RR – relative risk.

Q-wave in the first ECG was performed. In diabetic patients with Q wave in the first ECG, acute heart failure increased risk of death from IHD almost fourfold (RR=3.86, 95% CI 0.98–15.13, P=0.053) (data are not shown).

None of all analyzed factors had any significance on risk of recurrent MI during one year after a first-ever MI (data are not shown).

Discussion

The present study demonstrated that mortality after a first-ever MI was significantly different in patients with and without history of diabetes. The 28-day and one-year mortality rates were higher in diabetic than in nondiabetic MI patients. Diabetic patients with a first-ever acute MI were more likely to be older and women and had a higher incidence of acute heart failure, arterial hypertension, and obesity than nondiabetic patients.

It has been reported that diabetic patients have more comorbid risk factors including previous infarction and more severe IHD. Most studies have reported that diabetes is an independent predictor for mortality after MI (5, 8, 9). Older patients are most affected by diabetes, as the prevalence of disease increases with age, at least up to 75 years (1). From eight prospective studies, the multivariate-adjusted summary odds ratio for IHD mortality due to diabetes was 2.3 (95% CI 1.9–2.8) for men and 2.9 (95% CI 2.2–3.8) for women (10). Mursia *et al.* (11) showed that patients with diabetes were significantly older; were more likely to be women; had a history of prior MI or hypertension; were obese or were in Killip class II or greater; and had higher systolic blood pressure, pulse pressure, and heart rate, as well as lower left ventricular ejection fraction (LVEF). During 5-year follow-up, 31.3% of patients with diabetes and 20.1% of nondiabetic patients died (P<0.001).

The higher death and complication rates in diabetic patients appear to be multifactorial. Diabetes may be associated with severe IHD, systolic left ventricular dysfunction, autonomic neuropathy, and large infarct size (2, 12). A number of pathogenic mechanisms can worsen the ischemic injury by the superimposition of hypertension on diabetes (1). First, the coexistence of the two diseases leads to cardiac hypertrophy, enhancing susceptibility to ischemic damage. Second, hypertension is associated with the activation of neurohumoral mechanisms capable of exacerbating myocardial injury after an ischemia/reperfusion insult. Third, the severity of diabetic cardiomyopathy worsens when hypertension coexists. As there is a relation between glycometabolic dysregulation and heart failure, a meticulous regulation of glucose levels should be aimed for which may result in improvement in endothelial function and more efficient myocardial substrate utilization (12). Preservation of LVEF and prevention of heart failure are more effective in diabetic patients (13). In our study, data about LVEF and blood glucose level were not available, that is why we were not able to perform similar analysis.

Although early clinical studies suggest that diabetic patients with acute MI are more often present with atypical symptoms or remain unrecognized, later clinical studies showed that similar proportions of diabetic and nondiabetic patients had no chest pain during MI (14, 15). Our study is in agreement with these later studies since no statistically significant differences in symptoms between patients with and without history of diabetes were found. In a study by Richman *et al.* (16), no significant difference between nondiabetic and diabetic patients in the occurrence of the following complications after admission to the hospital was detected: congestive heart failure, nonsustained ventricular tachycardia, sustained ventricular tachycardia, cardiopulmonary resuscitation, and death. In the present study, diabetic patients with MI had a higher incidence of acute heart failure, but there was no significant difference in the incidence of arrhythmias and conduction disturbances between patients with and without history of diabetes.

Our study showed that Q wave and Q wave in the derivations reflecting lateral site of MI was significantly more prevalent among the diabetic than nondiabetic MI patients. Meanwhile, changes without Q wave, changes without Q wave in the derivations reflecting inferior site, ST elevation, and ST elevation in inferior site were more prevalent among nondiabetic patients. Gustafsson and coauthors (3) showed that there were no significant differences in the frequency of ST-segment elevation on the ECG between diabetic and nondiabetic patients. When only the demographic variables of age and sex were included as covariates in a multivariate analysis, mortality was increased in diabetic patients (3).

Multivariate analysis by Bouraoui and coauthors (17) showed that admission plasma glucose was a consistent predictor factor of in-hospital mortality (RR=1.2). Admission plasma glucose level was significantly higher in non-survivors with diabetes than in survivors (P=0.04). We identified several variables that were independently associated with 28-day and 1-year mortality in diabetic patients: female gender (for 28-day mortality) and acute heart failure (for

1-year mortality). Q wave in the derivations reflecting anterior location of MI in the first ECG was only one sign of ECG which was associated with significantly increased risk of death from IHD during one year after first-ever MI. Our study showed that in diabetic patients only anterior location of Q wave in the first ECG significantly increased risk of death during one year after MI.

Limitation of our study is that it was performed in a single community; therefore, the generalizability of our findings to other communities is uncertain. Another limitation is that our sample included persons only less than 65 years of age. The relationship between drug use or coronary angiography or thrombolysis and case fatality was not analyzed.

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Sergančiųjų cukriniu diabetu, ištiktų pirmojo miokardo infarkto, prognozė

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Raktažodžiai: miokardo infarktas, elektrokardiograma, cukrinis diabetas, prognozė, mirštamumas.

Santrauka. *Tikslas.* Nustatyti klinikinių požymių ir elektrokardiografinių pokyčių reikšmę prognozuojant mirtį per 28 dienas ir vienerius metus nuo pirmojo miokardo infarkto diabetu sergantiems ligoniams.

Metodai. Vertinti pirmos turimos ir užkoduotos elektrokardiogramos (elektrokardiogramų, užrašytų 25–64 m. Kauno gyventojams) 1983–1992 metais pirmojo miokardo infarkto ištiktiems pacientams. Elektrokardiogramos koduotos pagal Minesotos kodą, mirtys registruotos remiantis prospektyviojo mirčių registro duomenimis.

Rezultatai. Cukriniu diabetu sirgo 124 ligoniai, iš jų 65 (52,4 proc.) vyrai ir 59 (47,6 proc.) moterys. Mirštamumas per 28 dienas ($p=0,01$) ir vienerius metus ($p<0,001$) po pirmojo miokardo infarkto buvo didesnis sirgusiųjų cukriniu diabetu palyginti su nesirgusiais. Sirgusiems cukriniu diabetu ligoniams dažniau nei nesirgusiems šia liga miokardo infarktas komplikavosi ūminiu širdies nepakankamumu ($p<0,001$). Elektrokardiograma be pakitimų dažniau buvo išgyvenusiųjų nei mirusiųjų per 28 dienas po miokardo infarkto ir sirgusiųjų cukriniu diabetu ($p=0,01$). Ligoniams, sergantiems cukriniu diabetu, moteriškoji lytis didino mirties per 28 dienas riziką (SR=30,2, $p=0,02$). Ūminis širdies nepakankamumas (SR=4,48, $p=0,01$), Q dantelis priekinę sieną atspindinčiose derivacijose (SR=2,71, $p=0,04$) didino mirties per vienerius metus po pirmojo miokardo infarkto riziką ligoniams, sirgusiems cukriniu diabetu.

Išvados. Ligoniams, sirgusiems cukriniu diabetu, ūminis širdies nepakankamumas ir Q dantelis priekinę sieną atspindinčiose derivacijose didino mirties nuo išeminės širdies ligos riziką vienerių metų laikotarpiu po pirmojo miokardo infarkto. Moteriškoji lytis didino mirties nuo išeminės širdies ligos riziką per 28 dienas po miokardo infarkto sergantiesiems cukriniu diabetu.

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