Risk factors for heart failure in survivors after first myocardial infarction

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Key words: *myocardial infarction; heart failure; risk factors; case-control study.*

Summary. *Objective. We examined the prevalence and risk factors of heart failure among 25- to 64-year-old men treated in hospitals for first-time myocardial infarction.*

Material and methods. A nested case-control study included 448 men with first-time myocardial infarction, treated in Kaunas hospitals during 1997–2000. Questionnaires elicited information on demographic characteristics and health problems of respondents, psychological stress, and other risk factors. A multivariate logistic regression was used to determine adjusted risk factors for heart failure.

Results. Adjustment for age, education, smoking, blood pressure, body mass index, psychological stress, and impaired glucose tolerance showed that main risk factors for development of chronicle heart failure among myocardial infarction patients were impaired glucose tolerance (OR=2.32; 95% CI 1.38–3.88), hypertension (OR=1.51; 95% CI 1.01–2.25), and overweight (OR=1.60; 95% CI 1.00–2.57). Psychological stress and smoking also tended to increase the risk for heart failure. Acute heart failure was significantly associated with impaired glucose tolerance (OR=3.15; 95% CI 1.27–7.84).

Conclusion. Risk factors for heart failure were similar to those for coronary heart disease, and their combinations significantly increased the heart failure risk.

Introduction

Despite significant progress in the prevention and treatment of cardiovascular disease, epidemiologic data indicate that the incidence and prevalence of chronic heart failure have been increasing steadily in recent years (1). Heart failure is now recognized as a major public health problem among aging population (2–4). Variation in the prevalence of the syndrome may be related to the differences in methodology, case definition, assessment of heart failure (5), as well as differences in the prevalence of coronary heart disease in the populations (6, 7).

Manifestation of heart failure is associated with cardiac remodeling. Importance of the cardiac remodeling in the pathophysiology of heart failure was based on the left ventricular hypertrophy and dilatation as a consequent of hypertension. Mental stress, high-strain jobs were found to be also associated with higher blood pressure and left ventricular mass (8–11).

Data of Studies of Left Ventricular Dysfunction (SOLVD) registry show that coronary heart disease was the primary cause of heart failure in 69% of the patients, with 63% having previous myocardial infarction. History of hypertension was found in 43% of patients (12).

Risk factors for heart failure have been reported among patients with diagnosed coronary heart disease (13, 14) and recently in aged patients with myocardial infarction in the VALIANT (the VALsartan In Acute myocardial iNfarcTion) registry study (15). These studies have demonstrated that advancing age, coronary heart disease, hypertension, and diabetes are common risk factors for development of heart failure. Although the determinants and prognostic impact of heart failure in patients with acute coronary syndromes have been studied in large international studies (15, 16), little information is available for single risk factors impact on the development of heart failure complicating first-time myocardial infarction before the age of 64 years. The aims of the present study were to analyze the prevalence and risk factors of heart failure among 25- to 64-year-old men treated in hospitals for first-time myocardial infarction.

Material and methods

Study design and population. The study population was comprised of 25- to 64-year-old men residing in Kaunas city. All hospitalized patients with a

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first-time myocardial infarction from 1997 to 2000 were eligible for the study. More than 97% of myocardial infarction patients hospitalized in Kaunas area were treated in four cardiology departments. Specially trained staff identified the subjects for the registration of myocardial infarction cases in these departments.

Myocardial infarction cases were identified from two sources and were included at the time of disease onset. The sources were coronary and intensive care units within the cardiovascular departments in all hospitals in Kaunas and the hospital discharge register. A myocardial infarction case was a person with a clinical diagnosis coded I21 of the 10th revision of International Classification of Diseases (ICD-10) in the hospital registry. The criteria for myocardial infarction included: (i) symptoms according to the case history; (ii) specified changes in blood enzyme levels – creatine kinase and lactate dehydrogenase; and (iii) specified electrocardiographic changes (17). Altogether, 579 first-time myocardial infarction cases were registered among men aged 25–64 years. More than three-fourths (n=448, 77.4%) of patients were interviewed in the hospital during their first week of hospitalization. The reasons for exclusion from the study were: refusal to participate – 10.7%, atypical course of disease and treatment at home or in other than cardiology department – 9%, and difficulties in communication – 2.9%.

We adopted the criteria recommended by the Working Group of Heart Failure of the European Society of Cardiology (18). To meet the case definition for heart failure, patients had to have not only echocardiographic abnormalities, but also appropriate symptoms (shortness of breath, fatigue, fluid retention, or any combination of these symptoms) with clinical signs of fluid retention (pulmonary or peripheral) in the presence of an underlying abnormality of cardiac structure and function. Patients with acute heart failure (Killip class II–IV) and chronic severe and mild heart failure (codes I50.2–4) were assigned to the group of "cases" and compared to myocardial infarction patients without heart failure (controls).

Data on risk factors. Trained physicians interviewed the cases and controls using identical standardized questionnaires, which included questions on demographic, educational, and psychological factors, health behavior, and previous and ongoing health problems. Data on the participants' history of increased arterial blood pressure, diagnosed by a physician, were taken from the hospital records. The records were checked manually for all diagnoses. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

The respondent's perceived stress was measured by a set of seven questions, adapted from the L. Reeder stress scale (19), as follows: 1) In general I am tense and nervous; 2) I do not worry very much about my job; 3) My daily activities are very trying and stressful; 4) I seldom experience tension in my family relations; 5) There is a great amount of nervous strain related to my daily activities; 6) I often feel tension in my relations with other people; 7) At the end of the day I am completely exhausted mentally and physically. Four response options for each question (this describes me very well (1), fairly well (2), not very well (3), not at all (4)), scored 1 to 4, were used to define stress. We defined the stress measure as the sum of the scores, so that the potential values for stress ranged from 7 to 28. Values from 15 to 28 were considered to represent "no stress," and those from 7 to 14 were labeled "stress."

The participants were divided into two categories according to the educational level: eight or less years of schooling and secondary and university education.

Statistical analysis. The prevalence of heart failure by age was calculated by grouped logistic regression. Proportions were compared using a chi-square test. We examined the distribution of several known heart failure risk factors among the cases and controls.

To assess risk factors of heart failure, odds ratios (OR) and 95% confidence intervals (CI) were calculated by logistic regression for the univariate association between myocardial infarction patients suffering from heart failure (cases) and without the syndrome (controls). Factors associated with heart failure were then entered into multivariate logistic regression analysis to determine the independent importance of each of these factors. Crude effects were adjusted for potential confounding variables: age, education, smoking, blood pressure, BMI, impaired glucose tolerance, and stress. A value of $p<0.05$ was considered significant. For all epidemiological and statistical analyses, SPSS version 10.0 (SPSS Inc, Chicago, IL, USA) was used.

Results

From 1997 to 2000, 448 patients with first-time myocardial infarction were interviewed and enrolled into study: 208 patients were identified as having heart failure and 240 patients as not having the syndrome. Data on the prevalence of heart failure for 25- to 64-year-old men with first myocardial infarction show that syndrome was found in 46.4% of patients. Data

based on the clinical diagnosis of the syndrome indicate statistically insignificant differences in 25–44, 45–54, and 55–64-year age subgroups (Table 1). The prevalence of heart failure was 43.1, 48.1, and 46.2% in the age groups, respectively. No significant age differences in the prevalence of heart failure among age subgroups were observed, although among all heart failure cases, oldest patients made up the biggest part: patients aged 25–44 years – 13.5%, 45–54 years – 36.5%, and 55–64 years – 50.0% (Table 2). Mean age of heart failure group was 53.6±0.5 years and control group – 53.1±0.6 years (p=0.397). The incidence rate of acute heart failure was 9.8%.

To investigate whether the characteristics of heart failure cases and selected controls differed, the distribution of potential risk factors for heart failure in these two groups was compared (Table 2). As seen from Table 2, the group of patients who suffered from heart failure did not differ from control group regarding age, education, marital status, and smoking. A greater proportion of heart failure cases than controls had hypertension, increased BMI, impaired glucose tolerance,

Table 1. **Prevalence of heart failure among patients with first-time myocardial infarction (MI) by age strata**

Age group	All MI patients n=448	Heart failure	
		n=208	%
25–44 years	65	28	43.1
45–54 years	158	76	48.1
55–64 years	225	104	46.2

χ^2 for trend 0.051, df=2, p=0.822.

Table 2. **Distribution of potential risk factors for heart failure among cases and controls, crude odds ratios (OR) and 95% confidence intervals (CI)**

Risk factors	Cases (n=208)		Control (n=240)		Crude odds ratios	
	n	%	n	%	OR	95% CI
Age group						
25–44 years	28	13.5	37	15.4		
45–54 years	76	36.5	82	34.2	1.22	0.68–2.19
55–64 years	104	50.0	121	50.4	1.14	0.65–1.98
Education						
university, secondary	166	79.8	183	76.3		
8 years	42	20.2	57	23.8	0.81	0.52–1.27
Marital status						
married	184	88.5	210	87.5		
single	24	11.5	30	12.5	0.91	0.51–1.62
Smoking						
nonsmoker	54	26.0	53	22.1		
smoker	154	74.0	187	77.9	0.81	0.52–1.25
Blood pressure						
<140/90 mmHg	103	49.5	143	59.6		
≥140/90 mmHg	105	50.5	97	40.4	1.50	1.03–2.19
Body mass index						
20.1–25.0 kg/m^2	94	45.2	127	52.9		
≥25.1 kg/m^2	114	54.8	113	47.1	1.36	0.94–1.98
Psychological status						
no stress	37	17.8	57	23.8		
stress	171	82.2	183	76.3	1.44	0.91–2.29
Impaired glucose tolerance						
no	144	74.2	210	87.9		
yes	50	25.8	29	12.1	2.51	1.52–4.16

and expressed mental stress – the factors associated with ischemic heart disease. Crude odds ratios were 1.50 (95% CI 1.30–2.19), 1.36 (95% CI 0.94–1.98), 2.51 (95% CI 1.52–4.16), and 1.44 (95% CI 0.91–2.29), respectively. Table 3 shows the prevalence of risk factors for heart failure by cases and controls according to stratified analysis. To assess the odds ratios in reference strata, the cases without hypertension, diabetes, and overweight were included. In the groups of patients who have one of these risk factors or their combination, a significantly increased risk of heart failure was found.

To remove the effect of the differences in the prevalence of independent variables, crude odds ratios for the following identified predictors of heart failure were adjusted: blood pressure, BMI, impaired glucose tolerance, and psychological stress. After adjustment, the risk for acute heart failure remained significantly higher for 25–64-year-old men with impaired glucose tolerance (OR=3.15; 95% CI 1.27–7.84) (Table 4). There were no statistically significant excess risks of overweight and psychological stress. When these risks were additionally adjusted for differences in age, education, and smoking, results were similar. Among patients with mild and severe heart failure, hypertension increased the risk by 81% (OR=1.81; 95% CI 1.14–2.88), and excess risk associated with glucose intolerance was two times higher (OR=2.00; 95% CI 1.10–3.60). The risk associated with psychological stress was 20% greater than in those without, but the difference was statistically insignificant. Overweight significantly increased the risk for chronic heart failure.

Discussion

We analyzed the prevalence of heart failure in patients with first-time acute myocardial infarction before discharge and used a nested case-control study to provide predictors that were associated with the development of heart failure. All patients with a clinical diagnosis of myocardial infarction under 65 years, who responded to questionnaire, were entered into the study. In the present study, heart failure etiology was validated via hospital records. In patients with first-time myocardial infarction, the assessment of the prevalence of heart failure was based upon the unified criteria and case registration. Thus, we believe that the rate of misclassification is limited in this material. However, there were several sources of errors that may have caused a misclassification of the clinical diagnosis. These errors include diagnostic errors in silent cases and coding errors or other clerical errors in the recording of data. As we included only hospitalized patients with first-time myocardial infarction, who were interviewed, our sample does not represent all first episodes of myocardial infarction and heart failure cases. Therefore, some misclassification may have occurred with respect to the potential confounding factors, particularly the history of chronic disease. Using questionnaire data gathered for 77% of all the registered myocardial infarction events would have some effect on the prevalence of heart failure. The

Table 3. **Risk factors for heart failure (HF) among myocardial infarction patients, odds ratios (OR), 95% confidence intervals (CI), and p-values according to stratified analysis**

Risk factors	HF cases	Controls	Stratified		p
	n	n	OR	95% CI	
No hypertension and No IGT and No overweight	Reference group				
1. Only hypertension	105	97	1.82	1.12–2.98	0.0111
2. Only IGT	50	29	2.90	1.54–5.47	0.0003
3. Only overweight	114	113	1.70	1.05–2.74	0.0221
4. Only stress	171	183	1.57	1.00–2.47	0.0376
5. 3+4 combined	92	89	1.74	1.05–2.87	0.0215
6. 1+3 combined	70	52	2.26	1.31–3.93	0.0018
7. 2+3 combined	34	24	2.38	1.19–4.77	0.0075
8. 2+4 combined	47	24	3.29	1.70–6.41	0.0001
9. 1+2 combined	29	14	3.48	1.57–7.81	0.0007
10. 1–2+3+4 combined	21	9	3.92	1.54–10.23	0.001

IGT – impaired glucose tolerance.

Table 4. **Adjusted odds ratios (OR) and 95% confidence intervals (CI) for heart failure among men aged 25–64 years**

Risk factors	Killip class (II–IV)		Severe and mild heart failure	
	OR*	95% CI	OR*	95% CI
Hypertension (no/yes)	0.90	0.44–1.87	1.81	1.14–2.88
Overweight (no/yes)	0.33	0.15–0.75	1.60	1.00–2.57
Psychological stress (no/yes)	2.03	0.74–5.52	1.20	0.68–2.10
Impaired glucose tolerance (no/yes)	3.15	1.27–7.84	2.00	1.10–3.60
Age (<55/≥55 years)	1.23	0.58–2.61	0.78	0.47–1.28
Education (≤8/>8 years)	1.04	0.45–2.40	0.99	0.56–1.74
Smoking (no/yes)	0.66	0.30–1.43	1.32	0.73–2.37

* adjusted for hypertension, overweight, psychological stress, impaired glucose tolerance, age, education, and smoking.

limitations of this study also include the lack of detailed data collection for issues such as onset of heart failure. For this reason, we cannot provide specific information about the incidence rate of the syndrome and when heart failure occurred. Furthermore, we could not rule out the possibility that other environmental factors, which we have not studied, might have some effect on coronary heart disease and heart failure risk (20, 21).

Our data showed that the prevalence of heart failure among 25- to 64-year-old patients with myocardial infarction was 46.4%. Similar results have been reported by A. Ali *et al*. (22). These investigators examined clinical predictors of heart failure in patients with first acute myocardial infarction and found that after the fourth day of admission the heart failure was diagnosed in 41.6% of the patients. Data of other clinical study showed that 19.1% of patients admitted to the hospital with acute myocardial infarction had heart failure on admission; mean age of patients with syndrome and without it was 72.6 and 63.2 years, respectively (23).

Our data showed no differences in the prevalence of heart failure in age groups, but among myocardial infarction patients who had heart failure, the oldest patients (aged 55–64 years) made up 50.0%. The incidence rate of acute heart failure was 9.8%.

Patients in chronic heart failure group had higher rates of hypertension, overweight, impaired glucose tolerance and tended to be more frequently in stress, and they were likely to be current smokers. The published data are similar and show that hypertension and impaired glucose tolerance are the main risk factors for heart failure development (13, 23). The risk factors were particular important in subjects who developed heart failure before the age of 65 years. Even in the patients with normal epicardial coronary arteries who suffered from acute myocardial infarction diabetes and hypertension were the factors predictive of poor disease outcome (24).

The findings indicate that among myocardial infarction patients who had heart failure hypertension was observed in 50.5% and impaired glucose tolerance in 25.8% of cases. These data are similar to reported data from VALIANT myocardial infarction registry – 53.0% and 30.8%, respectively (15) – and other authors (23) – 54.6% and 33.3%, respectively.

It is commonly recognized that coronary heart disease and hypertension account for the vast majority of cases of heart failure in the general population (4), and in the present study these both factors were found in 50.5% of subjects. Data of stratified analysis showed that the odds ratio for heart failure associated with hypertension was 1.82 (95% CI 1.12–2.98), and for impaired glucose tolerance it was 2.90 (95% CI 1.54–5.47) as compared with subjects without these comorbidities. The risk for heart failure increased more than threefold in those with both risk factors (OR=3.48; 95% CI 1.57–7.81) and about fourfold in men who had four factors (hypertension, impaired glucose tolerance, overweight, and stress).

Conclusion

Hearth failure is frequently associated with acute myocardial infarction, and this frequently co-existed with hypertension, impaired glucose tolerance, and overweight.

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Sergančiųjų pirmuoju miokardo infarktu širdies nepakankamumo rizikos veiksniai

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Raktažodžiai: miokardo infarktas, širdies nepakankamumas, rizikos veiksniai, atvejo-kontrolės tyrimas.

Santrauka. *Darbo tikslas.* Straipsnyje nagrinėjami 25–64 metų vyrų, sergančių pirmuoju miokardo infarktu, širdies nepakankamumo riziką didinantys veiksniai.

Tyrimo medžiaga ir metodai. Lizdiniame atvejo-kontrolės tyrime dalyvavo 448 Kauno vyrai, susirgę pirmuoju miokardo infarktu ir gydyti ligoninėse. Naudojant klausimynus, sukaupti sirgusiųjų duomenys apie miokardo infarkto ir širdies nepakankamumo rizikos veiksnius. Širdies nepakankamumo riziką didinantiems veiksniams nustatyti naudojome daugiaveiksnę logistinę regresiją.

Rezultatai. Standartizacija pagal amžių, išsilavinimą, rūkymą, kraujospūdį, kūno masės indeksą, psichologinį stresą ir gliukozės toleranciją parodė, kad svarbiausi veiksniai, didinantys sergančiųjų pirmuoju miokardo infarktu lėtinio širdies nepakankamumo riziką, buvo gliukozės tolerancijos sutrikimas (ŠS=2,32; 95 proc. PI 1,38–3,88), hipertenzija (ŠS=1,51; 95 proc. PI 1,01–2,25) ir antsvoris (ŠS=1,60; 95 proc. PI 1,00–2,57). Psichologinis stresas ir rūkymas turėjo tendenciją didinti komplikacijų riziką. Ūminis širdies nepakankamumas buvo susijęs su gliukozės tolerancijos sutrikimu (ŠS=3,15; 95 proc. PI 1,27–7,84).

Išvados. Tyrimų rezultatai rodo, jog, esant sutrikusiai gliukozės tolerancijai, širdies nepakankamumui įtakos turi išeminės širdies ligos rizikos veiksniai, ypač atskirų veiksnių derinys.

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References

1. Kannel WB, Ho K, Thom T. Changing epidemiologic features of cardiac failure. Br Heart J 1994;72(Suppl):3-9.
2. Cowie MR, Wood DA, Coats AJS, Thompson SG, Poole-Wilson PA, Suresh V, et al. Incidence and aetiology of hearth failure. Eur Heart J 1999;20:421-8.
3. Remes J, Reunanen A, Aromaa A, Pyorala K. Incidence of hearth failure in Eastern Finland: a population-based surveillance study. Eur Hearth J 1992;13:588-93.
4. Wilhelmsen L, Rosengren A, Eriksson H, Lappas G. Hearth failure in the general population of men – morbidity, risk factors and prognosis. J Intern Med 2001;249:253-61.
5. Mosaterd A, Deckers JW, Hoes AW, Nederpel A, Smeets A, Linker DT, et al. Classification of hearth failure in population-based research: an assessment of six heart failure scores. Eur J Epidemiol 1997;13:491-502.
6. McMurray JJ, Sewart S. Epidemiology, aetiology, and prognosis of hearth failure. Heart 2000;83:596-602.
7. Bonneux L, Barendregt JJ, Meeter K, Bonsel GJ, van der Maas PJ. Estimating clinical morbidity due to ischemic heart disease and congestive heart failure: the future rise of heart failure. Am J Public Health 1994;84:202-8.
8. Schnall P, Pieper C, Schwartz J, Karasek RA, Schlussel Y, Devereux RB, et al. The relationship between job strain workplace, diastolic blood pressure, and left ventricular mass index. JAMA 1990;263:1929-36
9. Adams KF. New epidemiologic perspectives concerning mild-to-moderate heart failure. Am J Med 2001;110(7A):6-13.
10. Malinauskiene V, Theorell T, Grazuleviciene R, Malinauskas R, Azaraviciene A. Low job control and myocardial infarction risk in the occupational categories of Kaunas men, Lithuania. J Epidemiol Community Health 2004;58:131-5.
11. Malinauskiene V, Grazuleviciene R, Neiuwenhuijsen M, Azaraviciene A. Myocardial infarction risk and occupational categories in Kaunas 25–64-year-old men. Occup Environ Med 2002;59:745-50.
12. Bourassa MG, Gurne O, Bongdiwala ST, Ghall JK, Young JB, Rousseau M, et al. Natural history and patterns of current practice in heart failure. J Am Coll Cardiol 1993;22(Suppl A):14-9.
13. Kannel WB, Belanger AJ. Epidemiology of heart failure. Am Heart J 1991;121:951-7.
14. Hoffman RM, Psaty BM, Kronmal RA. Modifiable risk factors for incident heart failure in the Coronary Artery Surgery Study. Arch Intern Med 1994;154:417-23.
15. Velazquez EJ, Francis GS, Armstrong PW, Aylward PE, Diaz R, O'Connor ChM, et al. An international perspective on heart failure and left ventricular systolic dysfunction complicating myocardial infarction: the VALIANT registry. Eur Heart J 2004;25:1911-9.
16. Steg PG, Dabbous OH, Feldman LJ, Cohen-Solal A, Aumont MC, Lopez-Sendon J, et al. Determinants and prognostic impact of heart failure complicating acute coronary syndrome: observations from the Global Registry of Acute Coronary Events. Circulation 2004;109:494-9.
17. World Health Organisation MONICA Project. Monica Manual: monitoring of trends and determinants in cardiovascular disease. Geneva, Switzerland: Cardiovascular Diseases Unit, WHO; 1990.
18. The Task Force on Heart Failure of the European Society of Cardiology. Guidelines for the diagnosis of hearth failure. Eur

Heart J 1995;16:745-51.
19. Glasunov IS, Dowd JE, Baubiniene A, Grabauskas V, Sturmans F, Schuurman JH. The Kaunas Rotterdam Intervention Study: behavioral and operational components on health intervention programmes. Amsterdam: North-Holland Biomedical Press; 1981. p. 40-2.
20. Malinauskiene V, Grazuleviciene R, Theorell T, Azaraviciene A, Obelenis V, Azelis V. Psychosocial factors at work and myocardial infarction among men in Kaunas, Lithuania. Scan J Work Environ Health 2005;31(3):218-23.
21. Grazuleviciene R, Maroziene L, Dulskiene V, Malinauskiene V, Azaraviciene A, Laurinaviciene D, et al. Exposure to motor vehicle exhaust and myocardial infarction risk. Scan J Work Environ Health 2004;30(4):293-8.
22. Ali A, Rybicki B, Alan M, Wulbrecht N, Richer-Cornish K, Khaja F, et al. Clinical predictors of heart failure in patients with first acute myocardial infarction. Am Heart J 1999;138: 1133-9.
23. Wu A, Parsons L, Every N, Bates ER. Hospital outcomes in patients presenting with congestive heart failure complicating acute myocardial infarction. J Am Coll Cardiol 2002;40: 1389-94.
24. Da Costa A, Isaaz K, Faure E, Mourot S, Cerisier A, Lamaud M. Clinical characteristics, aetiological factors and long-term prognosis of myocardial infarction with an absolutely normal coronary angiogram. Eur Heart J 2001;22:1459-65.

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