Depression, anxiety, and risk factor control in patients after hospitalization for coronary heart disease: the EUROASPIRE III Study

Andrzej Pajak, Piotr Jankowski, Kornelia Kotseva, Jan Heidrich, Delphine de Smedt and Dirk De Bacquer

European Journal of Preventive Cardiology 2013 20: 331 originally published online 6 March 2012
DOI: 10.1177/2047487312441724

Original scientific paper

European Journal of Preventive Cardiology

European Journal of Preventive Cardiology
20(2) 331–340

DOI: 10.1177/2047487312441724
ejpc.sagepub.com
SAGE

Depression, anxiety, and risk factor control in patients after hospitalization for coronary heart disease: the EUROASPIRE III Study

Andrzej Pająk[1], Piotr Jankowski[1], Kornelia Kotseva[2], Jan Heidrich[3], Delphine de Smedt[4], Dirk De Bacquer[4] (on behalf of the EUROASPIRE Study Group)

Abstract

Objective: To assess in coronary heart disease (CHD) patients: (1) differences in the prevalence of depression and anxiety between samples selected from 22 countries; (2) the association of depression and anxiety with age, education, diagnostic category, favourable behaviours, use of cardioprotective drugs, and reaching the secondary prevention treatment targets.

Design: Cross-sectional study.

Methods: The study group consisted of 8580 patients from 22 European countries examined at least 6 months after hospitalization due to CHD. Depression and anxiety were assessed using Hospital Anxiety and Depression Scale (HADS).

Results: Prevalence of depression (HADS depression score $\geq$8) varied from 8.2% to 35.7% in men and from 10.3% to 62.5% in women. Prevalence of anxiety (HADS anxiety score $\geq$8) varied from 12.0% to 41.8% in men and from 21.5% to 63.7% in women. Older age, female sex, low education, and no history of invasive treatment were associated with more frequent depression and anxiety. Depression and anxiety were associated with less frequent modification of lifestyle. Depression was related with body mass index, waist circumference, fasting glucose, and more frequent self-reported diabetes but not with reaching the treatment targets for blood pressure and lipids.

Conclusions: High prevalence of depression and anxiety in CHD patients, and relation with less frequent lifestyle modification, call to integrate methods of identification and minimizing unfavourable effects of depression and anxiety into the cardiac rehabilitation and prevention programmes.

Keywords

Anxiety, cardiovascular risk, coronary artery disease, depression

Received 12 July 2011; accepted 13 February 2012

Introduction

In patients with acute myocardial infarction (AMI), depression appears to be related to the number of complications, duration of hospitalization, and cardiovascular risk after hospitalization.[1] In post-AMI patients, depression is related to an approximately 2–2.5-fold increased risk of recurrent coronary event as well as CVD and all-cause death.[2,3]

There are several mechanisms postulated to explain the relation between depression and CVD risk,

[1]Jagiellonian University Medical College, Kraków, Poland
[2]Imperial College London, London, UK
[3]Institute of Epidemiology and Social Medicine, University of Münster, Germany
[4]University, Ghent, Belgium

Corresponding author:
Andrzej Pająk, Department of Epidemiology and Population Studies, Institute of Public Health, Faculty of Health Sciences, Jagiellonian University Medical College, 20 Grzegórzecka St, 31–137 Kraków, Poland
Email: mmpajak@cyf-kr.edu.pl

including increased platelet activity,[4] inflammation,[5] changes in the immunological system and in hypothalamic–pituitary–adrenocortical axis,[6] and increased activity of the sympathetic nervous system, which is related to the development of the metabolic syndrome and arrhythmias.[7–9] Also the use of antidepressants were considered to increase cardiovascular risk.[10] There is good evidence that coronary heart disease (CHD) patients with depression are more exposed to well-known CVD risk factors, less prone to change unfavourable lifestyle, and less compliant to cardioprotective medication.[11–14] The causative role of depression is still debated as not all of the above relations are consistent across the studies[15] and attempts to reduce risk factors by improving mood in depressed patients are less encouraging.[16] It is also known that CHD, and AMI in particular, increases the risk of developing depression and anxiety.[17,18]

The evidence on the relation between anxiety and impaired CVD outcome was considered as less pronounced than for depression. However, anxiety was proved to be related to sudden death, poor quality of life, incident MI, and cardiovascular and all-cause mortality and in one study the effect of anxiety on survival was even stronger than the effect of depression.[19–23] Anxiety was also found to be interrelated with sympathetic activity and endothelial function.[24]

The Joint European Societies Guidelines on CVD prevention were issued in the period 1994–2007 aiming to improve the quality of life, reduce the risk of coronary events, and increase survival. The guidelines included recommendations on psychosocial risk factors including screening of CVD patients for depression.[25] The EUROASPIRE (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) studies have shown that integration of the guidelines with clinical practice varied largely by country and, despite improvement between the years 1995–96 and 2006–07, the average estimate of the effectiveness of CVD risk factors management in secondary prevention is still far from optimal.[26] In the rapidly changing clinical practice, up to now no comprehensive international information is available on the current quantitative relation between depression, anxiety, and lifestyle, exposure to CVD risk factors, and meeting the treatment goals in secondary prevention and no conclusion can be drawn on the extent to which the differences in the prevalence of depression and anxiety could explain poor control of CVD risk factors and lifestyle modification.

In the present substudy of the EUROASPIRE III survey, which was carried out in 2006–07, we aimed to assess in patients after hospitalization due to CHD:

1. Differences in the prevalence of depression and anxiety between samples selected from 22 countries;
2. The association of depression and anxiety with age, education, diagnostic category, favourable behaviours, use of cardioprotective drugs, and reaching the secondary prevention treatment targets.

Methods

The EUROASPIRE III survey was carried out in 22 European countries. A detailed description of the study design, samples, and methods was published earlier.[26] Briefly, within each country, one or more geographical areas with a defined population was selected and all hospitals serving this population were identified. The study included consecutive patients, men and women, at age $\geq$18 years and $<$80 years, who fulfilled one or more of the following diagnostic criteria: (1) coronary artery bypass graft operation (this includes emergency procedure for AMI); (2) percutaneous coronary intervention (this includes emergency procedure for AMI); (3) acute myocardial infarction (ST-elevation and non-ST-elevation MI); and (4) acute myocardial ischaemia but no evidence of infarction (troponin negative) were recruited for the study. Patients were invited for examination 6 months after the index event at earliest which consisted of a structured interview using a standard questionnaire, measurements of height, weight, and waist circumference, assessment of heart rate and blood pressure, and blood sample collection. The following information was obtained: personal and demographic details, education, employment status, history of diabetes, reported lifestyle, and other risk factor management in relation to smoking, diet, weight reduction, exercise, blood pressure, lipids, and glucose, and medication. Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ).[27] Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS).[28] The questionnaire was translated to local languages including a retranslation control procedure. In this report, scores $\leq$7 were considered as normal, 8–10 as mild depression or anxiety, and $>$10 as moderate or severe depression or anxiety.

Blood pressure was measured twice on the right upper arm in a sitting position using automatic digital sphygmomanometers Omron M5-I, Information on smoking was confirmed by the measurement of breath carbon monoxide (Smokerlyser, Bedfont Scientific, Model Micro 4). Current smoking was defined as self-reported smoking and/or a breath carbon monoxide exceeding 10 ppm.

Venous blood samples were collected for serum total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, calculated low-density lipoprotein (LDL) cholesterol, plasma glucose, and HbA1c in

patients with known diabetes. The samples were analysed in the central laboratory.

All data were collected electronically and submitted via internet to the data management centre where checks for completeness, internal consistency, and accuracy were run. All data were stored under the provisions of the national data protection regulations.

National coordinators were responsible for obtaining local Research Ethics Committees approvals. Written informed consent was obtained from each participant by the investigator by means of a signed declaration.

All statistical analyses were undertaken in the Department of Public Health, Ghent University, Belgium using the SAS system, release 9.1.3 (SAS Institute, Cary, North Carolina, USA). The distributions of depression and anxiety scores across levels of demographic characteristics were compared according to the Chi-squared test. The impact of the depression and anxiety scores on continuously scaled CHD risk factors was evaluated according to linear multilevel modelling. These hierarchical models accounted for the clustering of patients within centres.[29] Similarly, prevalence of self-reported lifestyle changes, use of cardioprotective drugs, and coronary risk factors were compared between categories of HADS depression and anxiety according to multilevel logistic modelling. Potential confounding due to differences in distributions of age, educational level, and diagnostic category was additionally adjusted for in the statistical models. Multilevel modelling was performed using PROC MIXED and PROC GLIMMIX procedures as implemented in the SAS system. A level of $\alpha = 0.05$ was a priori chosen to indicate statistical significance. Due to the expected inflation of the type I error due to multiple statistical testing, statistical significance was inferred at a p-value of 0.003 (Bonferoni correction).

Results

The total number of persons included into the analysis was 8580 including 6403 men and 2177 women. The size of the sample varied by country from 104 to 418 in men and from 13 to 191 in women. The age range was 21–83 years for men (mean $\pm$ SD 62.3 $\pm$ 9.5 years) and for women the age range was 36–82 years (65.9 $\pm$ 8.9).

Distribution of HADS depression and anxiety score by sex and by country is presented in Table 1. In general, depression symptoms were more prevalent in women out of whom 32.3% had depression, than in men in whom depression was found in 21.2%. Moderate or severe depression (depression score >10) was found in 7.4% of men and in 12.7% of women.

Table 1. Distribution of Hospital Anxiety and Depression Scale depression and anxiety scores by country in men and women

		Depression score (%)			Anxiety score (%)		
	N	<8	8–10	>10	<8	8–10	>10
Men							
Belgium	230	73.9	16.5	9.6	70.0	21.3	8.7
Bulgaria	374	70.3	17.9	11.8	67.9	19.5	12.6
Croatia	346	76.6	16.5	6.9	66.5	21.7	11.9
Cyprus	372	87.1	9.4	3.5	81.5	10.0	8.6
Czech Republic	376	80.6	12.8	6.7	85.6	8.5	5.9
Finland	158	86.7	9.5	3.8	88.0	8.9	3.2
France	211	75.8	14.7	9.5	69.7	14.7	15.6
Germany	418	79.7	13.6	6.7	77.5	14.6	7.9
Greece	104	68.3	26.0	5.8	64.4	8.7	26.9
Hungary	264	73.9	15.9	10.2	75.0	12.5	12.5
Ireland	293	91.8	7.2	1.0	73.0	18.1	8.9
Italy	298	89.3	8.4	2.4	83.9	11.1	5.0
Latvia	340	83.2	11.8	5.0	87.9	7.9	4.1
Lithuania	395	83.0	12.4	4.6	73.7	17.5	8.9
Poland	333	71.8	18.6	9.6	61.9	19.5	18.6
Romania	378	79.9	13.5	6.6	74.9	15.9	9.3
Russian Federation	261	72.0	18.8	9.2	58.2	26.4	15.3
Slovenia	213	64.3	20.7	15.0	59.6	25.8	14.6
Spain	369	78.1	12.2	9.8	62.3	19.8	17.9
The Netherlands	174	88.5	8.1	3.5	83.9	12.1	4.0
Turkey	269	68.8	17.1	14.1	72.5	17.5	10.0
United Kingdom	227	80.6	10.6	8.8	72.3	11.5	16.3
All men	6403	78.8	13.9	7.4	73.4	15.8	10.8
Women							
Belgium	39	79.5	12.8	7.7	46.2	35.9	18.0
Bulgaria	164	56.7	24.4	18.9	46.3	23.2	30.5
Croatia	101	66.3	23.8	9.9	46.5	23.8	29.7
Cyprus	54	53.7	33.3	13.0	57.4	31.5	11.1
Czech Republic	99	66.7	20.2	13.1	71.7	13.1	15.2
Finland	79	82.3	8.9	8.9	78.5	11.4	10.1
France	54	53.7	18.5	27.8	38.9	22.2	38.9
Germany	114	75.4	19.3	5.3	64.9	21.1	14.0
Greece	13	69.2	30.8	0.0	69.2	23.1	7.7
Hungary	191	66.5	19.4	14.1	49.2	20.9	29.8
Ireland	86	88.4	8.1	3.5	65.1	18.6	16.3
Italy	78	89.7	7.7	2.6	76.9	11.5	11.5
Latvia	178	79.8	10.1	10.1	75.3	15.7	9.0
Lithuania	112	69.6	20.5	9.8	55.4	19.6	25.0
Poland	139	69.1	21.6	9.4	48.9	25.9	25.2
Romania	143	62.9	26.6	10.5	53.9	21.0	25.2
Russian Federation	146	48.0	28.8	23.3	36.3	34.3	29.5
Slovenia	79	63.3	25.3	11.4	49.4	29.1	21.5
Spain	125	60.0	20.0	20.0	43.2	24.0	32.8
The Netherlands	39	87.2	5.1	7.7	74.4	15.4	10.3
Turkey	64	37.5	32.8	29.7	46.9	26.6	26.6
United Kingdom	80	82.5	11.3	6.3	57.5	20.0	22.5
All women	2177	67.7	19.7	12.7	55.6	21.9	22.5

Classification of scores: <8, normal; 8–10, mild; >10, moderate or strong.

Table 2. Distribution of Hospital Anxiety and Depression Scale depression and anxiety scores by age, diagnosis, and education

		Depression score (%)			Anxiety score (%)		
	N	<8	8–10	>10	<8	8–10	>10
Men							
Age (years)							
<50	684	81.6	11.4	7.0	67.8	18.7	13.5
50–59	1895	80.6	12.6	6.8	71.6	16.2	12.2
60–69	2390	79.0	13.9	7.1	75.9	15.0	9.1
≥70	1434	74.6	16.6	8.8	74.4	15.2	10.4
Significance		$p = 0.0009$			$p = 0.0003$		
Diagnostic category							
CABG	1317	80.8	13.7	5.5	80.3	13.6	6.2
PCI	2752	80.5	12.9	6.7	74.4	14.9	10.7
AMI	1226	77.2	14.2	8.7	70.1	18.5	11.4
Ischaemia	1108	73.9	16.1	10.0	66.8	17.6	15.6
Significance		$p < 0.0001$			$p < 0.0001$		
Educational level							
Primary or less	1418	74.7	15.4	9.9	68.9	17.8	13.3
Secondary	3650	78.7	14.0	7.3	73.3	16.0	10.7
High	1299	83.5	11.8	4.8	79.1	12.9	8.0
Significance		$p < 0.0001$			$p < 0.0001$		
Women							
Age (years)							
<50	108	74.1	20.4	5.6	46.3	21.3	32.4
50–59	436	67.0	19.5	13.5	49.5	24.1	26.4
60–69	878	69.7	18.9	11.4	58.7	19.9	21.4
≥70	755	64.8	20.5	14.7	57.0	23.1	20.0
Significance		$p = 0.09$			$p = 0.004$		
Diagnostic category							
CABG	374	72.2	16.6	11.2	60.2	20.3	19.5
PCI	761	70.6	19.7	9.7	60.3	18.8	20.9
AMI	454	63.9	21.2	15.0	53.7	25.8	20.5
Ischaemia	588	64.0	20.4	15.7	48.1	24.0	27.9
Significance		$p = 0.005$			$p < 0.0001$		
Educational level							
Primary or less	714	60.6	22.4	17.0	49.2	24.0	26.9
Secondary	1197	69.9	19.5	10.6	58.1	20.9	21.1
High	255	76.1	13.3	10.6	62.4	20.8	16.9
Significance		$p < 0.0001$			$p = 0.0002$		

Classification of scores: <8, normal; 8–10, mild; >10, moderate or strong. Significance according to the Chi-squared test. AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

There were substantial between-country differences in the prevalence of depression. In men, the lowest prevalence of depression was 8.2 and the highest 35.7% (Table 1). The proportion of men with moderate or severe depression was higher than 10% in four countries. The lowest proportion of women with depression was 10.3% and the highest 63.8%. In women, the prevalence of moderate or severe depression was higher than 10% in 10 countries and in four countries it exceeded 20%.

Anxiety was also more prevalent in women (44.4%) than in men (22.6%) (Table 1). Moderate or strong

Table 3. Self-reported lifestyle changes and use of cardioprotective drugs in relation to Hospital Anxiety and Depression Scale depression and anxiety scores

	Depression score (%)				Anxiety score (%)			
	<8	8–10	>10	*p*-value	<8	8–10	>10	*p*-value
Men								
Quit smoking[a]	51.0	43.5	35.0	<0.0001	50.4	46.2	40.8	0.004
Consuming less fat	82.4	81.1	76.2	0.008	81.8	82.0	81.2	0.27
Consuming more fruits and vegetables	78.8	75.1	74.3	0.02	78.6	76.7	75.8	0.18
Consuming more fish	67.7	62.6	59.1	0.002	67.4	62.9	64.6	0.008
Consuming less alcohol	60.8	61.2	58.4	0.24	60.9	59.6	61.0	0.30
Following diet to lose weight	43.6	40.2	36.6	0.006	42.8	42.0	42.5	0.26
Joining fitness/walking club	12.6	10.2	7.3	0.002	12.3	11.5	9.7	0.08
Doing more everyday activity	52.9	43.1	36.4	<0.0001	52.5	48.2	38.1	<0.0001
Use of antiplatelets	91.8	88.7	88.7	0.04	91.6	90.3	89.1	0.03
Use of beta-blockers	79.7	80.9	77.4	0.48	80.2	80.9	74.5	0.21
Use of ACE inhibitors	59.7	62.7	60.0	0.43	59.5	61.7	62.2	0.38
Use of diuretics	24.9	32.8	30.3	0.004	25.4	28.4	30.1	0.0003
Use of furosemide	8.8	13.3	13.5	0.0005	9.1	10.9	12.2	0.001
Use of statins	79.9	75.3	72.9	0.01	79.5	77.4	76.2	0.11
Use of glucose-lowering drugs[b]	16.4	18.8	19.2	0.27	16.4	17.5	20.2	0.0003
Women								
Quit smoking[a]	51.2	46.8	36.8	0.39	52.6	47.7	41.9	0.50
Consuming less fat	84.8	88.7	83.7	0.28	85.4	85.4	85.6	0.72
Consuming more fruits and vegetables	80.9	79.3	75.2	0.14	80.2	80.3	78.6	0.46
Consuming more fish	64.8	58.2	55.6	0.005	64.5	60.2	59.2	0.06
Consuming less alcohol	59.9	58.2	53.6	0.04	56.9	61.2	61.1	0.30
Following diet to lose weight	47.8	48.1	46.2	0.71	47.3	47.0	49.2	0.71
Joining fitness/walking club	15.2	7.9	6.5	0.0002	15.5	8.4	9.8	0.0002
Doing more everyday activity	47.0	37.6	31.0	0.0004	48.2	40.2	33.7	<0.0001
Use of antiplatelets	89.6	86.0	84.6	0.07	88.7	89.2	86.2	0.37
Use of beta-blockers	80.9	83.1	80.6	0.02	82.0	80.0	81.0	0.71
Use of ACE inhibitors	59.4	62.1	56.0	0.43	59.5	63.9	55.4	0.06
Use of diuretics	37.6	46.6	55.0	0.003	37.2	47.5	46.4	0.001
Use of furosemide	11.6	16.6	21.2	0.0003	11.7	15.5	17.2	0.005
Use of statins	78.1	73.8	65.9	0.39	77.5	76.1	70.7	0.23
Use of glucose-lowering drugs[b]	19.9	24.4	32.2	0.02	19.9	23.6	27.3	0.01

Classification of scores: <8, normal; 8–10, mild; >10, moderate or strong. [a]Among patients smoking in the month prior to the index event. [b]Insulin or oral anti-diabetic drugs. Significance adjusted for age, education, diagnostic category and country.

anxiety was found in 10.8% of men and in 22.5% of women. Similar to depression, there were large between-country differences in the prevalence of anxiety. The highest proportion of men with anxiety was 41.8% and the lowest 12%. The percentage of persons with moderate or severe anxiety was higher than 10% in 10 countries and in one country it was higher than 25%. In women, the highest prevalence of anxiety was 63.7% and the lowest 21.5%. In most countries, the proportion of women with moderate or severe anxiety was higher that 25% and only in two countries it was lower than 10%.

In men, depression was more prevalent in older age, whereas in women, differences according to age did not reach statistical significance. Anxiety was more prevalent in younger age irrespectively of sex. The proportion of depression and anxiety decreased with higher level of education in both sexes. Non-revascularized patients had higher prevalence of depression and

Table 4. Association between Hospital Anxiety and Depression Scale depression and anxiety scores and coronary heart disease risk factors

	Depression score		Anxiety score	
Variable	β ± SE	*p*-value	β ± SE	*p*-value
Men				
Body mass index (kg/m^2)	0.0458 ± 0.0149	0.002	0.0237 ± 0.0138	0.09
Waist circumference (cm)	0.1495 ± 0.0414	0.0003	0.0477 ± 0.0384	0.21
Systolic blood pressure (mmHg)	−0.1299 ± 0.0711	0.07	−0.1880 ± 0.0659	0.004
Diastolic blood pressure (mmHg)	−0.0261 ± 0.0419	0.53	0.0038 ± 0.0389	0.92
Total cholesterol (mmol/l)	−0.0018 ± 0.0041	0.66	0.0020 ± 0.0038	0.60
HDL cholesterol (mmol/l)	−0.0051 ± 0.0010	< 0.0001	−0.0021 ± 0.0009	0.02
LDL cholesterol (mmol/l)[a]	0.0006 ± 0.0014	0.68	0.0007 ± 0.0013	0.58
Fasting triglycerides (mmol/l)[a]	0.0067 ± 0.0021	0.002	0.0043 ± 0.0020	0.03
Fasting glucose (mmol/l)[a]	0.0025 ± 0.0010	0.01	0.0009 ± 0.0009	0.30
Total MET-minutes/week (IPAQ)[b]	−0.0674 ± 0.0059	< 0.0001	−0.0428 ± 0.0055	<0.0001
Smoking[c]	0.0657 ± 0.0095	<0.0001	0.0299 ± 0.0089	0.0008
Self-reported diabetes[c]	0.0444 ± 0.0087	<0.0001	0.0365 ± 0.0082	<0.0001
Women				
Body mass index (kg/m^2)	0.0911 ± 0.0295	0.002	0.0634 ± 0.0274	0.02
Waist circumference (cm)	0.2307 ± 0.0744	0.002	0.0788 ± 0.0690	0.25
Systolic blood pressure (mmHg)	−0.1098 ± 0.1232	0.37	0.0395 ± 0.1144	0.73
Diastolic blood pressure (mmHg)	0.0362 ± 0.0684	0.60	−0.0046 ± 0.0635	0.94
Total cholesterol (mmol/l)	0.0174 ± 0.0072	0.02	0.0144 ± 0.0067	0.03
HDL cholesterol (mmol/l)	−0.0020 ± 0.0018	0.26	0.0013 ± 0.0017	0.43
LDL cholesterol (mmol/l)[a]	0.0039 ± 0.0022	0.07	0.0033 ± 0.0020	0.11
Fasting triglycerides (mmol/l)[a]	0.0064 ± 0.0031	0.04	0.0040 ± 0.0030	0.18
Fasting glucose (mmol/l)[a]	0.0076 ± 0.0018	<0.0001	0.0022 ± 0.0017	0.19
Total MET-minutes/week (IPAQ)[b]	−0.0439 ± 0.0096	<0.0001	−0.0248 ± 0.0090	0.006
Smoking[c]	0.0293 ± 0.0187	0.12	0.0494 ± 0.0174	0.004
Self-reported diabetes[c]	0.0492 ± 0.0128	0.0001	0.0154 ± 0.0120	0.20

Linear regression beta coefficients and significance adjusted for age, education, diagnostic category, and country. [a]After natural log-transformation. [b]After natural log-transformation and adding 500 metmins. [c]According to logistic regression analysis. HDL, high-density lipoprotein; IPAQ, International Physical Activity Questionnaire; LDL, low-density lipoprotein; MET, metabolic equivalent of task.

anxiety than patients after myocardial revascularization (Table 2).

There were important differences in the proportion of patients who reported lifestyle changes by depression and anxiety category (Table 3). In men, the higher the depression score, the lower was the proportion of patients who reported cessation of smoking, who increased physical activity, and who reported favourable increase in consumption of fish. Similar decrease of the proportion of persons who reported favourable change in physical activity was found in women. The differences in the proportion of women who reported smoking cessation and change in fish consumption were not significant, although they were similar to differences in men.

In men and women, the higher the anxiety score, the lower was the proportion of patients who increased daily physical activity. Differences in the proportion of persons who reported favourable changes in diet by anxiety category were small and not significant. In both sexes, reported change in smoking and consumption of alcohol was not related to anxiety score.

In men and in women, higher depression and anxiety scores were associated with more frequent use of diuretics in particular furosemide. For the other diuretics the differences were not significant. More frequent use of glucose-lowering drugs was found in men with increased anxiety score.

Association between depression and anxiety scores and CVD risk factors are presented in Table 4. In men and women, the depression score was inversely related with physical activity and directly related with body mass index as well as with

Table 5. Association between Hospital Anxiety and Depression Scale depression and anxiety scores and coronary heart disease risk factors

	Depression score		Anxiety score	
	8–10 vs. <8	>10 vs. <8	8–10 vs. <8	>10 vs. <8
Men				
Smoking	1.22 (0.93–1.60)	1.48 (1.06–2.06)	0.93 (0.71–1.22)	1.05 (0.77–1.42)
Raised blood pressure[a]	1.00 (0.81–1.23)	0.95 (0.72–1.25)	0.98 (0.80–1.20)	0.85 (0.67–1.09)
Total cholesterol ≥ 4.5 mmol/l	0.94 (0.76–1.17)	1.20 (0.91–1.59)	0.99 (0.80–1.23)	0.89 (0.69–1.14)
LDL cholesterol ≥ 2.5 mmol/l	0.83 (0.65–1.07)	1.02 (0.73–1.42)	1.04 (0.81–1.33)	0.89 (0.67–1.20)
Fasting triglycerides ≥ 1.7 mmol/l	1.24 (0.96–1.59)	0.97 (0.69–1.38)	1.07 (0.83–1.38)	1.09 (0.81–1.47)
HDL cholesterol < 1/1.2 mmol/l[b]	1.14 (0.91–1.44)	1.18 (0.88–1.59)	1.08 (0.87–1.35)	0.78 (0.59–1.02)
Fasting glucose ≥ 7 mmol/l	1.22 (0.94–1.59)	1.07 (0.75–1.54)	1.11 (0.85–1.45)	1.04 (0.75–1.43)
Hba1c ≥ 6.5%[c]	1.05 (0.63–1.77)	1.89 (0.83–4.30)	1.84 (1.03–3.29)	1.31 (0.68–2.52)
Women				
Smoking	1.53 (0.05–45.8)	1.89 (0.04–10.2)	1.40 (0.92–2.12)	1.87 (1.13–3.10)
Raised blood pressure[a]	1.27 (0.62–2.59)	1.20 (0.51–2.81)	1.14 (0.81–1.59)	1.23 (0.88–1.73)
Total cholesterol ≥ 4.5 mmol/l	1.17 (0.71–1.93)	0.95 (0.53–1.72)	1.15 (0.82–1.62)	1.45 (1.02–2.07)
LDL cholesterol ≥ 2.5 mmol/l	1.33 (0.94–1.88)	1.18 (0.78–1.78)	0.87 (0.58–1.31)	1.38 (0.90–2.13)
Fasting triglycerides ≥ 1.7 mmol/l	1.11 (0.78–1.57)	1.23 (0.80–1.88)	1.79 (1.20–2.66)	1.57 (1.04–2.36)
HDL cholesterol < 1/1.2 mmol/l[b]	1.15 (0.76–1.74)	1.04 (0.62–1.73)	1.24 (0.89–1.72)	0.87 (0.62–1.22)
Fasting glucose ≥ 7 mmol/l	1.53 (1.03–2.27)	1.62 (1.00–2.63)	1.38 (0.90–2.11)	1.31 (0.85–2.02)
Hba1c ≥ 6.5%[c]	1.27 (0.91–1.77)	1.27 (0.85–1.90)	1.48 (0.65–3.36)	2.91 (1.17–7.23)

Values are odds ratio (95% CI) adjusted for age, education, diagnostic category, country, total metmins, and body mass index. [a]Systolic blood pressure≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg for non-diabetic patients and systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 80 mmHg for diabetic patients. [b]High-density lipoprotein cholesterol < 1 for men and < 1.2 mmol/l for women. [c]In patients with self-reported diabetes. LDL, low-density lipoprotein.

waist circumference. In both sexes, the increase in depression score was also related to more frequent self-reported diabetes, and in women only with higher fasting glucose. In men, there was an inverse relation between the depression score and HDL cholesterol and positive relation with smoking and fasting triglycerides. There was no significant relation between the depression score and blood pressure. In men and women, anxiety scores were directly related to smoking. Positive relation with self-reported diabetes and negative relation with physical activity were found only in men.

Relations between depression and anxiety scores and control of risk factors were less pronounced (Table 5). Compared to persons with no depression, there were more smokers among men with moderate or strong depression and more women with fasting glucose >7 mmol/l among women with mild and with moderate or strong depression. In women, moderate and strong anxiety was related to a higher proportion of patients with fasting triglicerydes >1.7 mmol/l and moderate or severe anxiety was associated with smoking, high total cholesterol and in diabetics with higher prevalence of elevated Hba1c.

Discussion

In this multi-national study involving patients with CHD from 22 countries, a large centre-variation in the prevalence of depression and anxiety was found. Depression and anxiety were more frequent in women than in men and the frequency increased with age and decreased with higher education level. After adjustment for covariates, depression and anxiety were related negatively to favourable lifestyle changes but their associations with compliance to medication were diverse. There was no association between depression or anxiety score with blood pressure but both were associated with higher exposure to smoking, low physical activity, dyslipidaemia and diabetes. However, the relations of depression with the probability of reaching prevention treatment targets for blood pressure and blood lipids were not significant. Moderate or severe anxiety was related to more frequent smoking, hypercholesterolaemia, and hypertriglicerydaemia and worse control of diabetes in women only.

To our knowledge, this is the largest European study which aimed to assess the prevalence of depression and anxiety symptoms and to examine their relation with

cardiovascular risk factors, lifestyle changes and compliance to cardioprotective medication in CHD patients. The assessment of the depression and anxiety long after hospitalization eliminated cases in which depression was related directly to hospitalization rather than a result of chronic condition or cardiac state. In contrast to persistent depression, in-hospital symptoms are weaker predictors of mortality after myocardial infarction.[30]

There are some limitations in the interpretation of the results of our study. First, in EUROASPIRE III identification of patients was done using clinical diagnosis of CHD which does not always meet the recommended diagnostic criteria. The average participation in the survey after the event was 73%.[26] Non-participants, especially those who did not survive until the examination, could have had higher prevalence of depression and anxiety. It should also be noted that patients were recruited from hospitals serving the defined area in particular countries but they cannot be regarded as representative for all CHD patients in the country. The main limitation comes from the cross-sectional design of the study and the results are inconclusive in terms of causal relationship. Further, the small number of recruited patients in some countries (particularly in women) could result that some relations were not statistically significant. For example, the average estimate of the proportion of persons who reported smoking cessation was similar in men and in women in each depression or anxiety category but the differences were significant only in men. The small number of recruited patients in some countries as well as cultural differences could account for the important differences in the prevalence of depression and anxiety between countries and between sexes in some countries.

In the earlier studies, the prevalence of major depression in CHD patients was estimated as 10–20% and about 40% of patients presented depressive and anxiety symptoms.[30–32] It is obvious that differences in the prevalence of depression and anxiety symptoms between the studies could be explained to a large extent by differences in the method of assessment.[31] In our study, the large variation in the prevalence was assessed using standardized methods of observation. Still, a part of the between-country variation could be referred to the differences in interpretation of the questionnaire which depended on the language and local culture. In the US population study, involving 200,000 participants, the average prevalence of depressive symptoms in the corresponding age group was similar (8.7–10.9%). However, between-state variation was smaller compared to our findings.[33]

We confirmed known relations between anxiety and depression with age and sex and we found that anxiety and depression were associated with an unhealthy lifestyle, i.e. low physical activity, unhealthy diet, and smoking.[1,34] In our study, a dose–response relationship between depression and anxiety and reported lifestyle changes was also found.

Earlier studies provided evidence that depression and anxiety are related to poorer compliance with medication.[12,14] In our study, the associations between depression and anxiety score and the use of cardioprotective medication can be partially explained by the differences in the patients' physical state. The more frequent use of furosemide in depressed and anxietic men and women could be partially explained by increased depression and anxiety in CHD patients with cardiac failure.[35] Our study did not confirm a relation between depression and thiazide duretics, as described earlier.[36]

Our findings have important implications for secondary prevention in CVD patients. Both European and American Guidelines on CVD prevention postulate screening of all CVD patients for depression.[25,32] However, up to date there is no firm evidence that screening with a subsequent medication or behavioural therapy improves cardiovascular outcome,[16,37] although recent studies suggest that selective serotonin reuptake inhibitors might reduce mortality and the risk of rehospitalization.[38] Further, in most countries cardiologists and primary care physicians who provide care for the majority of CHD patients after hospitalization are not trained to manage depression. However, our study confirmed, that depression and anxiety in CHD patients cannot be ignored. While waiting for conclusive results showing that treating depression or anxiety will improve the prognosis of patients with CHD, a prudent approach at present is to offer patients with clinically significant depression or anxiety treatment with psychotherapy or medications. For other patients, psychosocial risk factors should be assessed and their relevance in respect to quality of life and medical outcome should be discussed with patients.[25] The known independent effect on prognosis, high prevalence, clustering with other psychosocial risk factors, relation with lifestyle modification, and poorer compliance with medication call to integrate methods of identification and minimizing unfavourable effects of depression and anxiety into the cardiac rehabilitation and prevention programmes and to develop more effective methods of intervention.

Conclusion

CHD patients with low education, higher age, females, and those who do not undergo invasive treatment seem to be more likely to have depression and anxiety. Depression and anxiety appear as factors which increase difficulties in obtaining favourable lifestyle

modification. The effect of depression and anxiety on the other risk factors and reaching the treatment goals seems weaker and the relation between anxiety and reaching treatment goals in this study was found only in women.

Acknowledgements

EUROASPIRE III was carried out under the auspices of the European Society of Cardiology Euro Heart Survey Programme. EUROASPIRE study was originally an initiative of the ESC Working Group on Epidemiology and Prevention and the first survey was undertaken as part of the Joint ESC/EAS/ESH Implementation Group on Coronary Prevention following the publication of Joint European Societies recommendations on CHD prevention in 1994. The administrative organization and list of participating investigators and other research personnel is published elsewhere.[26]

Funding

The EUROASPIRE surveys were supported by unrestricted educational grants to the European Society of Cardiology from Astra Zeneca, Bristol-Myers Squibb, GlaxoSmithKline, Pfizer, Sanofi-Aventis, Servier, Merck/Schering Plough and Novartis. Contributions of Andrzej Pajak and Piotr Jankowski were supported by the grant of Polish Committee for Scientific Research (2P05D00830). Sponsors had no role in the design, data collection data analysis, data interpretation and writing of this report.

References

1. Hanssen TA, Nordrenhaug JE, Eide GE, et al. Anxiety and depression after acute myocardial infarction: an 18 month follow-up study with repeated measures and comparisson with a reference population. *Eur J Cardiovasc Prev Rehabil* 2009; 16: 651–659.
2. Van Melle J, DeJonge P, Spijkerman TA, et al. Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis. *Psychosom Med* 2004; 66: 814–822.
3. Nabi H, Shipley MJ, Vahtera J, et al. Effects of depressive symptoms and coronary heart disease and their interactive associations on mortality in middle-aged adults: the Whitehall II cohort study. *Heart* 2010; 96: 1645–1650.
4. Kuijpers PM, Hamulyak K, Strik JJ, et al. Beta-thromboglobulin and platelet factor 4 levels in post-myocardial infarction patients with major depression. *Psychiatry Res* 2002; 109: 207–210.
5. Baune BT, Neuhauser H, Ellert U, et al. The role of the inflammatory markers ferritin, transferrin and fibrinogen in the relationship between major depression and cardiovascular disorders – the German Health Interview and Examination Survey. *Acta Psychiatr Scand* 2010; 121: 135–142.
6. Jokinen J and Nordstrom P. HPA axis hyperactivity and cardiovascular mortality in mood disorder inpatients. *J Affect Disord* 2009; 116: 88–92.
7. Skilton MR, Moulin P, Terra JL, et al. Associations between anxiety, depression, and the metabolic syndrome. *Biol Psych* 2007; 62: 1251–1257.
8. Raikkonen K, Matthews KA and Kuller LH. Depressive symptoms and stressful life events predict metabolic syndrome among middle-aged women: a comparison of World Health Organization, Adult Treatment Panel III, and International Diabetes Foundation definitions. *Diabetes Care* 2007; 30: 872–877.
9. Cohen BE, Panguluri P, Na B, et al. Psychological risk factors and the metabolic syndrome in patients with coronary heart disease: findings from the Heart and Soul Study. *Psychiatry Res* 2010; 175: 133–137.
10. Smoller JW, Allison M, Cochrane BB, et al. Antidepressant use and risk of incident cardiovascular morbidity and mortality among postmenopausal women in the Women's Health Initiative Study. *Arch Intern Med* 2009; 169: 2128–2139.
11. Ziegelstein RC, Fauerbach JA, Stevens SS, et al. Patients with depression are less likely to follow recommendations to reduce cardiac risk during recovery from myocardial infarction. *Arch Int Med* 2000; 160: 1818–1823.
12. DiMatteo MR, Lepper HS and Croghan TW. Depression is a risk factor for non-compliance with medical treatment. Meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000; 160: 2101–2107.
13. Needham BL, Epel ES, Adler NE, et al. Trajectories of change in obesity and symptoms of depression: the CARDIA study. *Am J Pub Health* 2010; 100: 1040–1046.
14. Bane C, Hughes CM and McElnay JC. The impact of depressive symptoms and psychosocial factors on medication adherence in cardiovascular disease. *Pat Edu Counsel* 2006; 60: 187–193.
15. Gehi A, Musselman D, Otte C, et al. Depression and platelet activation in outpatients with stable coronary heart disease: findings from the Heart and Soul Study. *Psych Res* 2010; 175: 200–204.
16. Taylor CB, Conrad A, Wilhelm FH, et al. Does improving mood in depressed patients alter factors that may affect cardiovascular disease risk? *J Psych Res* 2009; 43: 1246–1252.
17. Hackett TP. Depression following myocardial infarction. *Psychosomatics* 1985; 26: 23–28.
18. Lane D, Carrol D, Ring Ch, et al. The prevalence and persistence of depression and anxiety following myocardial infarction. *Br J Health Psychol* 2002; 7: 11–21.
19. Roest AM, Martens EJ, de Jonge P, et al. Anxiety and risk of incident coronary heart disease: a meta-analysis. *J Am Coll Cardiol* 2010; 56: 38–46.
20. Rothenbacher D, Hahmann H, Wűsten B, et al. Symptoms of anxiety and depression in patients with stable coronary heart disease: prognostic value and consideration of pathogenetic links. *Eur J Cardiovasc Prev Rehabil* 2007; 14: 547–554.
21. Scherrer JF, Chrusciel T, Zeringue A, et al. Anxiety disorders increase risk for incident myocardial infarction in depressed and nondepressed Veterans Administration patients. *Am Heart J* 2010; 159: 772–779.

22. Denollet J, Maas K, Knottnerus A, et al. Anxiety predicted premature all-cause and cardiovascular death in a 10-year follow-up of middle-aged women. *J Clin Epidemiol* 2009; 62: 452–456.
23. Albert CM, Chae CU, Rexrode KM, et al. Phobic anxiety and risk of coronary heart disease and sudden cardiac death among women. *Circulation* 2005; 111: 480–487.
24. Narita K, Murata T, Hamada T, et al. Interactions among higher trait anxiety, sympathetic activity, and endothelial function in the elderly. *J Psychiatr Res* 2007; 41: 418–427.
25. Graham I, Atar D, Borch-Johnsen K, et al.; European Society of Cardiology (ESC); European Association for Cardiovascular Prevention and Rehabilitation (EACPR); Council on Cardiovascular Nursing; European Association for Study of Diabetes (EASD); International Diabetes Federation Europe (IDF-Europe); European Stroke Initiative (EUSI); Society of Behavioural Medicine (ISBM); European Society of Hypertension (ESH); WONCA Europe (European Society of General Practice/Family Medicine); European Heart Network (EHN); European Atherosclerosis Society (EAS). European guidelines on cardiovascular disease in clinical practice. Fourth Joint Task Force of the European Society of Cardiology and other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). *Eur J Cardiovasc Prev Rehabil* 2007; 14(Suppl 2): S1–S113.
26. Kotseva K, Wood D, De Backer G, et al.; EUROASPIRE Study Group. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. *Eur J Cardiovasc Prev* 2009; 16: 121–137.
27. International Physical Activity Questionnaire (IPAQ). Available at http://www.ipaq.ki.se/publications.htm.
28. Zigmond AS and Snaith RP. The hospital anxiety and depression scale. *Acta Psych Scand* 1983; 67: 361–370.
29. Brown H and Prescott R. *Applied mixed models in medicine*, 2nd ed. New York: John Wiley & Sons, 2006.
30. Lane D, Carroll D, Ring C, et al. In-hospital symptoms of depression do not predict mortality 3 years after myocardial infarction. *Int J Epidemiol* 2002; 31: 1179–1182.
31. Nicholson A, Kuper H and Hemingway H. Depression as an etiologic and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies. *Eur Heart J* 2006; 27: 2763–2774.
32. Lichtman JH, Bigger Jr JT, Blumenthal JA, et al. Depression and coronary heart disease: recommendations for screening, referral, and treatment: a science advisory from the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Psychiatric Association. *Circulation* 2008; 118: 1768–1775.
33. Strine TW, Mokdad AH, Balluz LS, et al. Depression and anxiety in the United States: findings from the 2006 Behavioral Risk Factor Surveillance System. *Psychiatr Serv* 2008; 59: 1383–1390.
34. Bonnet F, Irving K, Terra JL, et al. Anxiety and depression are associated with unhealthy lifestyle in patients at risk of cardiovascular disease. *Atherosclerosis* 2005; 178: 339–344.
35. Rutledge T, Reis V, Linke SA, et al. Depression in heart failure: a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. *J Am Coll Cardiol* 2006; 48: 1527–1537.
36. Okada F. Depression after treatment with thiazide diuretics for hypertension. *Am J Psych* 1985; 142: 1101–1102.
37. Thombs BD, de Jonge P, Coyne JC, et al. Depression screening and patient outcomes in cardiovascular care: a systematic review. *JAMA* 2008; 300: 2161–2171.
38. Pizzi C, Rutjes AW, Costa GM, et al. Meta-analysis of selective serotonin reuptake inhibitors in patients with depression and coronary heart disease. *Am J Cardiol*. 2011; 107: 972–979.