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Mental health is a risk factor for poor outcomes in cardiac patients: Findings from the national DenHeart survey

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ABSTRACT

Objective: To explore (i) the prevalence of cardiac risk factors (obesity, smoking, excessive alcohol consumption and medication non-adherence) among cardiac patients with depression and anxiety, (ii) associations between depression and anxiety scores and cardiac risk factors and (iii) the association of depression and anxiety and cardiac risk factors with mortality, and their population attributable risk.

Methods: A national cross-sectional study using patient-reported outcomes at discharge and national register data. For one year (April 15th 2013 to April 15th 2014) all patients discharged or transferred from the five Danish Heart Centres were included in the study. A total of 14,239 patients answered the HADS questionnaire, response rate 51%.

Results: Mean age was 64.8 years and 69% were male. Patients with depression or anxiety (HADS-D or HADS-A score ≥ 8) had 30% and 45%, respectively, higher odds of being current smokers; 19% and 37% higher odds of being obese and 31% and 24% higher odds of excessive alcohol consumption. Depressive patients had 34% higher odds of being non-adherent to their medication. At one-year follow-up, patients with depression (HADS-D score ≥ 11) had the highest attributable risk associated with mortality followed by: smoking, ischemic heart disease, anxiety, diabetes, hypertension chronic obstructive pulmonary disease and excessive alcohol consumption.

Conclusion: Depression and anxiety in patients with cardiac disease is associated with cardiac risk behaviour such as smoking, obesity, excessive alcohol consumption and medication non-adherence. Depression and anxiety have an attributable risk associated with mortality that is comparable to other well-known risk factors such as smoking.

1. Introduction

1.1. Background

Depression and anxiety are common conditions among cardiac patients as up to 15% of patients across different diagnoses report symptoms of depression and 25% report symptoms of anxiety [1–3]. Depression and anxiety may lead to cardiac risk behaviour, including unhealthy eating habits, smoking, excessive alcohol consumption and medication non-adherence [4–7]. These cardiac risk factors are known

Abbreviations: BMI, body mass index; CABG, coronary artery bypass graft; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HADS, Hospital Depression and Anxiety Scale; HR, hazard ratio; MI, myocardial infarction; OR, odds ratio; PAR%, population attributable risk percent; PCI, percutaneous coronary intervention; PRO, patient-reported outcome; PTSD, post-traumatic stress disorder; SD, standard deviation

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to increase the risk of poor outcomes, e.g. morbidity or mortality in cardiac patients [8]. In the DenHeart study, an association between symptoms of depression, anxiety and mortality has been established across cardiac diagnoses with a HR up to 2.29 (95% CI 1.81–2.90) [9]. The American Heart Association recommend that depression should be elevated to the status of a risk factor for adverse medical outcomes in patients with acute coronary syndrome [10]. However, this only applies for depression and acute coronary syndrome and not anxiety and quality of life and not for other cardiac diagnoses such as arrhythmia and heart failure.

Poor outcomes due to depression and anxiety could be explained by both physiological and behavioural processes. Psychological factors stimulate the autonomic nervous system, which triggers production of catecholamines, increases blood pressure, constricts coronary arteries and increases platelet activity. Consequently, patients suffer increased thrombogenesis, arrhythmogenesis, reduced heart rate variability, myocardial ischemia and impaired ventricular function [11]. Moreover, behavioural mechanisms are another link between mental status and cardiac disease. Individuals with symptoms of depression and anxiety are suggested to have an unhealthier food intake, smoke more, consume more drugs and/or alcohol, be less adherent to treatment, sleep poorly, and be less physically active [7]. These elements are risk factors associated with progression of cardiac disease and thus, subsequently, the identified adverse outcomes [12].

As both depression and anxiety symptoms and behavioural cardiac health risks are prevalent in cardiac patients it is relevant to investigate whether there is an association between symptoms of depression and anxiety and risk behaviour across cardiac diagnostic groups. If patients with depression or anxiety have a higher prevalence of poor cardiac risk behaviour they are at increased risk of adverse outcomes. It is also crucial to determine the attributable risk of depression and anxiety in prioritizing interventions to reduce mortality. Depression and anxiety are potentially modifiable which make the association with mortality clinically relevant. Furthermore, cardiac risk modification initiatives might be ineffective if depression and anxiety are not successfully treated.

Thus, the overall purpose was to gain insight into the mechanisms that cause higher mortality in cardiac patients with depression and anxiety.

1.2. Objectives

The objectives were, in cardiac disease patients, to explore (i) the prevalence of cardiac risk factors (obesity, smoking, excessive alcohol consumption and medication non-adherence) among patients with depression and anxiety, (ii) the associations between depression and anxiety scores and cardiac risk factors and (iii) the association of depression, anxiety and cardiac risk factors with mortality and their population attributable risk.

2. Methods

2.1. Study design

The DenHeart study was designed as a centre-based cohort study based on patient-reported data and national register data. All patients admitted to a Heart Centre were asked to fill out a paper-based questionnaire at hospital discharge to evaluate patient-reported outcomes (PROs) across cardiac diagnostic groups. The methods were thoroughly described in the published study protocol [13].

In previously published papers from the DenHeart study we reported diagnostic differences in symptoms of depression and anxiety between cardiac groups [3]. We also reported that depression and anxiety are predictors of both mortality and cardiac events after 1 year across cardiac diagnoses [9]. For the current paper we take the next step and try to explain the association between depression/anxiety and mortality/cardiac events by looking at cardiac risk factors. This paper is investigating if patients´ with depression and anxiety have more risk factors (e.g. smoking and obesity) potentially leading to the poorer outcomes already documented from the DenHeart study [9]. Furthermore, we wanted to follow up on the American Heart Association suggestion of elevating depression as a risk factor [10] by investigating the population attributable risk of depression and anxiety on mortality compared to other known risk factors.

2.2. Setting and participants

For one year (April 15th 2013 to April 15th 2014) all patients discharged or transferred from the five Danish Heart Centres were included in the study.

2.3. Eligibility criteria

All patients were unselected and consecutively included. Patients under 18 years of age, without a Danish civil registration number and unable to understand Danish were excluded from the study. For ethical reasons, patients who were unconscious when transferred were also excluded.

2.4. Recruitment

Patients were asked to complete and return the questionnaire before they left the hospital or to do so at home within three days of discharge and return it by mail. Patients who were transferred to another hospital were asked to fill out the questionnaire at final discharge.

Patients were recruited by a ward nurse or by a research assistant nurse. All nurses at the Heart Centres, approximately 800, were informed about the study and procedures at ward meetings. Moreover, guidelines were distributed and a website established (www.DenHeart.dk). The questionnaire was distributed with a postage pre-paid envelope to facilitate its return.

2.5. Data sources/measurement

The DenHeart questionnaire consisted of a series of well-validated questionnaires and a number of ancillary questions. The questionnaire consisted of 80 questions. It was tested for feasibility in a small sample and took approximately 20 min for patients to fill out. Among other questionnaires, the Hospital Depression and Anxiety Scale (HADS) was included in the DenHeart survey. HADS is a 14-item questionnaire that assesses levels of depression and anxiety in medically ill patients admitted to non-psychiatric hospital clinics. The scale offers two scores, HADS-D and HADS-A, and consists of seven questions to assess depression and seven to assess anxiety [14]. For each of the questions the respondent chooses from four responses to indicate the extent to which each applies for the last week. HADS is a valid and internally consistent measure, with a mean Cronbach's alpha of 0.82 and 0.83 for the HADS-D and HADS-A, respectively [15]. Scores of 0 to 7 for either subscale are regarded as normal and scores of 8 to 10 suggest the possible presence of a mood disorder. Scores of 11 and above indicate the probable presence of a mood disorder [16]. In this paper, when we report depression and anxiety it is based on this patient-reported questionnaire. For the sake of readability, we use “depression and anxiety” and not possible or probable depression and anxiety throughout the paper.

The survey also included nine questions about health and health behaviour from the Danish Health and Morbidity Survey and the Danish National Health Survey [17, 18] and one question regarding medication adherence.

Data from the following Danish national registers were collected on all identified patients at baseline: The Danish Civil Registration System [19], The Danish National Patient Register [20], and the Danish Education Registers [21].

To combine questionnaire data with data from the registers all questionnaires were matched with a hospital discharge from the National Patient Register. This was executed by matching the date the patient filled out the questionnaire or the date the questionnaire was received with a discharge from a relevant hospital documented in the National Patient Register. To calculate the number of possible responders, a list of all patients discharged from a Heart Centre in the study period was reviewed. Patients without a relevant cardiac diagnosis or cardiac observation diagnosis were not counted among possible responders.

Information co-morbidity and ICD-10 primary action diagnosis was obtained from the National Patient Register. Responders were divided into seven diagnostic groups: ischemic heart disease: I10.9, I20-I25, T823D, Z95.1, Z95.5; arrhythmia: I44-I46, I46.9, I47-I49, Z95.0,R00.0, R00.1, R00.2, R00.8A, T75.0, T75.4, T82.1, T82.8; heart failure: I11.0, I42.0-I43.8, I50, I51.7, R57.0; congenital heart disease: Q00-Q99, I27.8A, I27.9, I28.0; infectious heart disease: I30.0-I32.0, I33, I38.9-I39.0, I40.0-I41.8, I32.8, I39.8, I51.4, T82.6, T82.7; heart transplant: T86.2-T86.3, Z94.1, Z94.3; heart valve disease: I05.0-I06.0, I34.0-I37.2, I39.1, I39.2, I51.1A, Z95.2-Z95.4. Two further groups were defined: other diagnoses: D15.1, E78.0, E78.5, I11.9, I26.0, I27.0, I27.2, I27.8, I27.9A, I51.0, I51.3B, I51.8, I51.9, I71.0-I71.4, I71.6, I71.9, J81.9, J96.0, J96.9, S25.0, S26.0, S26.8, S26.9, Z95.8, Z95.9 and observation for heart disease: R01.1, R06.0, R07.1-R07.4, R42.9, R55.9, Z03.4, Z03.5, Z82.4.

Tu comorbidity index scores [22] were calculated using information on primary and secondary diagnoses for all patients going back 10 years before the index discharge. The Tu scores incorporate congestive heart failure, cardiogenic shock, arrhythmia, pulmonary oedema, malignancy, diabetes, cerebrovascular disease, acute/chronic renal failure and chronic obstructive pulmonary disease. All diagnoses are weighted equally.

Information on cardiac risk factors was obtained from self-reported data. Obesity was defined as a body mass index (BMI) ≥ 30. Smoking was defined as current daily smoking. Excessive alcohol intake was defined as a weekly consumption exceeding 21 units for men and 14 for women, in accordance with the Danish Health Authority. Medication non-adherence was defined as forgetting to take prescribed medication more than once a week among patients who took medication prior to their hospital admission.

Information on deaths during the first-year post-discharge was obtained from the Danish Civil Registration System.

2.6. Bias

Several decisions were made to minimize the risk of bias. Preplanned outcomes and objectives were described in the protocol [13]. Data collection was standardized by guidelines and information meetings to minimize inter-observer variability. All patients were included consecutively from the Heart Centres over one year to avoid selection and chronology bias. To evaluate transfer bias all non-responding patients were followed up in the registers to allow for comparisons on essential parameters [3].

2.7. Study population

The study population entailed all patients with a cardiac diagnose discharged from the five Danish Heart Centres during the inclusion period. The five Heart Centres diagnose and treat around 45,000 patients every year, of whom approximately 35,000 have a cardiac condition. Patients admitted with non-cardiac illnesses were excluded. The response rate was 51%. In total 14,239 patients completed the HADS questionnaire (Fig. 1). The proportions of patients in each diagnostic group are comparable among responders and non-responders and they have similar sociodemographic and clinical characteristics [3]. A higher mortality rate was detected among non-responders [9]. This could mean that the population attributable risks have been underestimated in this study.

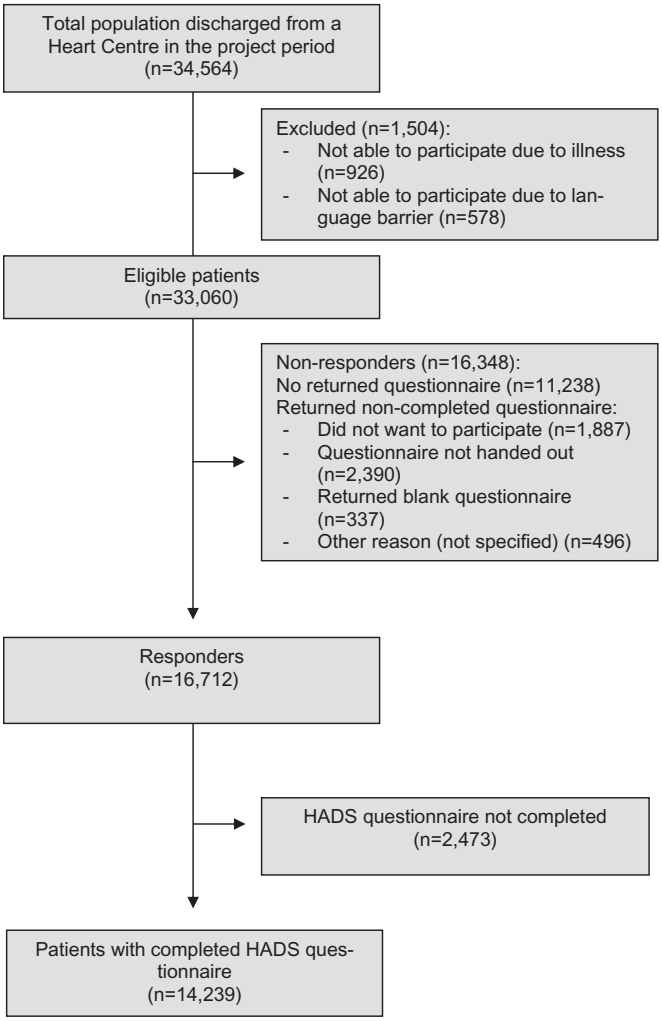

Fig. 1. Flowchart

2.8. Statistical methods

All statistical analyses of continuous outcomes were based on standard regression methods and the normal distribution. Categorical data were compared using χ^2 test and Cochran-Armitage Trend Test, respectively. Continuous data were compared using one-way Anova. Associations between HADS scores and risk factors were tested using logistic regression adjusted for age, sex, marital status, educational level, Tu comorbidity index score and cardiac diagnostic group (ischemic heart disease, arrhythmia, heart failure, congenital heart disease, infectious heart disease, heart valve disease, heart transplant or other diagnoses) [13].

The population attributable risk percent (PAR%) is the reduction in incidence (mortality) that would be observed if the population was entirely unexposed compared with its current (actual) exposure pattern. PAR% was calculated using the following formula: $p(RR - 1/RR)$, where the notation p is the proportion of cases exposed to the risk factor and RR is the Hazard Ratio (HR) (results from Cox's proportional hazard models with age as underlying time scale) in the exposed compared with the unexposed group.

Originally, the plan was to use weighting to deal with missing data in the analyses [13]. However, responders and the total population discharged were very similar in terms of age, sex, diagnoses and

Table 1
Demographic and clinical profile for responders stratified by HADS scores.

	All responders	Patients with HADS-A < 8	Patients with HADS-A 8–10	Patients with HADS-A ≥11	Patients with HADS-D < 8	Patients with HADS-D 8–10	Patients with HADS-D ≥11
n	14,239	9369	2329	1978	11,144	1652	982
Male, %	69	73	65	59**	70	66	66**
Age, mean (SD)	64.8 (12.6)	65.3 (12.4)	63.4 (13.0)	62.5 (12.4)**	64.6 (12.6)	65.8 (12.3)	64.1 (12.4)**
Married, %	64	66	62	60**	66	60	58**
Educational level, %							
Basic school	31	29	32	35**	29	36	34**
Upper secondary or vocational education	43	43	44	44	44	42	45
Higher education	23	25	21	18	25	19	18
No information	2	2	2	3	2	3	4
Co-morbidity ten years back, %							
Hypertension	35	33	38	39**	33	43	46**
Ventricular arrhythmia	5	5	5	5	5	6	5
Ischemic heart disease	42	41	43	47**	41	48	54**
Myocardial infarction	18	18	18	22**	17	21	25**
PCI	18	17	18	20*	17	21	24**
CABG	4	4	4	5	4	5	6*
Diabetes	13	12	15	16**	11	19	22**
Heart failure	18	17	19	19*	16	22	26**
Renal disease	4	3	4	4	3	5	7**
Chronic obstructive pulmonary disease	7	5	8	10**	5	10	13**
Tu co-morbidity score, %							
0	41	42	42	38**	43	34	32**
1	34	33	32	36	33	35	33
2	16	16	16	15	16	17	20
≥3	9	8	10	11	8	14	16

HADS-A = Hospital Depression and anxiety Scale – Anxiety; HADS-D = Hospital Depression and anxiety Scale – Depression; SD = standard deviation; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft.

** $p < .01$

* $p < .05$.

education. In all analyses observations with missing data were excluded. All analyses were conducted using SAS version 9.3.

2.9. Ethics approval

The study complies with the Declaration of Helsinki. According to Danish legislation, surveys do not have to be approved by an ethics committee system (H-4-2013-FSP) but rather by the Danish Data Protection Agency (2007–58-0015/30–0937). Use of register data was permitted by The Danish National Board of Health (FSEID-0001131). DenHeart is registered at ClinicalTrials.gov (NCT01926145) and approved by the Institutional Boards of the Heart Centres. Patients signed an informed consent.

3. Results

3.1. Participants

Socio-demographic and clinical profiles are presented in Table 1 for all responders and responders stratified by HADS scores.

Mean age was 64.8 years (standard deviation (SD) 12.6), 69% were male and 64% were married. Looking at co-morbidity ten years back the following seem to be increasingly prevalent with increasing HADS scores: hypertension, ischemic heart disease, myocardial infarction (MI), percutaneous coronary intervention (PCI), diabetes and chronic obstructive pulmonary disease (COPD), Table 1.

Obesity, current smoking and medication non-adherence was significantly more prevalent among patients with increasing HADS scores. For excessive alcohol consumption, no significant differences were found between patients with increasing HADS scores, Table 2.

3.2. Predictors of cardiac risk factors

Compared with patients scoring 8 and below, patients with a HADS-D score ≥ 11 were 45% more likely to be current smokers (odds ratio (OR) = 1.45 (1.22–1.72)) and patients with a HADS-A score ≥ 11 were 30% more likely (OR = 1.30 (1.14–1.49)), Table 3.

Patients with HADS-D scores 8–10 and ≥ 11 were 42% and 37% more likely to be obese, respectively (OR = 1.42 (1.26–1.61) and (OR = 1.37 (1.18–1.60). Furthermore, patients with a HADS-A score 8–10 and ≥ 11 were 17% and 19% more likely to be obese, respectively (OR = 1.17 (1.05–1.31) and (OR = 1.19 (1.06–1.34), Table 3.

Patients with a HADS-D score 8–10 were 26% more likely to have an excessive alcohol consumption compared with patients with a HADS-D score < 8 (OR = 1.26 (1.03–1.54). Patients with HADS-A scores 8–10 and ≥ 11 were 21% and 31% more likely to have excessive alcohol consumption, respectively (OR = 1.21 (1.01–1.44) and (OR = 1.31 (1.08–1.58), Table 3.

Patients with HADS-D scores 8–10 and ≥ 11 were 33% and 34% more likely to be non-adherent to their medication, respectively, compared with patients with a HADS-D score < 8 (OR = 1.33 (1.14–1.56) and (OR = 1.34 (1.09–1.64). No significant results were found for HADS-A and medication non-adherence, Table 3.

The HRs and PAR%s of nine potential risk factors for all-cause mortality are shown in Table 4. The highest PAR% was HADS-D > 11 (10.5%), followed by smoking (7.8%), ischemic heart disease (7.4%) and HADS-A > 11 (7.3%).

4. Discussion

Patients reporting symptoms of anxiety and depression were more likely to be current smokers, obese and have an excessive alcohol intake. Patients with depressive symptoms were more likely to be non-compliant to their medication. Furthermore, the highest population

Table 2
Prevalence of behavioural cardiac risk factors among patients stratified by HADS scores.

	Patients with HADS-A < 8	Patients with HADS-A 8–10	Patients with HADS-A ≥ 11	p[a]b, c	Patients with HADS-D < 8	Patients with HADS-D 8–10	Patients with HADS-D ≥ 11	p[a]
n	9369	2329	1978		11,144	1652	982	
BMI ≥ 30, n (%)	2027 (23)	590 (27)	517 (28)	< 0.0001	2400 (23)	467 (31)	276 (30)	< 0.0001
Current smoker, n (%)	1063 (12)	319 (14)	355 (18)	< 0.0001	1322 (12)	242 (15)	180 (19)	< 0.0001
Alcohol intake above high-risk limit, n (%)	658 (8)	179 (9)	151 (8)	> 0.10	785 (8)	128 (9)	76 (9)	> 0.10
Medication non-adherence, n (%)	399 (5)	121 (6)	113 (7)	0.01	476 (5)	196 (7)	70 (8)	0.0001

HADS-A = Hospital Depression and anxiety Scale – Anxiety, HADS-D = Hospital Depression and anxiety Scale – Depression, BMI = body mass index.
[a] Cochran-Armitage Trend Test of differences between groups.
[b] The Danish Health Authority defines the high-risk limit for alcohol consumption as a weekly intake of > 21 standard drinks for men and > 14 standard drinks for women.
[c] Medication non-adherence is defined as forgetting to take prescribed medication more than once a week.

attributable risk associated with one-year mortality was found in depression symptoms followed by smoking, ischemic heart disease and anxiety symptoms.

This paper presents two interesting findings. First, in cardiac patients there is a clear association between depression, anxiety and cardiac risk behaviour. Second, depression and anxiety symptoms have high attributable risk associated with mortality in a model including the risk factors that we traditionally intervene upon: hypertension, ischemic heart disease, diabetes, chronic obstructive pulmonary disease, smoking, BMI > 30 and excessive alcohol intake.

Psychological issues such as depression were previously found to impact modification of health-related behaviour e.g. physical activity, food consumption and medication compliance in rehabilitation [6]. Alcohol use has also previously been linked to depression and anxiety with poor outcomes such as heart disease and mortality [23, 24]. Studies have also linked anxiety to health-related risk behaviour, for instance in patients with post-traumatic stress disorder (PTSD) where behavioural factors, specifically smoking, alcohol and sleep disturbances, mediated the association between PTSD and heart rate variability based indices of autonomic nervous system dysregulation [4]. Smoking has also previously been linked to depression and anxiety with up to 93% and 44% increased odds of smoking in patients with major depression or generalized anxiety disorder [5, 25, 26]. Conversely, smokers had 85% increased odds of depression and 71% increased odds for anxiety in an international study of more than one hundred thousand people [27].

Looking at the population attributable risks associated with one-year all-cause mortality for depression (10.5%) and anxiety (7.3%), it is reasonable to ask if this is really the full picture? Probably not. Even though this paper shows an association between depression and anxiety symptoms and health-related behaviour that could explain some of the risk, the influence of risk behaviour might not have short-term effects. Depression and anxiety was previously found to be significantly associated with the onset of heart disease in a prospective study. However, the median time after psychological diagnosis (assessed according to DSM-IV criteria) to onset of heart disease ranged from 7 to 48 years [24]. The physiological effect of stress as explained in the introduction could be the explanatory mechanism, and we believe that a connection has been established, but the true extent of the risk still needs to be verified or adjusted. Of particular interest are the results of the 2004 InterHeart study which surprisingly showed how only smoking and cholesterol were stronger risk factors for development of ischemic heart disease than psycho-social factors, followed by obesity, hypertension, eating habits, exercise, diabetes and alcohol intake [12]. Our findings confirm these results, except for obesity which seems to be protective of mortality one year after hospital discharge.

Lifestyle modification initiatives at the general practitioners, the hospitals and in cardiac rehabilitation must incorporate screening and treatment of depression and anxiety to prevent morbidity and mortality in cardiac patients.

4.1. Strengths and limitations

We succeeded in including many patients across cardiac diagnoses

Table 3
Depression and anxiety as predictors of cardiac risk factors.

	Current smoker	BMI ≥ 30	Alcohol intake above high risk limit[a]	Medicine non-adherence[b]
	OR (95% CI)[c]	OR (95% CI)[c]	OR (95% CI)[c]	OR (95% CI)[c]
HADS-A				
HADS-A < 8	1	1	1	1
HADS-A 8–10	1.06 (0.93–1.21)	1.17 (1.05–1.31)*	1.21 (1.01–1.44)*	1.13 (0.91–1.40)
HADS-A ≥ 11	1.30 (1.14–1.49)*	1.19 (1.06–1.34)*	1.31 (1.08–1.58)*	1.17 (0.93–1.47)
HADS-D				
HADS-D < 8	1	1	1	1
HADS-D 8–10	1.17 (1.01–1.36)*	1.42 (1.26–1.61)*	1.26 (1.03–1.54)*	1.33 (1.14–1.56)*
HADS-D ≥ 11	1.45 (1.22–1.72)*	1.37 (1.18–1.60)*	1.24 (0.96–1.60)	1.34 (1.09–1.64)*

BMI = body mass index; HADS-A = Hospital Anxiety and Depression Scale – Anxiety; HADS-D = Hospital Anxiety and Depression Scale – Depression; OR = odds ratio; CI = confidence interval.
[a] The Danish Health Authority defines the high-risk limit for alcohol consumption as a weekly intake of > 21 standard drinks for men and > 14 standard drinks for women.
[b] Medication non-adherence is defined as forgetting to take prescribed medication more than once a week. Patients who did not take any medication are excluded from this analysis.
[c] Logistic regression adjusted for age, sex, marital status, educational level, Tu co-morbidity index score and diagnostic group.
* Significance level set at 0.05.

Table 4
Hazard ratio (HR) and population attributable risk percent (PAR%) for one-year, all-cause mortality risk factors.

	Deaths (%)	Prevalence (exposure)	Crude[1]			Adjusted for all potential risk factors displayed in the table + age and sex[1]			No. of respondents
			HR	95% CI	PAR%	HR	95% CI	PAR%	
HADS-D > 11	162 (6.2)	19.1	2.90	(2.37–3.55)	12.5	2.21	(1.66–2.95)	10.5	13,758
Ever smoker	302 (3.2)	67.9	1.55	(1.23–1.96)	24.1	1.13	(0.85–1.48)	7.8	13,812
HADS-A > 11	166 (3.9)	31.5	1.91	(1.56–2.34)	15.0	1.30	(0.98–1.73)	7.3	13,656
Hypertension	212 (4.3)	35.1	1.46	(1.20–1.77)	11.1	1.12	(0.87–1.45)	3.8	14,219
Ischemic heart disease	227 (3.8)	42.5	1.31	(1.08–1.58)	10.1	1.21	(0.94–1.56)	7.4	14,219
Diabetes	94 (5.1)	13.0	1.87	(1.48–2.36)	6.0	1.56	(1.15–2.11)	4.7	14,219
COPD	71 (7.5)	6.6	2.42	(1.87–3.13)	3.9	1.93	(1.38–2.68)	3.2	14,219
BMI ≥ 30	81 (2.5)	24.4	1.07	(0.83–1.37)	1.6	0.85	(0.63–1.14)	−4.3	13,230
High alcohol intake	31 (3.1)	7.9	1.22	(0.84–1.74)	1.4	1.36	(0.92–2.01)	2.1	12,894

from the five national Heart Centres in Denmark. Furthermore, we included both psycho-social and more traditional cardiac risk factors in the data analyses.

Patients who were too ill or did not speak or understand Danish were excluded. As the most severely ill patients were non-responders the responding patients may not have been entirely representative of the total target population. Also, mortality was higher in non-responders [9].

Data from the national registers were used. The National Patient Register is known internationally to be the most complete of its kind [20].

Self-reported data are not objective and consequently, bias may exist. In self-reporting of e.g. physical activity, alcohol consumption and weight, social desirability bias can occur, as respondents answer according to what they believe is socially acceptable [28, 29].

The most critically ill cardiac patients in Denmark are treated at the five Heart Centres. In 47 regional or local hospitals cardiac patients are treated medically for e.g. hypertension and heart failure. These patients were underrepresented in the DenHeart study.

The study lacks data on duration of symptoms of depression and anxiety and data on comorbid psychiatric diagnoses which could affect early mortality. Furthermore, the study does not offer a complete overview of all risk factors.

In previous national health surveys, we experienced that age and socio-economic situation play an important role for non-response. Likewise, regional differences of about 15% in response rates have been found [18, 30]. This study was carried out in Denmark and while international treatment guidelines are implemented, variances may exist internationally within cardiac care as well as culture and social behaviour. The patients admitted to the Heart Centres are often elderly and severely ill, which may influence the response rate. In general, studies presenting PROs often have a lower response rate than other studies [29].

5. Conclusion

Symptoms of depression and anxiety are associated with cardiac risk factors such as smoking, obesity, excessive alcohol consumption and medication non-adherence. Depression and anxiety seem to have high attributable risk associated with mortality after one year, comparable to other known risk factors, smoking and ischemic heart disease. This might be partly moderated by risk behaviour.

5.1. Perspective

Future research should look further into the causative mechanisms linking depression and anxiety to poor outcomes in cardiac patients both from a biological and behavioural perspective. Recent theory suggests that stress-response such as anxiety is constantly there but then if safety is perceived, the stress response is under tonic prefrontal inhibition, reflected by e.g. high heart rate variability. Doubt of safety can lead to disinhibiting the default stress response, also in the absence of a real threat. If a person doesn't know how to recognize safety patterns, general insecurity arises resulting in anxiety and the somatic health risks [31]. This might explain why so many cardiac patients suffer from anxiety, even a long time after an actual threat existed. They have not learned to recognize safety patterns. Furthermore, their heart disease and likely poor fitness due to an unhealthy lifestyle could affect their capability to deal with stressors. Challenges are perceived to be somewhat more difficult and are overestimated in acknowledgement of a sick body [31]. Future research should investigate these phenomena in more detail. Depression and anxiety are linked to mortality and must be taken seriously and treated if they persist after a period of normal recovery e.g. 6–8 weeks after a cardiac event. Non-pharmacological interventions based on cognition seem an option [32] and are currently being tested further [33].

In the DenHeart study a pre-specified protocol is followed and future papers will report on the PROs as predictors of readmission, costs and labour market affiliation.

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Conflicts of interest

None.

Contributors

SKB conceived the idea for the study. All designed the study. KJ and OE performed the statistical analyses. SKB wrote the first draft of the manuscript. All revised the manuscript critically. All have given their final approval of the version to be published.

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