



Patient-reported outcomes, sociodemographic and clinical factors are associated with 1-year mortality in patients with ischemic heart disease—findings from the DenHeart cohort study

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Abstract

Purpose In patients with ischemic heart disease, the objectives were (1) to explore associations between patient-reported outcomes, sociodemographic, and clinical factors at discharge and 1-year all-cause mortality and (2) to investigate the discriminant predictive performance of the applied patient-reported outcome instruments on 1-year all-cause mortality.

Methods Data from the Danish national DenHeart cohort study were used. Eligible patients ($n = 13,476$) were invited to complete a questionnaire-package, of which 7167 (53%) responded. Questionnaires included the 12-item Short form health survey (SF-12), Hospital anxiety and depression scale (HADS), EQ-5D, HeartQoL, Edmonton symptom assessment scale (ESAS), and ancillary questions on, e.g., social support. Clinical and demographic characteristics were obtained from registers, as were data on mortality. Comparative analyses were used to investigate differences in patient-reported outcomes. Mortality associations were explored using multifactorially adjusted Cox regression analyses. Predictive performance was analyzed using receiver operating characteristics (ROC).

Results Patient-reported outcomes at discharge differed among those alive versus those deceased at one year, e.g., depression (HADS-Depression ≥ 8) 19% vs. 44% ($p < 0.001$). Associations with 1-year mortality included feeling unsafe about returning home from the hospital; hazard ratio (HR) 2.07 (95% CI 1.2–3.61); high comorbidity level, HR 3.6 (95% CI 2.7–4.8); and being unmarried, HR 1.60 (95% CI 1.33–1.93). Best predictive performance was observed for SF-12 physical component summary (Area under the curve (AUC) 0.706).

Conclusion Patient-reported health, sociodemographic, and clinical factors are associated with 1-year mortality. We propose systematic screening with robust predictive tools to identify patients at risk and healthcare initiatives to explore and offer effective treatment to modify patient-reported health indicators.

Keywords Coronary artery disease (MeSH) · Myocardial ischemia (MeSH) · Patient-reported outcome measures (MeSH) · ROC curve (MeSH) · Mortality (MeSH) · Surveys and questionnaires (MeSH)

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Plain English summary

Ischemic heart disease is the most common heart disease and a leading cause of death globally. Patients' own view of their physical and emotional health is known to be a reliable indicator of their risk of dying. Studies are still needed to identify which patient-rated health factors are the most important and which questionnaires, measuring these factors, are the strongest to predict mortality. In our study, roughly 7000 patients responded to questionnaires about their health-related quality of life, physical symptoms, and emotional distress. After one year, we collected information on mortality and combined the data. We found that some of the most important factors in predicting death within the first year were symptoms of depression, having other illnesses and feeling unsafe about returning home from the hospital. The results can be used to develop a questionnaire-package with the ability to identify those patients at risk of dying with high precision. Health care providers can not only use this information to allocate extra resources to these patients but also use the questionnaire data to address relevant physical and emotional problems that traditional health assessments do not reveal.

Introduction

Ischemic heart disease is a leading cause of death globally and in Europe alone responsible for roughly 20% of all deaths yearly [1, 2]. Even though incidence and mortality rates have decreased in middle- and high-income countries, mortality risk remains high for patients with a poor cardiac risk factor profile [1]. Compiling evidence has shown that patients' self-reported physical and psycho-emotional health, in addition to more well-known clinical and health behavior risk factors, are important components in risk factor profile assessment [1, 3].

Evidence supporting the prognostic relevance of patient-reported outcomes have consistently demonstrated their association with serious adverse outcomes, including mortality [4–11]. Depression, in particular, has been strongly linked to mortality in patients with coronary artery disease, and a large meta-analysis found a 32% increased mortality risk for those with depressive symptoms, and a recent large study found a two-fold mortality risk for those diagnosed with depression [10, 11]. Health-related quality of life, anxiety, and symptom burden are other patient-reported outcomes that have been found to be associated with mortality, although the current evidence is not consistent [4–9]. In previous DenHeart research, we found a more than threefold risk of 1-year mortality for

those with symptoms of depression and a 76% increased risk for those with anxiety symptoms among patients with ischemic heart disease [5].

Identifying poor physical and psycho-emotional health requires insight into the patients' perceptions of their health, and high-quality patient-reported outcome measures can be used as tools to gain and quantify this insight [12]. The need for applying such measures in cardiovascular research, as well as in clinical practice, has been highlighted in European as well as American position papers [12–14]. Future work, however, is needed to solidify the prognostic value of patient-reported outcomes and to identify which patient-reported outcomes are the most predictive on mortality. Published literature investigating patient-reported health and mortality in patients with ischemic heart disease often report on small, selected patient populations, and studies exploring the predictive effect of various patient-reported outcome measures on mortality are lacking.

Objectives

The objectives of this study in patients with ischemic heart disease were (1) to investigate the associations between patient-reported outcomes including social support, disease management, and health behavior, as well as sociodemographic and clinical factors at discharge and 1-year all-cause mortality and (2) to investigate the predictive performance of the applied patient-reported outcome measures on mortality.

Methods

Study design

Data for this study were derived from the Danish national DenHeart study which is a cohort study including data from a questionnaire survey linked with complete baseline and follow-up register data. The published study protocol describes the design and methods in detail [15] and a brief overview is presented in the following.

Setting and participants

All patients discharged or transferred from a Danish heart center, between April 2013 and April 2014, were invited to participate in the survey. The questionnaire consisted of six standardized patient-reported outcome measures and 16 ancillary questions. The 80-item questionnaire took on average 20 min to complete. The patient's assigned staff nurse assessed the patient's eligibility for inclusion and either recruited the patient or noted the appropriate exclusion criteria. Patients were invited to either complete the questionnaire and return it before discharge or at home within three

days following discharge. Patients transferred to another hospital were asked to complete the questionnaire at final discharge or within the following three days. Patients were excluded if they were younger than 18 years old, did not have a Danish civil registration number, or were considered incapable of reporting patient-reported outcomes (i.e., due to physical, cognitive, or linguistic impairment). The current study uses data only on patients with ischemic heart disease as an action diagnosis based on the International classification of diseases 10 (ICD-10) codes: I20–I25. The sample was divided into three subgroups: (1) IHD/AP subgroup: diagnoses reflecting chronic ischemic heart disease and stable angina (ICD-10: I20.1–I20.9, I24–I25); (2) non-STEMI/UAP subgroup: non-ST-elevation myocardial infarction and unstable angina (ICD-10: I20.0, I21.4–I21.9); and (3) STEMI subgroup: ST-elevation myocardial infarction (ICD-10: I21.0, I21.1, and I21.3). One-year follow-up data on all patients were collected retrospectively via national registers.

Variables, data sources, and measurements

Register data

Sociodemographic and clinical characteristics were obtained on all patients from the following national registers: the Danish national patient register [16], the Danish civil registration system [17], and the Danish Education Register [18]. Data included sex, age, marital status, length of hospital stay, educational level, and comorbidities. Comorbidities were collected 10 years back and were used for the calculation of the Tu comorbidity index score [19] excluding the DenHeart index admission. The score includes the following comorbidities: arrhythmia, cardiogenic shock, congestive heart failure, pulmonary edema, malignancy, diabetes, cerebrovascular diseases, chronic obstructive pulmonary disease, and acute and chronic renal failure. All diagnoses are weighed equally [19]. Education was categorized into three levels: (1) Basic (primary school); (2) medium (high school and vocational training); or (3) higher level (short-, medium-, and long-term higher education or research education). Comorbidity levels were divided into three categories using the Tu comorbidity index scores: (1) 0 for none; (2) 1–2 for moderate level; and (3) 3+ for high level.

Patient-reported outcome measures

In the current study, we used five of the standardized questionnaires and nine ancillary questions from the DenHeart survey. These were chosen to provide an overall reflection of the patient's physical and mental health, and all are outcomes that have been reported as influencing health outcomes. The standardized questionnaires are described briefly below.

The 12-item Short form health survey (SF-12) is a generic measure of self-rated health that can be amassed into a Physical component summary (PCS) and Mental component summary (MCS). Higher scores indicate better perceived health status [20]. Estimated minimal clinically important differences (MCIDs) of 3 and 2 points for the PCS and MCS, respectively, have been proposed [21].

The Hospital anxiety and depression scale (HADS) is a 14-item scale, offering two subscales measuring symptoms of anxiety (HADS-A) and symptoms of depression (HADS-D) [22]. Scores range from 0 to 21 and a score of eight or above indicates the possible presence of a mood disorder [22]. Proposed MCID is 1.7 points for both HADS subscales [23].

The EQ-5D-5L measures current health status [24]. It covers five dimensions including mobility, self-care, usual activities, pain/discomfort, and anxiety and depression rated on a five-point scale. A Visual analogue scale (VAS) is also included, ranging from 0 to 100 of self-perceived health with endpoints labeled as 'best imaginable health state' and 'worst imaginable health state.' Scores can be calculated into a summarized score for the five dimensions (EQ-5D index score) and a VAS score (EQ-5D VAS). Higher scores indicate better perceived health state [24]. For the EQ-5D index and VAS scores, suggested MCIDs are 0.051 and 6.9 points, respectively [25].

The HeartQoL is a heart disease-specific questionnaire developed in patients with ischemic heart disease measuring cardiac health-related quality of life [26]. The 14-item scale provides an overall global score (HeartQoL global), a 10-item physical subscale score (HeartQoL physical), and a 4-item emotional subscale score (HeartQoL emotional). Scores range from 0 to 3, with 3 indicating the best cardiac health-related quality of life [26]. A MCID estimate for the HeartQoL subscales is proposed as 0.35 point [27].

The Edmonton symptom assessment scale (ESAS) allows patients to rate their symptoms on a 10-point numeric rating scale [28]. The nine symptoms included are pain, fatigue, nausea, drowsiness, appetite, dyspnea, depression, anxiety, and well-being, and scores can be summarized into the ESAS distress score. Higher scores indicate the presence and intensity of symptoms [28]. We report the summary score and the individual symptoms fatigue and dyspnea in this study. For the ESAS, MCID estimates are suggested to be four points for the total score and one point for the individual symptom scores [29].

All instruments have been validated in patients with coronary artery disease [26, 30], except the ESAS [29]. All have been shown to be valid and reliable with internal consistency of scales/subscales exceeding an acceptable Cronbach's alpha suggested as 0.70 [30, 31]. Additional information on the applied instruments including information on validity, reliability, and minimal important differences have been

described elsewhere [15, 32]. Standardized patient-reported outcome measures were analyzed as continuous variables except the HADS which was dichotomized using the proposed cut-off score of ≥ 8 .

Ancillary questions included the following: two questions reflecting social support (*Does it ever happen that you are alone, even though you want to be with others?*, and *Do you have someone to talk to if you have problems or need support?*); two questions reflecting disease management (*Do you feel safe about returning home from the hospital?*, and *Do you know which symptoms should elicit contact to health care after your discharge?*); and finally, four questions reflecting health behavior, height and weight, smoking, alcohol consumption, and physical activity. Questions reflecting social support and health behavior were derived from the Danish National Health Survey [33] and questions on disease management from the Danish national survey of patient experiences [34].

Data from the questionnaire were linked at the individual level with the relevant hospital discharge from the Danish National Patient Register and subsequently with data from other national registers.

Outcomes

One-year follow-up data on all-cause mortality were collected from the Danish civil registration system, which is a nationwide register with none lost to follow-up [17]. Data were collected at least one year following inclusion of the last participant.

Statistical methods

Continuous data are presented as mean and Standard deviation (SD) and categorical data as frequencies and percentages. Baseline characteristics, patient-reported outcomes, and mortality rates were analyzed using descriptive statistics. Differences in time to death among diagnostic subgroups and between survey responders and non-responders were analyzed using the log-rank test and visualized in Kaplan–Meier survival plots.

Associations with 1-year mortality were explored, by firstly analyzing differences in standardized patient-reported outcomes among those alive and those deceased at one year using Student's *t* test for continuous variables and Pearson's Chi-square test for categorical variables. Secondly, self-reported indicators of social support, disease management, and health behavior, as well as sociodemographic and clinical characteristics, and their associations with 1-year mortality were analyzed using Cox proportional hazards models with time to death as the underlying timescale and censoring on death. The assumptions on proportional hazards were assessed and verified. The standardized patient-reported

outcomes were not explored in regression models as these have been reported in a prior DenHeart study [5]. The pre-selected indicator variables tested were chosen based on clinical relevance and prior research. Possible covariates were explored and significant differences among key variables were found between groups alive and deceased (Online resource 1). These were included as adjustment variables to reduce bias from confounding. The preselected indicator variables were tested individually and adjusted for sex, age, marital status, length of hospital stay, educational level, diagnostic subgroup, and the Tu comorbidity index score. Results are reported as hazard ratios (HRs) with 95% confidence intervals (CIs) and visualized in forest plots.

Receiver operating characteristic (ROC) curves with the Area under the curve (AUC) were generated to evaluate the crude discriminant predictive effect of the instruments and their subscales on 1-year mortality. This included the SF-12 PCS and MCS, the HADS-A and HADS-D, the EQ 5D index score and EQ-5D VAS plus the HeartQoL global and ESAS summary score. To allow for comparison, the HADS-A, HADS-D, and ESAS summary scores were reversed before analysis, as these scores indicate a poorer outcome with a high score as opposed to the remaining patient-reported outcomes. In general, an AUC of 0.5 suggests no predictive discrimination and 0.7 to 0.8 is considered acceptable [35].

A *p*-value of less than 0.05 was considered statistically significant. All analyses were done using IBM SPSS version 25.

Results

Participants

A total of 34,564 patients were discharged or transferred during the study period, 14,115 (41%) with ischemic heart disease. Eligible patients ($n = 13,476$) were invited to complete a questionnaire and 7167 responded (53%) (Fig. 1). The total sample consisted of 70% males, mean age was 66 years, SD 11, and 61% were married (Table 1). Looking into subgroups, more STEMI patients were male, younger and unmarried and had the lowest comorbidity of any group with 74% having no comorbidities compared with 57% in the non-STEMI/UAP group and 51% in the chronic IHD/AP group (Table 1). Baseline characteristics by responder group are presented as supplementary data (Online resource 2).

Descriptive data

Table 2 presents the patient-reported outcomes in patients alive and patients deceased at 1-year follow-up. Missing data in summary scores were 19% for the SF-12 but did not

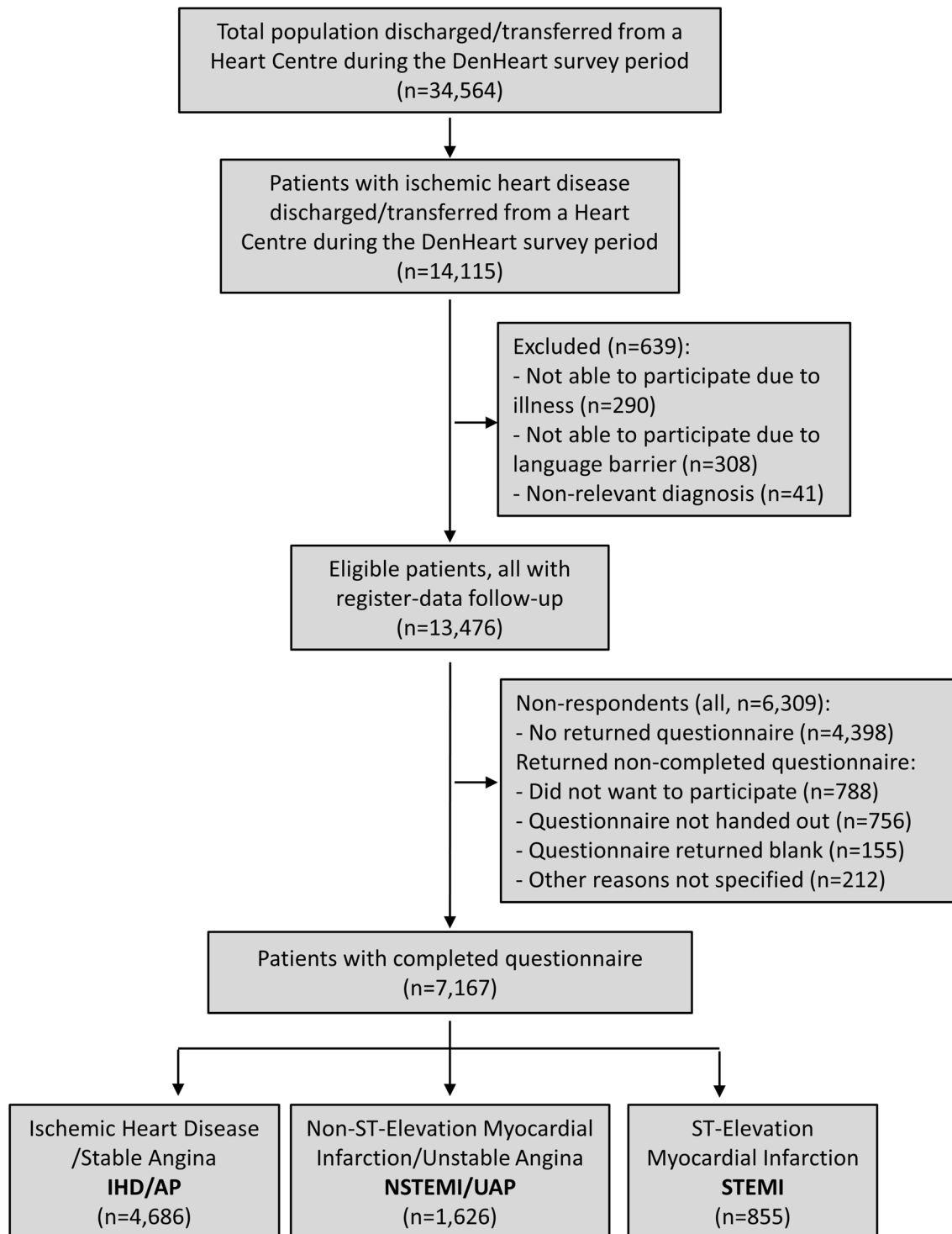


Fig. 1 Patient flow-chart

exceed 5% for the remainder of the patient-reported outcome measures.

Scores for patients deceased at one year were significantly worse for all standardized patient-reported outcomes except the proportion of patients with a HADS-anxiety score ≥ 8 .

Lack of social support and poor disease management was significantly more prevalent in the deceased compared with alive patients at 1-year follow-up except for ‘not knowing whom to contact with questions about disease treatment.’ No associations were observed with the different indicators of

Table 1 Sociodemographic and clinical characteristics

	Total population	IHD/AP	NSTEMI/UAP	STEMI
N	13,476	7764	3722	1990
Male, <i>n</i> (%)	9446 (70)	5407 (70)	2547 (68)	1492 (75)
Age, <i>years</i> , mean (SD)	66 (11)	66 (10)	66 (12)	63 (13)
Married, <i>n</i> (%)	8253 (61)	4876 (63)	2240 (60)	1137 (57)
Length of hospital stay, <i>days</i> , mean (SD)	2.0 (2.8)	1.8 (2.5)	2.1 (3.4)	2.5 (2.4)
Educational level, <i>n</i> (%)				
Basic school	5583 (43)	3196 (42)	1569 (44)	818 (43)
Upper secondary or vocational school	4953 (38)	2858 (38)	1351 (38)	744 (39)
Higher education	2510 (19)	1487 (20)	674 (19)	349 (18)
No information	430 (3)	223 (3)	128 (3)	79 (4)
Tu co-morbidity index score ^a , <i>n</i> (%)				
0	7561 (56)	3969 (51)	2126 (57)	1466 (74)
1–2	5058 (38)	3220 (42)	1352 (36)	486 (24)
3+	857 (6)	575 (7)	244 (7)	38 (2)
Co-morbidities, <i>n</i> (%)				
Hypertension	4936 (37)	3315 (43)	1251 (34)	370 (19)
Diabetes	2132 (16)	1418 (18)	546 (15)	167 (8)
Heart failure	1511 (11)	1063 (14)	383 (10)	65 (3)
Chronic obstructive pulmonary disease	1309 (10)	797 (10)	384 (10)	128 (6)

IHD ischemic heart disease, AP angina pectoris, NSTEMI Non-ST-segment elevation myocardial infarction, UAP unstable angina pectoris, STEMI ST-segment elevation myocardial infarction, SD standard deviation

^aTu co-morbidity score is an index score calculating the rate of co-morbidity based on predefined diagnoses. Comorbidities are calculated ten years back excluding index admission

health behavior, with the exception of poor physical fitness level (Table 2).

The overall 1-year mortality for the sample was 4% but varied among diagnostic subgroups with the lowest mortality rate of 3% in the chronic IHD/AP group and 6% in both the non-STEMI/UAP and the STEMI groups. The rates also varied between responders and non-responders with a mortality rate of 2% among responders and 7% among non-responders. Significant differences in time to death were identified both among diagnostic subgroups and responder groups (Fig. 2a and b).

Outcome data

Figure 3a depicts associations with 1-year mortality among selected self-reported indicators of social support, disease management, and health behavior. Associations with 1-year mortality included poor physical fitness level, HR 2.23 (95% CI 1.56–3.17); feeling unsafe about returning home from the hospital, HR 2.07 (95% CI 1.18–3.61); and feeling alone occasionally or frequently, HR 1.63 (95% CI 1.12–2.37) (Fig. 3a). Among selected clinical and sociodemographic variables in the total population, depicted in Fig. 3b, associations were high comorbidity level score three and above, HR 3.6 (95% CI 2.7–4.8); STEMI group, HR 2.9 (95% CI

2.3–3.7); and being unmarried, HR 1.60 (95% CI 1.33–1.93) (Fig. 3b).

The best discriminant performance on 1-year mortality was observed for the SF-12 physical component summary (AUC 0.706), the EQ 5D VAS (AUC 0.666), and the HADS-D (AUC 0.653) (Fig. 4).

Discussion

Key results

In this large unselected population of patients with ischemic heart disease, we found significant differences in patient-reported outcomes between those alive and those deceased at 1-year follow-up. Strong associations with 1-year mortality included feeling unsafe about returning home from hospital, high comorbidity level, and being unmarried. The best discriminant performance was observed for the self-rated physical health and symptoms of depression.

Interpretation

Patient-reported outcomes at discharge were not only statistically significantly different between patients alive and deceased at one year but also exceeded MCIDs for

Table 2 Patient-reported outcomes on self-rated health, symptoms of anxiety and depression, quality of life, symptom distress, social network, disease management, and health behavior by vital status

Responders <i>n</i> = 7167	Alive at follow-up	Deceased at follow-up	<i>p</i> ^a
N (%)	7005	162	
<i>Standardized questionnaires</i>			
SF-12, mean (SD)			
Physical component summary (PCS)	41.78 (10.81)	34.01 (10.86)	<0.001
Mental component summary (MCS)	48.60 (10.77)	44.90 (11.54)	<0.001
HADS			
HADS-Anxiety, mean (SD)	5.90 (4.20)	6.86 (4.81)	0.006
HADS-Anxiety ≥ 8, <i>n</i> (%)	2198 (33)	61 (40)	0.052
HADS-Depression, mean (SD)	4.30 (3.67)	6.54 (4.51)	<0.001
HADS-Depression ≥ 8, <i>n</i> (%)	1298 (19)	67 (44)	<0.001
EQ-5D 5L, mean (SD)			
EQ-5D index score	0.76 (0.15)	0.67 (0.20)	<0.001
EQ-5D VAS	68.84 (19.58)	56.69 (23.23)	<0.001
HeartQoL, mean (SD)			
HeartQoL global	1.75 (0.76)	1.34 (0.78)	<0.001
HeartQoL physical	1.61 (0.85)	1.15 (0.81)	<0.001
HeartQoL emotional	2.10 (0.83)	1.85 (0.94)	<0.001
ESAS, mean (SD)			
ESAS summary score	20.41 (16.73)	27.91 (18.76)	<0.001
Fatigue	4.02 (2.90)	5.03 (3.00)	<0.001
Dyspnea	2.60 (2.64)	3.61 (3.02)	<0.001
<i>Ancillary questions</i>			
Social support, <i>n</i> (%)			
Feeling alone “sometimes or often”	1793 (26)	59 (39)	<0.001
“Never or almost never” having someone to talk to about problems or in need of support	275 (4)	15 (10)	0.001
Disease management, <i>n</i> (%)			
“Feeling unsafe or very unsafe” about returning home after hospitalization	318 (5)	18 (12)	<0.001
Not knowing what symptoms should elicit contact to GP or hospital	474 (7)	19 (13)	0.028
Not knowing whom to contact with questions about disease/treatment	386 (6)	9 (6)	0.962
Health behavior, <i>n</i> (%)			
Body mass index (BMI) ≥ 30	1697 (26)	32 (24)	0.706
“Less good/poor” physical fitness level	2293 (33)	89 (59)	<0.001
Current smoker	1039 (15)	21 (14)	0.676
Current or ever smoker	4995 (73)	115 (77)	0.349
Alcohol intake above high-risk limit ^b	532 (8)	11 (8)	0.928

SF-12 medical outcome scale short form-12, HADS hospital anxiety and depression scale, EQ-5D EuroQoL 5 dimensions 5 levels, ESAS Edmonton symptom assessment scale

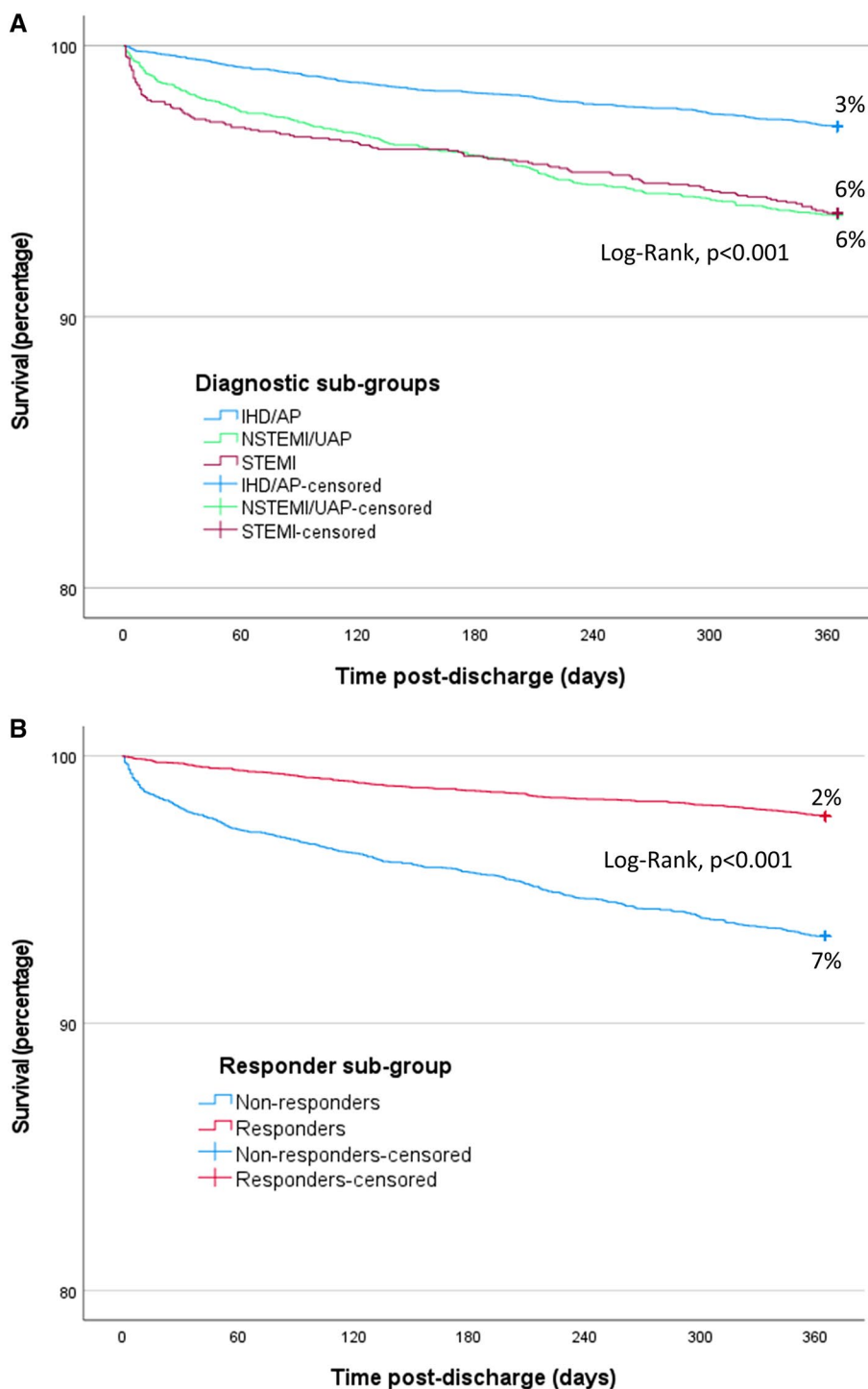
^aDifferences between groups were tested using Students *t* test for continuous variables and Pearson χ^2 test for categorical variables. Significance level, *p* < 0.05

^bThe Danish Health Authority defined the high-risk limit for alcohol consumption as a weekly intake exceeding 21 units for men and 14 units for women at the point of inclusion

most scores. These included MCS and PCS (mental and physical health) of the SF-12; HADS-D (symptoms of depression); EQ-5D index and VAS scores (health status); HeartQoL global and physical subscales (disease-specific global and physical quality of life); and the ESAS total, fatigue, and dyspnea symptom scores. The HADS-A

(symptoms of anxiety) and HeartQoL emotional (disease-specific emotional quality of life) did not exceed suggested MCIDs. Using MCIDs as a tool to interpret results might give an indication of the clinical relevance of a result. This is particularly relevant when working with patient-reported outcomes where a statistically significant scale

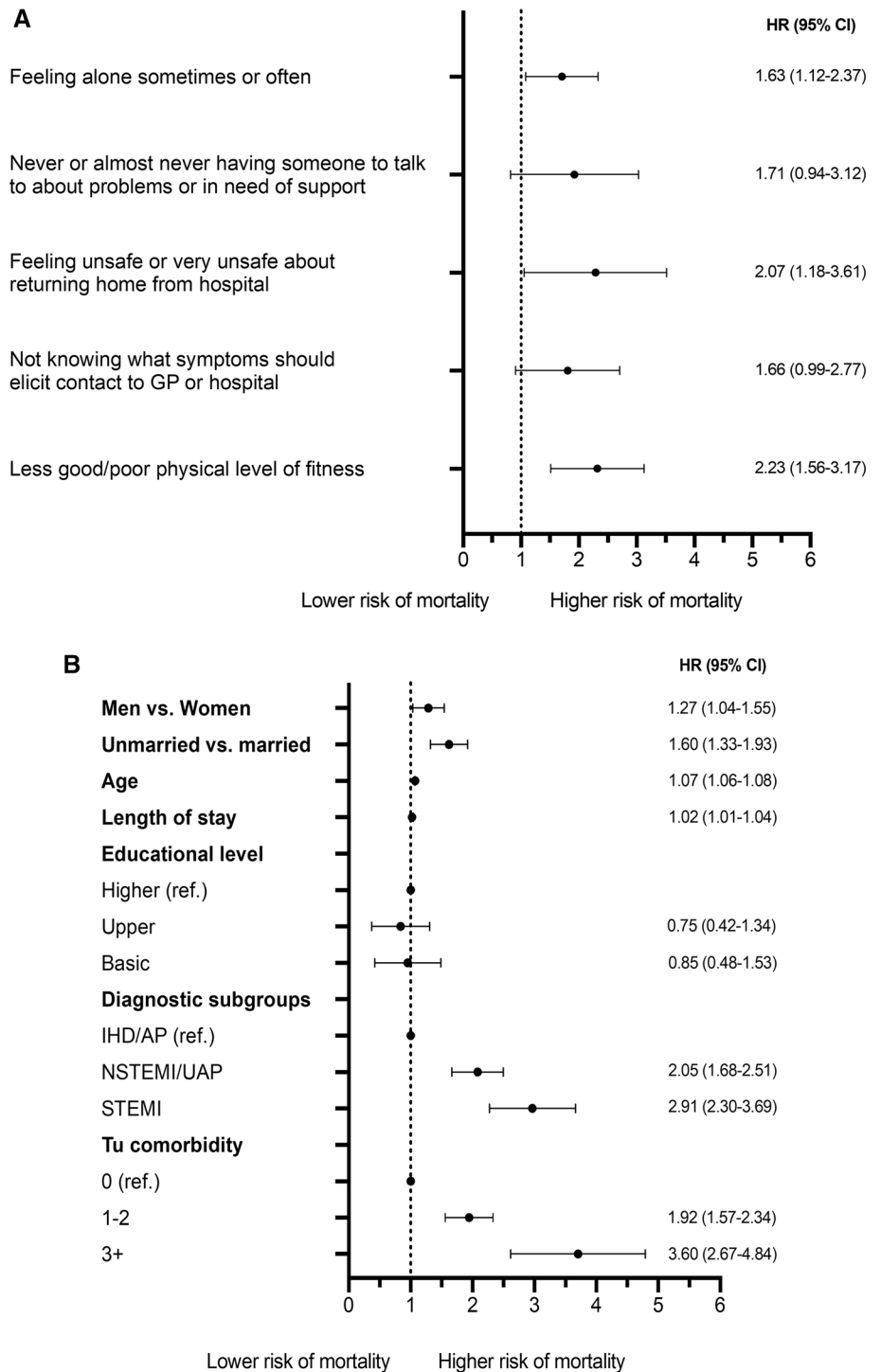
Fig. 2 Kaplan–Meier survival curves—**a** Diagnostic sub-groups and **b** Survey responder groups (Total population, $n = 13,476$)



score difference may, in fact, make no real difference to the patients or clinicians. The validity of a MCID is thus important, and a review has highlighted that multiple methods are applied in estimating MCIDs leading to different results [36]. Researchers should take this into account and consider the method and context in which the estimates have been produced and how this relates to the conclusions of their own work.

Our findings are generally in line with previous research, adding to the compiling evidence of a strong link between poor patient-reported health indicators and mortality, particularly convincing for depression [4–11]. Nonetheless, mental health still seems to go unrecognized and under-treated in cardiac patients [37], and the recent cardiovascular disease statistics from the European Society of Cardiology state that although psychological and social factors are well

Fig. 3 Associations with 1-year mortality—**a** Among self-reported indicators of social support, disease management, and health behavior (Responders, $n = 7167$) and **b** among selected clinical and sociodemographic variables (Total population, $n = 13,476$). Indicator variables were tested individually and adjusted for sex, age, marital status, length of hospital stay, educational level, diagnostic subgroup, and the Tu comorbidity index score



established as cardiovascular risk factors, they are still not included in standardized assessment [1].

Self-reported indicators of lack of support and poor disease management were also, for the most part, significantly different among alive and deceased. Remarkably, self-reported indicators of health behavior covering more conventional cardiac risk factors such as obesity and smoking revealed no difference, except for poor physical fitness

levels. Responses about health behavior at hospital discharge following a cardiac event may inaccurately reflect prior health behavior, and these factors are also known to be prone to social desirability bias [13], which may explain why the expected differences are not found. Even so, obesity, excessive alcohol use, and particularly smoking are well-established cardiac risk factors [3], although perhaps getting a disproportionate amount of attention compared with

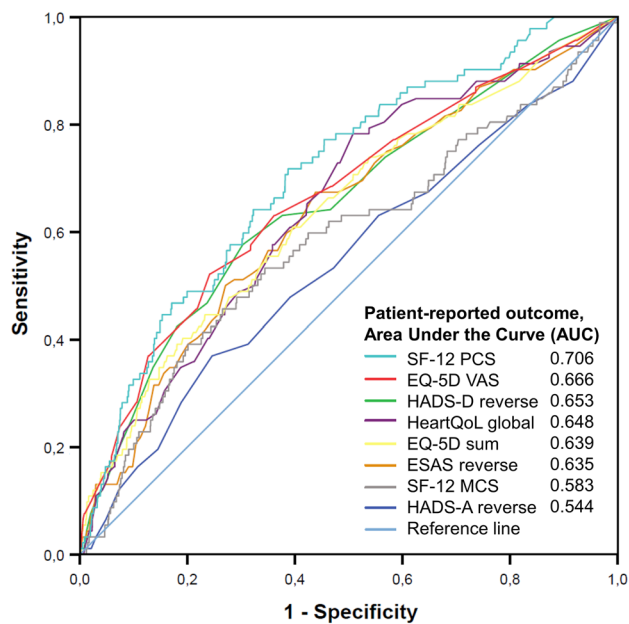


Fig. 4 Receiver operating characteristic (ROC) curves of included patient-reported outcome measures (Responders, $n = 7167$)

psychological and social factors that may warrant a much higher priority. In 2004, the large international INTERHEART study identified nine risk factors associated with incident myocardial infarction, and looking at the population attributable risks, they identified psychosocial factors as the third most attributable risk factor, only superseded by hypercholesterolemia and smoking and succeeded by more traditional risk factors, such as obesity, exercise, and alcohol intake [3] that are all factors traditionally intervened upon. Concordantly, previous DenHeart research found the three strongest population attributable risk factors of 1-year mortality, in a mixed population with cardiac disease, to be symptoms of depression, smoking, and anxiety [38]. The same study found that both anxiety and depression were associated with cardiac risk behavior including smoking, excessive eating, excessive alcohol consumption, and medication non-adherence, thus underpinning the close biobehavioral relationship between poor mental health and cardiac risk factors and, presumably, the causative mechanisms behind poor mental health and mortality risk [38]. Jointly, these findings bring into question whether it might be more appropriate to intervene upon psychological and social factors to not only alleviate the related distress and suffering for patients but also to reduce the increased risk of poor outcomes that are associated both directly and indirectly via the harmful health behavior choices these patients may make.

Looking at associations with 1-year mortality among clinical and sociodemographic variables, most results were in concordance with previous research [5], except for lower educational level not being associated with mortality, which

is in contrast to other research in this area [39], however coincides with prior DenHeart findings [40]. Being unmarried was associated with 1-year mortality which was supported by our supplementary data, where 62% in the alive group were married compared to 46% in the deceased group (Online resource 1). Feeling lonely and feeling unsafe about returning home from the hospital were also associated with 1-year mortality, which are both presumably linked to living alone and having little or no social support. Living alone has consistently been found to be linked to the progression of cardiovascular disease as well as increased morbidity and mortality [41]. Interestingly, our prior DenHeart research found that feeling lonely was more predictive of poor outcomes than living alone and women who felt lonely had an almost three-fold mortality risk and men who felt lonely a two-fold mortality risk, whereas living alone only predicted 1-year mortality in men with a 34% increased risk [42].

In this study, we also explored the discriminant predictive effect of the instruments applied in order to provide insight into what measures might be most appropriate to include in the prognostic assessment in clinical practice. Physical health, measured by SF-12 PCS, was the only instrument with an acceptable AUC as a predictive tool, which seems apparent considering that poor self-rated physical health is a likely reflection of disease severity, which, in turn, is strongly linked to mortality [43]. Health measured by EQ-5D VAS and depression measured by the HADS-D had values just below the acceptable, however, in light of the substantial supportive evidence behind physical health and depression as linked to mortality [5–7, 9–11]; it seems reasonable that these instruments can offer a reliable predictive indication. Surprisingly, anxiety measured by HADS-A showed the lowest discriminant effect, indicating no discriminant predictive effect. Though several studies, including prior DenHeart research, have found associations between anxiety and mortality [4, 5, 8], the evidence is not consistent [4, 6, 9]. Anxiety is a more transient and variable state and presumably associations depend heavily on the time-point of data collection. DenHeart survey data were collected once at hospital discharge, and it is likely that a proportion of patients reporting symptoms of anxiety at discharge recover in the months following. Although an association can be demonstrated, the discriminant predictive effect may still be weak. This indicates that associations found in regression analysis may not be sufficient to conclude that an instrument will be able to predict an outcome. Further exploration within subgroups is also needed, as it is known that reporting varies substantially according to, for instance, sex and age. Thus, much more methodological work is needed to be able to include patient-reported outcomes in predictor models along with other relevant prognostic factors to accurately assess risk for each individual patient. Although the predictive performance of HADS-A was poor, it is

important to acknowledge that anxiety as a permanent condition is agonizing for patients and has been linked to harmful health behavior and adverse outcomes [5, 36]. In a large study of patients with coronary heart disease, Moser and colleagues found that symptoms of anxiety measured at two time-points, and thus considered persistent, independently predicted morbidity and mortality, thus concluding that for anxiety to be a valid prognostic tool, it should be measured at multiple time-points [44]. More work is needed to explore when and how to screen for anxiety in order to detect those patients at risk who may benefit from treatment.

The health issues that patient-reported outcomes are indicative of are multiple and complex and require equally multifaceted and perhaps complex interventions. Cardiac rehabilitation has consistently been proven effective in improving particularly physical health and quality of life [45]. Though the term quality of life is commonly used in healthcare research, and is highlighted as an important patient outcome [1, 2], it has been argued for years that the term is being misused [46–48]. The claimed quality of life questionnaires usually measure the patients' self-rated health, and although the term health-related quality of life is still very widely used in an attempt to more appropriately reflect the concept, more recent position papers use the term patient-reported outcome and patient-reported health status [13, 14]. For mental health concerns, the evidence is not robust, however, and approaches such as mindfulness and cognitive behavioral therapy have shown promising results and are safe and relatively inexpensive [49–51]. Lack of social support is arguably a societal problem in many high-income countries, where family structures have changed dramatically over the past century. Offering health care initiatives that can remedy loneliness and lack of support in a long-term and meaningful way for the individual is not feasible. Peer-support and additional attention to the needs and concerns of these patients following discharge are presumably the best we can offer as professionals.

Strengths and limitations

Our study included a large unselected sample of patients with ischemic heart disease. We used validated standardized patient-reported outcome measures, often used in cardiac populations, thus offering estimates that can be used for comparison and as benchmarks. We linked patient-reported data with high-quality register data with none lost to follow-up. These data allowed for the reduction of bias due to confounding factors in adjusted analysis, thus providing robust estimates. Although the DenHeart study aimed to include all patients and efforts were made to increase the response rate and secure complete data, the response rate in the overall study was 53%. Our data showed significant differences among responders and non-responders in baseline variables

as well mortality rates, indicating that the most vulnerable patients were not included in this study. We expect that these non-responders would report worse patient-reported outcomes, thus possibly leading to underestimated results. Although we had access to information on several known confounding factors from registers and self-reported data, additional information about the burden of illness related to previous and current hospitalizations might have strengthened the study. Particularly the chronic IHD/AP group, included at various stages in their illness and with a large variation in the burden of disease, might have been too heterogeneous a group to assess as one. Adjustments in ROC analysis might have given insight into the predictive effect of the isolated instruments; however, we wanted to uncover the prognostic value as it would commonly be used in clinical practice, thus unadjusted. Repeated follow-up patient-reported outcome assessment could potentially have given insight into how these might evolve over time and have widened the perspective on the self-perceived illness trajectory. Not all patient-reported outcomes were validated in patients with ischemic heart disease, thus questioning the validity of results related to these. Also, not all MCID estimates were produced in cardiac patients; thus, interpretation should be considered indicative rather than conclusive. Multiple testing and mass-significance are potentially a problem in this study. The Bonferroni correction methods could have been applied to counteract this problem. Exploratory analysis, however, should always be interpreted with caution and be regarded as hypothesis-generating rather conclusive. Thus, the P values reported are uncorrected.

Conclusion

Patient-reported health status, symptoms of anxiety and depression, symptom burden, and disease-specific quality of life were expectedly and significantly different at discharge among patients alive versus patients deceased one year following. Strongest associations with 1-year all-cause mortality were high comorbidity, STEMI, poor physical fitness level, and feeling unsafe about returning home from the hospital. Predictive discriminant performance estimates of the patient-reported outcome instruments on mortality showed self-rated physical health (SF-12 PCS) to be a robust predictive tool, and probably also health status (EQ-5D VAS) and symptoms of depression (HADS-D) are acceptable.

The findings may guide clinicians and researchers in choosing appropriate patient-reported outcome measures. We propose systematic screening using robust predictive tools to identify patients at risk and healthcare initiatives to explore and offer effective treatment to modify poor patient-reported health indicators.

Generalizability

The study was carried out in Denmark. Differences among countries in health behavior, socioeconomic status, and healthcare provision are likely to impact public health and mortality in general, and generalizability of results may therefore be limited to similar cultural contexts. Generalizability of results is probably compromised by selection bias as our sample was not completely representative of the target population.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11136-021-02956-5>.

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Author contributions SKB conceived the idea for the DenHeart survey and TBR for the current sub-study. TBR and BB performed the statistical analyses. TBR drafted the manuscript. All co-authors revised the manuscript critically.

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Data availability The data underlying this article will be shared on reasonable request to the corresponding author.

Declarations

Conflict of interest Authors have no competing interests.

Ethical approval The study was approved by the national data protection agency (reg. 2007-58-0015/30-0937). The Danish National Board of Health approved the use of register data (FSEID-01131). The study fully complies with the declaration of Helsinki and was registered at ClinicalTrials.gov (NCT 019-6145) and approved by the institutional boards of the participating heart centers. Surveys are not required by Danish legislation to be approved by humans' ethics committee.

Consent to participate All included patients signed informed consent.

Consent for publication With their informed consent, participants agreed to the publication of results.

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