Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

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Complete List of Authors:	Berg, Selina; Rigshospitalet, Heart Centre Svanholm, Jette; Aarhus University Hospital, Department of Cardiology Lauberg, Astrid; Aalborg University Hospital, Department of Cardoilogy and Department of Cardiothoracic Surgery Borregaard, Britt; Odense University Hospital, Department of Thoracic, Cardiac and Vascular Surgery Herning, Margrethe; Gentofte Hospital, Department of Cardiology Mygind, Anna; Aarhus University Hospital, Department of Cardiology Christensen, Anne; Rigshospitalet, Heart Centre Christensen, Anne; National Institute of Public Health, Ekholm, Ola; National Institute of Public Health, Juel, Knud; National Institute of Public Health, Thrysøe, Lars; Odense University Hospital, Department of Cardiology
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Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

Selina Kikkenborg Berg, RN, MScN, Ph.D.[1,2]
Jette Svanholm, RN, MSc, Ph.D.[3]
Astrid Lauberg, RN, MScN[4]
Britt Borregaard, RN, MPQM[5]
Margrethe Herning, RN, MED[2]
Anna Mygind, MSPH, Ph.D.[3]
Anne Vinggaard Christensen, MSPH[1]
Anne Illemann Christensen, MSPH[6]
Ola Ekholm, MSc[6]
Knud Juel, Ph.D.[6]
Lars Thrysøe, RN, MLP, Ph.D.[7]

1. The Heart Centre, Unit 2151, Rigshospitalet, Copenhagen University Hospital Blegdamsvej 9, 2100 Copenhagen, Denmark
2. Department of Cardiology, Gentofte University Hospital, Niels Andersens Vej 65, 2900 Hellerup, Denmark
3. Department of Cardiology, Aarhus University Hospital, Brendstrupgaardsvej 100, 8200 Aarhus N, Denmark
4. Department of Cardiology and Department of Cardiothoracic Surgery, Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg, Denmark
5. Department of Thoracic, Cardiac and Vascular Surgery, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense C, Denmark
6. National Institute of Public Health, University of Southern Denmark, Øster Farimagsgade 5A, 1353 Copenhagen, Denmark
7. Department of Cardiology, Odense University Hospital, University of Southern Denmark, Sdr. Boulevard 29, 5000 Odense C, Denmark

Corresponding author:

Selina Kikkenborg Berg, PhD.
Copenhagen University Hospital, Rigshospitalet
The Heart Centre, unit 2152
Blegdamsvej 9
2100 Copenhagen
Denmark
E-mail: selina@rh.dk
Tel: +45 3545 9526

Abstract

Introduction: Patient reported health status, including symptom burden, functional status and quality of life, is an important measure of health. Differences in health status between diagnostic groups within cardiology have only been sparsely investigated. These outcomes may predict morbidity, mortality, labour market affiliation and health care utilization in various diagnostic groups. A national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population has been designed as the DenHeart survey.

Methods and analysis: DenHeart is designed as a cross-sectional survey with register based follow-up. All diagnostic groups at the five national Heart Centres are included during one year (April 15th 2013 to April 15th 2014) and asked to fill out a questionnaire at hospital discharge. The total eligible population, both responders and non-responders, will be followed in national registers. The following instruments are used: SF-12, HADS, EQ-5D, B-IPQ, HeartQoL and ESAS. The following variables are collected from national registers: action diagnosis, procedures, co-morbidity, length of hospital stay, type of hospitalisation, visits to GP and other agents in primary health care, dispensed prescription medication, vital status, and cause of death. Labour market affiliation, sick leave, early retirement pension, educational degree and income will be collected from registers. Frequency distributions and multiple logistic regression analyses will be used to describe and assess differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors. Cox proportional hazards regression models with age as the time scale will be used to investigate associations between patient reported outcomes at baseline and morbidity/mortality, labour market affiliation and health care utilization after one year.

Ethics and dissemination: The study complies with the Declaration of Helsinki. The study has been approved by the Danish Data Protection Agency: 2007-58-0015/30-0937. Study findings will be disseminated widely through peer reviewed publications and conference presentations.

Trial registration: ClinicalTrials.gov: NCT01926145.

Introduction

Patient reported health status, which includes symptom burden, functional status and quality of life, is an important measure of health. Validated patient health status surveys, including disease specific instruments for patients with cardiovascular disease, allow quantification of critical patient-centred outcomes and additional research is needed to better understand the determinants[1] and the predicting factors of patients' health status. Previous studies suggest an association between heart disease, self-reported health and morbidity and mortality, and that patient reported outcome measures can predict prolonged hospital stay, future quality of life, return to work, morbidity and mortality in cardiac patients.[2-7] Quality of life scores seem to provide important prognostic information independent of traditional clinical data, as higher scores have been associated with longer survival in patients with ventricular arrhythmias and coronary artery disease.[8, 9] However no studies have included all diagnostic groups within cardiology and comparisons among diagnostic groups are lacking. The overall aim of the DenHeart survey is to gain knowledge about patient reported outcome measures regarding health among cardiac patients at hospital discharge. Knowledge about patients' own perception of their health status and predicting factors can help to guide inpatient practice and outpatient follow-up. Furthermore, a survey combined with register data can be used to evaluate differences among diagnostic groups and predicting factors for patient reported outcome measures at hospital discharge and long-term morbidity and mortality. Also, economic analysis of healthcare utilisation and work ability status in a large cohort of cardiac patients is needed. Therefore, the DenHeart study is designed as a national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population.

Objectives

The objectives of the DenHeart study are to describe: (i) differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors and (ii) patient reported outcomes at hospital discharge as a predictor of a) morbidity and mortality, b) labour market affiliation and c) health care utilization after one year.

Methods and analysis

Study design

The DenHeart study is designed as a cross-sectional survey with register based follow-up. All cardiac patients are asked to fill out a questionnaire at hospital discharge to evaluate patient reported outcomes. Furthermore, the total eligible population, both responders and non-responders, will be followed in national registers.

Setting and participants

The five Heart Centres in Denmark are including patients during a one year period, from April 15th 2013 to April 15th 2014. One centre began data collection later, May 1st 2013. Four heart centres have both medical and surgical wards, one centre medical wards only. All cardiac patients discharged or transferred to a local hospital from one of the Heart Centres are potential participants in the study. Patients are unselected and consecutively included at hospital discharge. Included patients are asked to complete and return a questionnaire before they leave the hospital or alternatively to do so at home within 3 days of discharge and return it by mail. Patients who are transferred to another hospital are given the questionnaire at discharge from the Heart Centre and asked to fill it out at the

day of hospital discharge or alternatively to do so at home within 3 days of discharge and then return it by mail.

Eligibility criteria

All diagnostic groups within cardiology are included. Patients with ischemic heart disease (e.g. coronary angiography, percutaneous coronary intervention), heart failure (e.g. coronary artery bypass graft, heart transplantation), arrhythmia (e.g. ablation, labyrinth, pacemaker, implantable cardioverter defibrillator), heart valve disease (e.g. stent, valve replacement), endocarditis and congenital heart disease (e.g. atrium septum defect, patent ductus arteriosus, patent foramen ovale, coarctatio) are diagnosed and treated at the Heart Centres. Infrequent conditions such as thorax-trauma are also included.

Patients under 18 years of age and patients without a Danish civil registration number are excluded from the study. For ethical reasons, patients who are unconscious when transferred are also excluded.

Reasons for non-response are recorded which allows for sub-analyses of these groups. On the front page of the questionnaire there is a box that enables the patient or nurse to tick off the reason for non-response: “Does not wish to participate”, “Not able to participate because of illness”, “Not able to participate because of language barrier”, “Questionnaire not handed out” and “Other”.

Recruitment

Patients are recruited at hospital discharge (the same day or the day before discharge) by the ward nurse in charge of the discharge of the individual patients or by a research nurse. All nurses at the centres, approximately 800, have been informed about the study and procedures at ward meetings, guidelines have been distributed and a website created

(www.DenHeart.dk). When informing patients about the study and handing out the questionnaire, nurses also distribute a postage pre-paid envelope to them to return the questionnaire in, either at the ward or after discharge. No reminders are sent to patients as the time window of three days post discharge makes it impossible. Distribution and return rates are monitored to allow for interventions if the rates drop during data collection.

Data sources/measurement

The following patient reported outcome measures are used: Short-form 12 (SF-12), Hospital Anxiety and Depression Scale (HADS), EQ-5D, Brief Illness Perception Questionnaire (B-IPQ), HeartQoL and Edmonton Symptom Assessment Scale (ESAS).

SF-12: The SF-12 is a 12-item version of the SF-36 and is a brief, reliable measure of overall health. The questionnaire measures eight domains of health: physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health with higher scores indicating better health status. The items cover the previous four weeks and results are expressed in terms of two summary scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS).[10] A Cronbach's alpha of 0.87 and 0.84 for PCS-12 and MCS-12 respectively have been reported in a population of coronary heart disease patients.[11] The SF-12 is a suitable for studies focusing on patient-based assessment of physical and mental health.[10] Furthermore it is used in the National Health Surveys and outcomes can be compared.

HADS: HADS is a 14-item questionnaire that assesses levels of depression and anxiety in medically ill patients. The scale offers two scores, HADS-A and HADS-D, and consists of seven questions to assess anxiety and seven questions to assess depression.[12] 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 0.83 and 0.82 for the HADS-A and HADS-D respectively.[13] Scores of 0 to 7 for either subscale are regarded as normal and scores of 8 to 10 suggest the presence of a mood disorder. Scores of 11 and above indicate the probable presence of a mood disorder.[14]

EQ-5D: The EQ-5D is a standardised instrument for measuring current health status that provides a simple descriptive profile and a single index value that can be used in clinical and economic evaluation of health care and in population health surveys. The questionnaire covers five dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into three levels: no problems, some or moderate problems or extreme problems. The questionnaire consists of a descriptive system produced in a standard layout that enables the respondent to classify his/her health according to the five dimensions and a Visual Analogue Scale that enables the respondent to provide a self-rating of his/her own health. Higher scores indicate better health status.[15] An overall Cronbach's alpha of 0.73 has been found in a population of coronary heart disease patients.[11]

B-IPQ: B-IPQ is a short questionnaire that assesses cognitive and emotional representations of illness on the basis of eight items. The eight items each represent a dimension of the respondent's perception of his or her own illness. Five items assess current cognitive representations of illness: consequences, timeline, personal control, treatment control and identity. Two items assess emotional representations of illness: concern and emotions. The last item assesses illness comprehensibility. A higher score on the B-IPQ reflects a more threatening view of illness. B-IPQ has good test-retest reliability

measured with Pearson correlations and has shown good predictive validity among patients recovering from myocardial infarction.[16]

HeartQoL: HeartQoL is an illness specific questionnaire that measures quality of life (QoL) in cardiac patients. The questionnaire covers the previous four weeks and produces a global score and two subscales. A physical and an emotional scale with higher scores indicating better QoL status. HeartQoL is a new questionnaire developed on the basis of items from three widely used questionnaires for specific groups of cardiac patients (Seattle Angina Questionnaire, MacNew Heart Disease Health-related Quality of Life Questionnaire and Minnesota Living with Heart Failure questionnaire). The questionnaire has proven to be a reliable instrument with a Cronbach's alpha between 0.80-0.91 for the global score and each subscale and to be responsive in patients with a wide spectrum of diagnoses.[17-19]

ESAS: ESAS is a 10 item questionnaire that allows patients to rate their current symptoms on a visual numeric scale. The following symptoms are included: pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, shortness of breath and distress. Higher scores indicate the presence and intensity of the symptoms. ESAS has proven to be a valid instrument to measure cancer patients' self-reported symptoms with an overall Cronbach's alpha of 0.79.[20] However, the scale has not yet been evaluated in cardiac patients.

Besides the validated questionnaires, thirteen questions about health behaviour, sense of security and use of medicines are included in the questionnaire. This amounts to a total of 62 items. The questionnaire was pre-tested for feasibility by 12 (10 male, 2 female) patients aged 52-81 years old (mean 65.9) on medical and surgical wards at three of the

Heart Centres, and the introduction and layout was adjusted afterwards. The questionnaire takes about 20 minutes to complete.

Variables from registers

Because all Danish citizens have a unique personal identification number, linkage between the national registers and other data sources is feasible. Therefore, the Danish registers offer a great number of possibilities for national epidemiological studies.[21]

For the DenHeart study, data are drawn at baseline and follow-up after one year from the following registers:

The Danish Civil Registration System:[22] Gender, age, marital status.

The Danish National Patient Register:[23] Action diagnosis, other diagnoses, procedures, length of hospital stay, type of hospitalisation (acute, heart related, other).

The Danish National Health Service Register:[24] Contact with general practitioners and other agents in primary health care.

Registers on personal labour market affiliation:[25] Labour market affiliation, sick leave, early retirement pension.

Population Education Register:[26] Educational degree.

The Income Statistics Register:[27] Income.

Data handling and record keeping

Questionnaires are mailed from the Heart Centres or from the patients' home to a scanning agency (Express A/S). Questionnaires are scanned and the file delivered to The National Institute of Public Health, University of Southern Denmark and placed on a secure

hard drive. When the data collection is finished, the entire dataset will be reviewed in order to remove ineligible respondents, e.g. pulmonary trauma. Furthermore, the entire population of patients discharged from the Heart Centres during the data collection period will be drawn from the National Patient Register. This will be reviewed in order to remove irrelevant discharges, in accordance with the inclusion criteria.

Data monitoring

In order to monitor trial conduct, reports are continuously delivered from the scanning agency in order to identify the need for adjustments. A data file is delivered every two weeks during the first three months and every month thereafter throughout the entire data collection period. The data file includes a list of received questionnaires ranked by centre and unit, and information on whether the questionnaire has been completed on the front page. The numbers are compared to the number of patients discharged at unit level in the same period. Assessments of response rates are done and adjustments made if needed. Low response rates in a unit will lead to contact with the unit concerned to learn the reason why and actions to increase them. Returned questionnaires will be screened for systematic errors.

Study size

The study size is not derived statistically, as it consists of the total population of patients discharged from the five Heart Centres in the project period. The five Heart Centres diagnose and treat about 45,000 patients per year. These patients are diagnosed with numerous diseases and conditions and the aim is to describe differences, not only among the most common diagnoses but also the infrequent ones. Thus, all patients discharged from national Heart Centres over one year are included in order to secure as high a level of specificity as possible. Furthermore, by including a large number of participants, a

shorter follow-up time is needed. Besides the primary objectives, further ancillary and spin-off analyses will be prepared. Clearly, power calculations cannot be performed prospectively for all potential analyses based on data from the DenHeart study. Moreover, adverse outcomes have very different incident rates.

Response rate

The final response rate is calculated based on discharge data from the National Patient Register. For calculating the actual number of eligible patients, the following are not included: patients without a Danish civil registration number, patients living in Greenland (no register follow-up possible), patients with two admissions within 24 hours, patients deceased in hospital and outpatient visits. Patients admitted for less than 24 hours without a procedure and readmitted with a procedure within one month are counted once.

Patients who have filled out more than one questionnaire during the project period due to repeated hospitalizations will only be counted once (the first questionnaire returned) in the final count of the response rate. The repeated measurements may be included in sub-analyses.

Statistical methods

Objective 1: For each diagnostic group, age (mean), sex distribution and patient reported outcomes at hospital discharge distribution will be reported. Differences between groups will be tested by use of ANOVA tests for continuous variables and chi-squared tests for categorical variables. Multivariate logistic regression will be used to investigate the relationship between diagnostic group and patient reported outcomes when controlling for response date (number of days since hospital discharge), age, sex and other possible

confounders, and in-hospital predicting factors (e.g. procedure, duration of index hospital admission, acute/elective admission, stay at intensive care unit, complications).

Objective 2a: For each diagnostic group, the crude associations between patient reported outcome measures at hospital discharge and all-cause and cardiac morbidity and all-cause and cardiac mortality after one year, will be described and assessed using ANOVA tests for continuous variables and chi-squared tests for categorical variables. In addition, multivariate Cox proportional hazards regression models, with age as the time scale, will be used to examine the associations between patient reported outcome measures at baseline and all-cause morbidity and mortality and cardiac morbidity and mortality when adjusting for response date, sex, co-morbidity and other potential confounding factors at baseline.

Objective 2b: For each diagnostic group, the crude associations between patient reported outcome measures at hospital discharge and labour market affiliation (employment status, sick leave, early retirement pension) after one year will be described and assessed using the ANOVA tests for continuous variables and chi-squared tests for categorical variables. Multivariate Cox proportional hazards regression models, with age as the time scale, will also be carried out to investigate the associations between patient reported outcome measures at baseline and labour market affiliation when adjusting for potential confounding factors (e.g. response date, sex, co-morbidity).

Objective 2c: For each diagnostic group, the crude associations between patient reported outcomes measures at hospital discharge and health care utilization (hospitalizations, contact with general practitioner, medical specialist, and physiotherapist) after one year, will be described and assessed using the ANOVA tests for continuous variables and chi-

squared tests for categorical variables. Multivariate Cox proportional hazards regression models, with age as the time scale, will be used to analyse the association between patient reported outcome measures at baseline and health care utilization when adjusting for potential confounding variables (e.g. response date, sex, co-morbidity).

Weighting

It is possible to link both respondents and non-respondents in the survey on an individual level to different administrative registers. Thus, non-response weights will be computed based on register information (e.g. sex and age) in order to reduce non-response bias. Patients with a low probability of response will be given a higher weight in the analyses to represent the larger number of non-respondents with similar characteristics. Accordingly, patients more likely to respond will be given a lower weight.

Spin-off projects

Several spin-off analyses will be prepared and conducted, e.g. a three year follow up analysis on the primary outcomes, the association between patient reported outcomes at discharge and cardiac events over time, patient reported outcomes and medication compliance and patient reported outcomes as a screening tool in clinical practice. A follow-up survey after two to five years is being considered.

Ethics and dissemination

The study is conducted in accordance with the Declaration of Helsinki. According to Danish legislation, surveys should not be approved by an ethics committee system but only by the Danish Data Protection Agency, no. 2007-58-0015/30-0937. The DenHeart survey is approved by the Institutional Boards of the Heart Centres and registered at ClinicalTrials.gov (NCT01926145).

The National Institute of Public Health stores data from the DenHeart survey. Access to data can only be provided to investigators after approval from the Publication Committee. All study results will be published in international research journals and conference presentations.

Discussion

Study population

The five Heart Centres treat the most critically ill cardiac patients in Denmark. Approximately 47 regional or local hospitals treat cardiac patients medically and care for terminally ill cardiac patients. These patients are underrepresented in the DenHeart study. The patients in this study represent the patients with diagnoses where medical, invasive or surgical treatment is possible, and patients with rare conditions such as heart transplant and congenital heart disease. Furthermore, four of the five Heart Centres have a local hospital function treating all cardiac diagnoses. One surgical unit did not wish to participate in the study.

Patients who are hospitalised several times in the project period will be asked to fill out the questionnaire each time. Repeated measures will only be used in sub-analyses. For reporting of primary outcomes, patients will only be counted once (the first questionnaire returned).

Variables

The majority of the outcome measures included in the questionnaire is comprised of validated and standardised instruments to assess patient reported outcomes, which enhances the validity of the questionnaire. However, in the interpretation of the results, it

must be taken into account that patients with different cardiac conditions differ regarding how much their health status has changed prior to admission to hospital, and that some of the instruments have long recall.

Confounding factors

From previous national health surveys, we know that age and socioeconomic position play a significant role for non-response. Also, regional differences of about 15 % in response rates have been documented.[28, 29] The patients treated at the Heart Centres are often aged and severely ill, which may be reflected in the response rates. This will be accounted for by reporting both actual responses as well as weighted data for the underrepresented groups in the analyses. However, several different initiatives are being conducted by the centres to optimize response rates. Nurses are reminded to hand out the questionnaires at local meetings, by posters in the ward and logo-pens, and response rates are continuously shared with the ward nurses in order to secure motivation among the approximately 800 nurses involved in the distribution of questionnaires. Letters are sent to the local hospitals that receive patients from the Heart Centres asking to remind the patients to fill out the questionnaire at discharge to home. Some centres are mailing questionnaires to patients after discharge when they are not handed out in hospital. As this is a national multicentre study, regional differences in ways to enhance the response rates may occur. All of these different strategies fall within the frame of the DenHeart study and timeframe for responding.

Contributorship

SKB conceived the study. SKB, AVC, MH, LT, BB, JS, AM, AL, AIC, KJ and OE initiated the study design and implementation. KJ, AIC and OE provided statistical expertise in the clinical trial design. All contributed to the refinement of the study protocol.

Funding

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Competing interest

No competing interests have been declared by the authors.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Page 2-3
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses Page 5
Methods		
Study design	4	Present key elements of study design early in the paper Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 5-6
Participants	6	*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants Page 6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Page 7-10
Bias	9	Describe any efforts to address potential sources of bias Page 11, 14, 16
Study size	10	Explain how the study size was arrived at Page 11-12
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Not applicable (analyses not done yet)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

		(*e*) Describe any sensitivity analyses Page 12-14
Results	**No results as this is a research protocol**	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives Not applicable (no results yet)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Not applicable (no results yet)
Generalisability	21	Discuss the generalisability (external validity) of the study results Not applicable (no results yet)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Page 17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

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Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

Selina Kikkenborg Berg, RN, MScN, Ph.D.[1,2]
Jette Svanholm, RN, MSc, Ph.D.[3]
Astrid Lauberg, RN, MScN[4]
Britt Borregaard, RN, MPQM[5]
Margrethe Herning, RN, MED[2]
Anna Mygind, MSPH, Ph.D.[3]
Anne Vinggaard Christensen, MSPH[1]
Anne Illemann Christensen, MSPH[6]
Ola Ekholm, MSc[6]
Knud Juel, Ph.D.[6]
Lars Thrysøe, RN, MLP, Ph.D.[7]

1. The Heart Centre, Unit 2151, Rigshospitalet, Copenhagen University Hospital Blegdamsvej 9, 2100 Copenhagen, Denmark
2. Department of Cardiology, Gentofte University Hospital, Niels Andersens Vej 65, 2900 Hellerup, Denmark
3. Department of Cardiology, Aarhus University Hospital, Brendstrupgaardsvej 100, 8200 Aarhus N, Denmark
4. Department of Cardiology and Department of Cardiothoracic Surgery, Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg, Denmark
5. Department of Thoracic, Cardiac and Vascular Surgery, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense C, Denmark
6. National Institute of Public Health, University of Southern Denmark, Øster Farimagsgade 5A, 1353 Copenhagen, Denmark
7. Department of Cardiology, Odense University Hospital, University of Southern Denmark, Sdr. Boulevard 29, 5000 Odense C, Denmark

Corresponding author:

Selina Kikkenborg Berg, PhD.
Copenhagen University Hospital, Rigshospitalet
The Heart Centre, unit 2152
Blegdamsvej 9
2100 Copenhagen
Denmark
E-mail: selina@rh.dk
Tel: +45 3545 9526

Abstract

Introduction: Patient reported health status, including symptom burden, functional status and quality of life, is an important measure of health. Differences in health status between diagnostic groups within cardiology have only been sparsely investigated. These outcomes may predict morbidity, mortality, labour market affiliation and health care utilization in various diagnostic groups. A national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population has been designed as the DenHeart survey.

Methods and analysis: DenHeart is designed as a cross-sectional survey with register based follow-up. All diagnostic groups at the five national Heart Centres are included during one year (April 15th 2013 to April 15th 2014) and asked to fill out a questionnaire at hospital discharge. The total eligible population, both responders and non-responders, will be followed in national registers. The following instruments are used: SF-12, HADS, EQ-5D, B-IPQ, HeartQoL and ESAS. The following variables are collected from national registers: action diagnosis, procedures, co-morbidity, length of hospital stay, type of hospitalisation, visits to GP and other agents in primary health care, dispensed prescription medication, vital status, and cause of death. Labour market affiliation, sick leave, early retirement pension, educational degree and income will be collected from registers. Frequency distributions and multiple logistic regression analyses will be used to describe and assess differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors. Cox proportional hazards regression models with age as the time scale will be used to investigate associations between patient reported outcomes at baseline and morbidity/mortality, labour market affiliation and health care utilization after one year.

Ethics and dissemination: The study complies with the Declaration of Helsinki. The study has been approved by the Danish Data Protection Agency: 2007-58-0015/30-0937. Study findings will be disseminated widely through peer reviewed publications and conference presentations.

Introduction

Patient reported health status, which includes symptom burden, functional status and quality of life, is an important measure of health. Validated patient health status surveys, including disease specific instruments for patients with cardiovascular disease, allow quantification of critical patient-centred outcomes and additional research is needed to better understand the determinants[1] and the predicting factors of patients' health status. Previous studies suggest an association between heart disease, self-reported health and morbidity and mortality, and that patient reported outcome measures can predict prolonged hospital stay, future quality of life, return to work, morbidity and mortality in cardiac patients.[2-7] Quality of life scores seem to provide important prognostic information independent of traditional clinical data, as higher scores have been associated with longer survival in patients with ventricular arrhythmias and coronary artery disease.[8, 9] However no studies have included all diagnostic groups within cardiology and comparisons among diagnostic groups are lacking. The overall aim of the DenHeart survey is to gain knowledge about patient reported outcome measures regarding health among cardiac patients at hospital discharge. Knowledge about patients' own perception of their health status and predicting factors can help to guide inpatient practice and outpatient follow-up. Furthermore, a survey combined with register data can be used to evaluate differences among diagnostic groups and predicting factors for patient reported outcome measures at hospital discharge and long-term morbidity and mortality. Also, economic analysis of healthcare utilisation and work ability status in a large cohort of cardiac patients is needed. Therefore, the DenHeart study is designed as a national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population.

Objectives

The objectives of the DenHeart study are to describe: (i) differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors and (ii) patient reported outcomes at hospital discharge as a predictor of a) morbidity and mortality, b) labour market affiliation and c) health care utilization after one year.

Methods and analysis

Study design

The DenHeart study is designed as a cross-sectional survey with register based follow-up. All cardiac patients are asked to fill out a questionnaire at hospital discharge to evaluate patient reported outcomes. Furthermore, the total eligible population, both responders and non-responders, will be followed in national registers.

Setting and participants

The five Heart Centres in Denmark are including patients during a one year period, from April 15th 2013 to April 15th 2014. One centre began data collection later, May 1st 2013. Four heart centres have both medical and surgical wards, one centre medical wards only. All cardiac patients discharged or transferred to a local hospital from one of the Heart Centres are potential participants in the study. Patients are unselected and consecutively included at hospital discharge. Included patients are asked to complete and return a questionnaire before they leave the hospital or alternatively to do so at home within 3 days of discharge and return it by mail. Patients who are transferred to another hospital are given the questionnaire at discharge from the Heart Centre and asked to fill it out at the

day of hospital discharge or alternatively to do so at home within 3 days of discharge and then return it by mail.

Eligibility criteria

All diagnostic groups within cardiology are included. Patients with ischemic heart disease (e.g. coronary angiography, percutaneous coronary intervention), heart failure (e.g. heart transplantation), arrhythmia (e.g. ablation, labyrinth, pacemaker, implantable cardioverter defibrillator), heart valve disease (e.g. valve replacement), endocarditis and congenital heart disease (e.g. atrium septum defect, patent ductus arteriosus, patent foramen ovale, coarctatio) are diagnosed and treated at the Heart Centres. Infrequent conditions such as thorax-trauma are also included. Patients are grouped by their primary action diagnose and will only be included in one group.

Patients under 18 years of age and patients without a Danish civil registration number are excluded from the study. For ethical reasons, patients who are unconscious when transferred are also excluded.

Reasons for non-response are recorded which allows for sub-analyses of these groups. On the front page of the questionnaire there is a box that enables the patient or nurse to tick off the reason for non-response: “Does not wish to participate”, “Not able to participate because of illness”, “Not able to participate because of language barrier”, “Questionnaire not handed out” and “Other”.

Recruitment

Patients are recruited at hospital discharge (the same day or the day before discharge) by the ward nurse in charge of the discharge of the individual patients or by a research nurse. All nurses at the centres, approximately 800, have been informed about the study and procedures at ward meetings, guidelines have been distributed and a website created (www.DenHeart.dk). When informing patients about the study and handing out the questionnaire, nurses also distribute a postage pre-paid envelope for the return of the questionnaire, either at the ward or after discharge. No reminders are sent to patients as the time window of three days post discharge makes it impossible. Distribution and return rates are monitored to allow for interventions if the rates drop during data collection. No specific cut off is set for low rates calling for interventions. Instead monthly discussions on each site and in the national research group are undertaken allowing for discussions and ideas for reminding the staff to hand out the questioners. *Data sources/measurement*
The following patient reported outcome measures are used: Short-form 12 (SF-12), Hospital Anxiety and Depression Scale (HADS), EQ-5D, Brief Illness Perception Questionnaire (B-IPQ), HeartQoL and Edmonton Symptom Assessment Scale (ESAS). Both EQ5D and SF-12 are generic health instruments. SF-12 is included to be able to compare to a national general population and EQ5D is included due to a different scale composition.

SF-12: The SF-12 is a 12-item version of the SF-36 and is a brief, reliable measure of overall health. The questionnaire measures eight domains of health: physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health with higher scores indicating better health status. The items cover the previous four weeks and results are expressed in terms of two summary scores: the

Physical Component Summary (PCS) and the Mental Component Summary (MCS).[10] A Cronbach's alpha of 0.87 and 0.84 for PCS-12 and MCS-12 respectively have been reported in a population of coronary heart disease patients.[11] The SF-12 is a suitable for studies focusing on patient-based assessment of physical and mental health.[10] Furthermore it is used in the National Health Surveys and outcomes can be compared.

HADS: 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-A and HADS-D, and consists of seven questions to assess anxiety and seven questions to assess depression.[12] 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 0.83 and 0.82 for the HADS-A and HADS-D respectively.[13] Scores of 0 to 7 for either subscale are regarded as normal and scores of 8 to 10 suggest the presence of a mood disorder. Scores of 11 and above indicate the probable presence of a mood disorder.[14]

EQ-5D: The EQ-5D is a 6-item standardised instrument for measuring current health status that provides a simple descriptive profile and a single index value that can be used in clinical and economic evaluation of health care and in population health surveys. The questionnaire covers five dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into three levels: no problems, some or moderate problems or extreme problems. . The sixth item a Visual Analogue Scale enables the respondent to provide a self-rating of his/her own health. Higher scores indicate better health status.[15] An overall Cronbach's alpha of 0.73 has been found in a population of coronary heart disease patients.[11]

B-IPQ: B-IPQ is a short 8-item questionnaire that assesses cognitive and emotional representations of illness. The eight items each represent a dimension of the respondent's perception of his or her own illness. Five items assess current cognitive representations of illness: consequences, timeline, personal control, treatment control and identity. Two items assess emotional representations of illness: concern and emotions. The last item assesses illness comprehensibility. A higher score on the B-IPQ reflects a more threatening view of illness. B-IPQ has good test-retest reliability measured with Pearson correlations and has shown good predictive validity among patients recovering from myocardial infarction.[16]

HeartQoL: HeartQoL is an 14-item illness specific questionnaire that measures quality of life (QoL) in cardiac patients. The questionnaire covers the previous four weeks and produces a global score and two subscales. A physical and an emotional scale with higher scores indicating better QoL status. HeartQoL is a new questionnaire developed on the basis of items from three widely used questionnaires for specific groups of cardiac patients (Seattle Angina Questionnaire, MacNew Heart Disease Health-related Quality of Life Questionnaire and Minnesota Living with Heart Failure questionnaire). The questionnaire has proven to be a reliable instrument with a Cronbach's alpha between 0.80-0.91 for the global score and each subscale and to be responsive in patients with a wide spectrum of diagnoses.[17-19] ESAS: ESAS is a 10-item questionnaire that allows patients to rate their current symptoms on a visual numeric scale. The following symptoms are included: pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, shortness of breath and distress. Higher scores indicate the presence and intensity of the symptoms. ESAS has proven to be a valid instrument to measure cancer patients' self-reported symptoms with an overall Cronbach's alpha of 0.79.[20] Even though ESAS was developed

for palliative care in cancer patients, the ESAS has been used in cardiac populations and there was found modest correlation to NYHA class and heart failure questionnaires.[21] Besides the validated questionnaires, 16 questions about health behaviour, cardiac symptoms, sense of security and use of medicines are included in the questionnaire. This amounts to a total of 80 items. The questionnaire was pre-tested for feasibility by 12 (10 male, 2 female) patients aged 52-81 years old (mean 65.9) on medical and surgical wards at three of the Heart Centres, and the introduction and layout was adjusted afterwards. The questionnaire takes about 20 minutes to complete.

Variables from registers

Because all Danish citizens have a unique personal identification number, linkage between the national registers and other data sources is feasible. Therefore, the Danish registers offer a great number of possibilities for national epidemiological studies.[22]

For the DenHeart study, data are drawn at baseline and follow-up after one year from the following registers:

The Danish Civil Registration System:[23] Gender, age, marital status.

The Danish National Patient Register:[24] Action diagnosis, other diagnoses, procedures, length of hospital stay, type of hospitalisation (acute, heart related, other).

The Danish National Health Service Register:[25] Contact with general practitioners and other agents in primary health care.

Registers on personal labour market affiliation:[26] Labour market affiliation, sick leave, early retirement pension.

Population Education Register:[27] Educational degree.

The Income Statistics Register:[28] Income.

Data handling and record keeping

Questionnaires are mailed from the Heart Centres or from the patients' home to a scanning agency (Express A/S). Questionnaires are scanned and the file delivered to The National Institute of Public Health, University of Southern Denmark and placed on a secure hard drive. When the data collection is finished, the entire dataset will be reviewed in order to remove ineligible respondents, e.g. pulmonary trauma. Furthermore, the entire population of patients discharged from the Heart Centres during the data collection period will be drawn from the National Patient Register. This will be reviewed in order to remove irrelevant discharges, in accordance with the inclusion criteria.

Data monitoring

In order to monitor trial conduct, reports are continuously delivered from the scanning agency in order to identify the need for adjustments. A data file is delivered every two weeks during the first three months and every month thereafter throughout the entire data collection period. The data file includes a list of received questionnaires ranked by centre and unit, and information on whether the questionnaire has been completed on the front page. The numbers are compared to the number of patients discharged at unit level in the same period. Assessments of response rates are done and adjustments made if needed. Low response rates in a unit will lead to contact with the unit concerned to learn the reason why and actions to increase them. Returned questionnaires will be screened for systematic errors.

Study size

The study size is not derived statistically, as it consists of the total population of patients discharged from the five Heart Centres in the project period. The five Heart Centres diagnose and treat about 45,000 patients per year. These patients are diagnosed with numerous diseases and conditions and the aim is to describe differences, not only among the most common diagnoses but also the infrequent ones. Thus, all patients discharged from national Heart Centres over one year are included in order to secure as high a level of specificity as possible. Furthermore, by including a large number of participants, a shorter follow-up time is needed. Besides the primary objectives, further ancillary and spin-off analyses will be prepared. Clearly, power calculations cannot be performed prospectively for all potential analyses based on data from the DenHeart study. Moreover, adverse outcomes have very different incidence rates.

Response rate

The final response rate is calculated based on discharge data from the National Patient Register. For calculating the actual number of eligible patients, the following are not included: patients without a Danish civil registration number, patients living in Greenland (no register follow-up possible), patients with two admissions within 24 hours, patients deceased in hospital and outpatient visits. Patients admitted for less than 24 hours without a procedure and readmitted with a procedure within one month are counted once.

Even though patients are encouraged to fill out the questionnaire within 3 days all questionnaires completed within 4 weeks of discharge are included in the analyses.

Patients who have filled out more than one questionnaire during the project period due to repeated hospitalizations will only be counted once (the first questionnaire returned) in the

final count of the response rate. The repeated measurements may be included in sub-analyses.

Statistical methods

Objective 1: For each diagnostic group, age (mean), sex distribution and patient reported outcomes at hospital discharge distribution will be reported. Differences between groups will be tested by use of ANOVA tests for continuous variables and chi-squared tests for categorical variables. Multivariate logistic regression will be used to investigate the relationship between diagnostic group and patient reported outcomes when controlling for response date (number of days since hospital discharge), age, sex and other possible confounders, and in-hospital predicting factors (e.g. procedure, duration of index hospital admission, acute/elective admission, stay at intensive care unit, complications).

Objective 2a: For each diagnostic group, the crude associations between patient reported outcome measures at hospital discharge and all-cause and cardiac morbidity and all-cause and cardiac mortality after one year, will be described and assessed using ANOVA tests for continuous variables and chi-squared tests for categorical variables. In addition, multivariate Cox proportional hazards regression models, with age as the time scale, will be used to examine the associations between patient reported outcome measures at baseline and all-cause morbidity and mortality and cardiac morbidity and mortality when adjusting for response date, sex, co-morbidity and other potential confounding factors at baseline.

Objective 2b: For each diagnostic group, the crude associations between patient reported outcome measures at hospital discharge and labour market affiliation (employment status, sick leave, early retirement pension) after one year will be described and assessed using

the ANOVA tests for continuous variables and chi-squared tests for categorical variables. Multivariate Cox proportional hazards regression models, with age as the time scale, will also be carried out to investigate the associations between patient reported outcome measures at baseline and labour market affiliation when adjusting for potential confounding factors (e.g. response date, sex, co-morbidity).

Objective 2c: For each diagnostic group, the crude associations between patient reported outcomes measures at hospital discharge and health care utilization (hospitalizations, contact with general practitioner, medical specialist, and physiotherapist) after one year, will be described and assessed using the ANOVA tests for continuous variables and chi-squared tests for categorical variables. Multivariate Cox proportional hazards regression models, with age as the time scale, will be used to analyse the association between patient reported outcome measures at baseline and health care utilization when adjusting for potential confounding variables (e.g. response date, sex, co-morbidity).

Weighting

It is possible to link both respondents and non-respondents in the survey on an individual level to different administrative registers. Thus, non-response weights will be computed based on register information (e.g. sex and age) in order to reduce non-response bias. Patients with a low probability of response will be given a higher weight in the analyses to represent the larger number of non-respondents with similar characteristics. Accordingly, patients more likely to respond will be given a lower weight.

Spin-off projects

Several spin-off analyses will be prepared.

Ethics and dissemination

The study is conducted in accordance with the Declaration of Helsinki. According to Danish legislation, surveys should not be approved by an ethics committee system but only by the Danish Data Protection Agency, no. 2007-58-0015/30-0937. The DenHeart survey is approved by the Institutional Boards of the Heart Centres and registered at ClinicalTrials.gov (NCT01926145). Patients sign informed consent stating that participation is voluntary and that further information from patient records may be obtained.

The National Institute of Public Health stores data from the DenHeart survey. Access to data can only be provided to investigators after approval from the Publication Committee. All study results will be published in international research journals and conference presentations.

Discussion

Study population

The five Heart Centres treat the most critically ill cardiac patients in Denmark. Approximately 47 regional or local hospitals treat cardiac patients medically and care for terminally ill cardiac patients. These patients are underrepresented in the DenHeart study. The patients in this study represent the patients with diagnoses where medical, invasive or surgical treatment is possible, and patients with rare conditions such as heart transplant and congenital heart disease. Furthermore, four of the five Heart Centres have a local hospital function treating all cardiac diagnoses. One surgical unit did not wish to participate in the study.

Patients who are hospitalised several times in the project period will be asked to fill out the questionnaire each time. Repeated measures will only be used in sub-analyses. For

reporting of primary outcomes, patients will only be counted once (the first questionnaire returned).

Variables

The majority of the outcome measures included in the questionnaire is comprised of validated and standardised instruments to assess patient reported outcomes, which enhances the validity of the questionnaire. However, in the interpretation of the results, it must be taken into account that patients with different cardiac conditions differ regarding how much their health status has changed prior to admission to hospital, and that some of the instruments have long recall.

Confounding factors

From previous national health surveys, we know that age and socioeconomic position play a significant role for non-response. Also, regional differences of about 15 % in response rates have been documented.[29, 30] The patients treated at the Heart Centres are often aged and severely ill, which may be reflected in the response rates. This will be accounted for by reporting both actual responses as well as weighted data for the underrepresented groups in the analyses. However, several different initiatives are being conducted by the centres to optimize response rates. Nurses are reminded to hand out the questionnaires at local meetings, by posters in the ward and logo-pens, and response rates are continuously shared with the ward nurses in order to secure motivation among the approximately 800 nurses involved in the distribution of questionnaires. Letters are sent to the local hospitals that receive patients from the Heart Centres asking to remind the patients to fill out the questionnaire at discharge to home. Some centres are mailing questionnaires to patients after discharge when they are not handed out in hospital. Mailed questionnaires are sent

with overnight post service allowing the questionnaire to be filled out within the 3 days. As this is a national multicentre study, regional differences in ways to enhance the response rates may occur. All of these different strategies fall within the frame of the DenHeart study and timeframe for responding.

Contributorship

SKB conceived the study. SKB, AVC, MH, LT, BB, JS, AM, AL, AIC, KJ and OE initiated the study design and implementation. KJ, AIC and OE provided statistical expertise in the clinical trial design. All contributed to the refinement of the study protocol.

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Competing interest

No competing interests have been declared by the authors.

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Selina Kikkenborg Berg, RN, MScN, Ph.D.[1,2]
Jette Svanholm, RN, MSc, Ph.D.[3]
Astrid Lauberg, RN, MScN[4]
Britt Borregaard, RN, MPQM[5]
Margrethe Herning, RN, MED[2]
Anna Mygind, MSPH, Ph.D.[3]
Anne Vinggaard Christensen, MSPH[1]
Anne Illemann Christensen, MSPH[6]
Ola Ekholm, MSc[6]
Knud Juel, Ph.D.[6]
Lars Thrysøe, RN, MLP, Ph.D.[7]

1.The Heart Centre, Unit 2151, Rigshospitalet, Copenhagen University Hospital Blegdamsvej 9, 2100 Copenhagen, Denmark
2. Department of Cardiology, Gentofte University Hospital, Niels Andersens Vej 65, 2900 Hellerup, Denmark
3.Department of Cardiology, Aarhus University Hospital, Brendstrupgaardsvej 100, 8200 Aarhus N, Denmark
4. Department of Cardiology and Department of Cardiothoracic Surgery, Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg, Denmark
5. Department of Thoracic, Cardiac and Vascular Surgery, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense C, Denmark
6.National Institute of Public Health, University of Southern Denmark, Øster Farimagsgade 5A, 1353 Copenhagen, Denmark
7. Department of Cardiology, Odense University Hospital, University of Southern Denmark, Sdr. Boulevard 29, 5000 Odense C, Denmark

Corresponding author:

Selina Kikkenborg Berg, PhD.
Copenhagen University Hospital, Rigshospitalet
The Heart Centre, unit 2152
Blegdamsvej 9
2100 Copenhagen
Denmark
E-mail: selina@rh.dk
Tel: +45 3545 9526

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Abstract

Introduction: Patient reported health status, including symptom burden, functional status and quality of life, is an important measure of health. Differences in health status between diagnostic groups within cardiology have only been sparsely investigated. These outcomes may predict morbidity, mortality, labour market affiliation and health care utilization in various diagnostic groups. A national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population has been designed as the DenHeart survey.

Methods and analysis: DenHeart is designed as a cross-sectional survey with register based follow-up. All diagnostic groups at the five national Heart Centres are included during one year (April 15th 2013 to April 15th 2014) and asked to fill out a questionnaire at hospital discharge. The total eligible population, both responders and non-responders, will be followed in national registers. The following instruments are used: SF-12, HADS, EQ-5D, B-IPQ, HeartQoL and ESAS. The following variables are collected from national registers: action diagnosis, procedures, co-morbidity, length of hospital stay, type of hospitalisation, visits to GP and other agents in primary health care, dispensed prescription medication, vital status, and cause of death. Labour market affiliation, sick leave, early retirement pension, educational degree and income will be collected from registers. Frequency distributions and multiple logistic regression analyses will be used to describe and assess differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors. Cox proportional hazards regression models with age as the time scale will be used to investigate associations between patient reported outcomes at baseline and morbidity/mortality, labour market affiliation and health care utilization after one year.

Ethics and dissemination: The study complies with the Declaration of Helsinki. The study has been approved by the Danish Data Protection Agency: 2007-58-0015/30-0937. Study findings will be disseminated widely through peer reviewed publications and conference presentations.

Trial registration: ClinicalTrials.gov: NCT01926145.

Introduction

Patient reported health status, which includes symptom burden, functional status and quality of life, is an important measure of health. Validated patient health status surveys, including disease specific instruments for patients with cardiovascular disease, allow quantification of critical patient-centred outcomes and additional research is needed to better understand the determinants[1] and the predicting factors of patients' health status. Previous studies suggest an association between heart disease, self-reported health and morbidity and mortality, and that patient reported outcome measures can predict prolonged hospital stay, future quality of life, return to work, morbidity and mortality in cardiac patients.[2-7] Quality of life scores seem to provide important prognostic information independent of traditional clinical data, as higher scores have been associated with longer survival in patients with ventricular arrhythmias and coronary artery disease.[8, 9] However no studies have included all diagnostic groups within cardiology and comparisons among diagnostic groups are lacking. The overall aim of the DenHeart survey is to gain knowledge about patient reported outcome measures regarding health among cardiac patients at hospital discharge. Knowledge about patients' own perception of their health status and predicting factors can help to guide inpatient practice and outpatient follow-up. Furthermore, a survey combined with register data can be used to evaluate differences among diagnostic groups and predicting factors for patient reported outcome measures at hospital discharge and long-term morbidity and mortality. Also, economic analysis of healthcare utilisation and work ability status in a large cohort of cardiac patients is needed. Therefore, the DenHeart study is designed as a national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population.

Objectives

The objectives of the DenHeart study are to describe: (i) differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors and (ii) patient reported outcomes at hospital discharge as a predictor of a) morbidity and mortality, b) labour market affiliation and c) health care utilization after one year.

Methods and analysis

Study design

The DenHeart study is designed as a cross-sectional survey with register based follow-up. All cardiac patients are asked to fill out a questionnaire at hospital discharge to evaluate patient reported outcomes. Furthermore, the total eligible population, both responders and non-responders, will be followed in national registers.

Setting and participants

The five Heart Centres in Denmark are including patients during a one year period, from April 15th 2013 to April 15th 2014. One centre began data collection later, May 1st 2013. Four heart centres have both medical and surgical wards, one centre medical wards only. All cardiac patients discharged or transferred to a local hospital from one of the Heart Centres are potential participants in the study. Patients are unselected and consecutively included at hospital discharge. Included patients are asked to complete and return a questionnaire before they leave the hospital or alternatively to do so at home within 3 days of discharge and return it by mail. Patients who are transferred to another hospital are given the questionnaire at discharge from the Heart Centre and asked to fill it out at the

day of hospital discharge or alternatively to do so at home within 3 days of discharge and then return it by mail.

Eligibility criteria

All diagnostic groups within cardiology are included. Patients with ischemic heart disease (e.g. coronary angiography, percutaneous coronary intervention), heart failure (e.g. ~~coronary artery bypass graft,~~ heart transplantation), arrhythmia (e.g. ablation, labyrinth, pacemaker, implantable cardioverter defibrillator), heart valve disease (e.g. ~~stent,~~ valve replacement), endocarditis and congenital heart disease (e.g. atrium septum defect, patent ductus arteriosus, patent foramen ovale, coarctatio) are diagnosed and treated at the Heart Centres. Infrequent conditions such as thorax-trauma are also included. Patients are grouped by their primary action diagnose and will only be included in one group.

Patients under 18 years of age and patients without a Danish civil registration number are excluded from the study. For ethical reasons, patients who are unconscious when transferred are also excluded.

Reasons for non-response are recorded which allows for sub-analyses of these groups. On the front page of the questionnaire there is a box that enables the patient or nurse to tick off the reason for non-response: “Does not wish to participate”, “Not able to participate because of illness”, “Not able to participate because of language barrier”, “Questionnaire not handed out” and “Other”.

Recruitment

Patients are recruited at hospital discharge (the same day or the day before discharge) by the ward nurse in charge of the discharge of the individual patients or by a research nurse. All nurses at the centres, approximately 800, have been informed about the study and

procedures at ward meetings, guidelines have been distributed and a website created (www.DenHeart.dk). When informing patients about the study and handing out the questionnaire, nurses also distribute a postage pre-paid envelope for the ~~to them to~~ return of the questionnaire ~~in~~, either at the ward or after discharge. No reminders are sent to patients as the time window of three days post discharge makes it impossible. Distribution and return rates are monitored to allow for interventions if the rates drop during data collection. No specific cut off is set for low rates calling for interventions. Instead monthly discussions on each site and in the national research group are undertaken allowing for discussions and ideas for reminding the staff to hand out the questioners.

Data sources/measurement

The following patient reported outcome measures are used: Short-form 12 (SF-12), Hospital Anxiety and Depression Scale (HADS), EQ-5D, Brief Illness Perception Questionnaire (B-IPQ), HeartQoL and Edmonton Symptom Assessment Scale (ESAS). Both EQ5D and SF-12 are generic health instruments. SF-12 is included to be able to compare to a national general population and EQ5D is included due to a different scale composition.

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SF-12: The SF-12 is a 12-item version of the SF-36 and is a brief, reliable measure of overall health. The questionnaire measures eight domains of health: physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health with higher scores indicating better health status. The items cover the previous four weeks and results are expressed in terms of two summary scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS).[10] A Cronbach's alpha of 0.87 and 0.84 for PCS-12 and MCS-12 respectively have been reported in a population of coronary heart disease patients.[11] The SF-12 is a suitable for

studies focusing on patient-based assessment of physical and mental health.[10] Furthermore it is used in the National Health Surveys and outcomes can be compared.

HADS: 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-A and HADS-D, and consists of seven questions to assess anxiety and seven questions to assess depression.[12] 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 0.83 and 0.82 for the HADS-A and HADS-D respectively.[13] Scores of 0 to 7 for either subscale are regarded as normal and scores of 8 to 10 suggest the presence of a mood disorder. Scores of 11 and above indicate the probable presence of a mood disorder.[14]

EQ-5D: The EQ-5D is a 6-item standardised instrument for measuring current health status that provides a simple descriptive profile and a single index value that can be used in clinical and economic evaluation of health care and in population health surveys. The questionnaire covers five dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into three levels: no problems, some or moderate problems or extreme problems. ~~The questionnaire consists of a descriptive system produced in a standard layout that enables the respondent to classify his/her health according to the five dimensions and a~~. The sixth item a Visual Analogue Scale ~~that~~ enables the respondent to provide a self-rating of his/her own health. Higher scores indicate better health status.[15] An overall Cronbach's alpha of 0.73 has been found in a population of coronary heart disease patients.[11]

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B-IPQ: B-IPQ is a short 8-item questionnaire that assesses cognitive and emotional representations of illness ~~on the basis of eight items~~. The eight items each represent a dimension of the respondent's perception of his or her own illness. Five items assess current cognitive representations of illness: consequences, timeline, personal control, treatment control and identity. Two items assess emotional representations of illness: concern and emotions. The last item assesses illness comprehensibility. A higher score on the B-IPQ reflects a more threatening view of illness. B-IPQ has good test-retest reliability measured with Pearson correlations and has shown good predictive validity among patients recovering from myocardial infarction.[16]

HeartQoL: HeartQoL is an 14-item illness specific questionnaire that measures quality of life (QoL) in cardiac patients. The questionnaire covers the previous four weeks and produces a global score and two subscales. A physical and an emotional scale with higher scores indicating better QoL status. HeartQoL is a new questionnaire developed on the basis of items from three widely used questionnaires for specific groups of cardiac patients (Seattle Angina Questionnaire, MacNew Heart Disease Health-related Quality of Life Questionnaire and Minnesota Living with Heart Failure questionnaire). The questionnaire has proven to be a reliable instrument with a Cronbach's alpha between 0.80-0.91 for the global score and each subscale and to be responsive in patients with a wide spectrum of diagnoses.[17-19]

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ESAS: ESAS is a 10-item questionnaire that allows patients to rate their current symptoms on a visual numeric scale. The following symptoms are included: pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, shortness of breath and distress. Higher scores indicate the presence and intensity of the symptoms. ESAS has proven to be a valid instrument to measure cancer patients' self-reported symptoms with an overall

Cronbach's alpha of 0.79.[20] ~~However, the scale has not yet been evaluated in cardiac patients~~Even though ESAS was developed for palliative care in cancer patients, the ESAS has been used in cardiac populations and there was found modest correlation to NYHA class and heart failure questionnaires.[21]

Besides the validated questionnaires, ~~thirteen~~ 16 questions about health behaviour, cardiac symptoms, sense of security and use of medicines are included in the questionnaire. This amounts to a total of 8062 items. The questionnaire was pre-tested for feasibility by 12 (10 male, 2 female) patients aged 52-81 years old (mean 65.9) on medical and surgical wards at three of the Heart Centres, and the introduction and layout was adjusted afterwards. The questionnaire takes about 20 minutes to complete.

Variables from registers

Because all Danish citizens have a unique personal identification number, linkage between the national registers and other data sources is feasible. Therefore, the Danish registers offer a great number of possibilities for national epidemiological studies.[22]

For the DenHeart study, data are drawn at baseline and follow-up after one year from the following registers:

The Danish Civil Registration System:[23] Gender, age, marital status.

The Danish National Patient Register:[24] Action diagnosis, other diagnoses, procedures, length of hospital stay, type of hospitalisation (acute, heart related, other).

The Danish National Health Service Register:[25] Contact with general practitioners and other agents in primary health care.

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Registers on personal labour market affiliation:[26] Labour market affiliation, sick leave, early retirement pension.

Population Education Register:[27] Educational degree.

The Income Statistics Register:[28] Income.

Data handling and record keeping

Questionnaires are mailed from the Heart Centres or from the patients' home to a scanning agency (Express A/S). Questionnaires are scanned and the file delivered to The National Institute of Public Health, University of Southern Denmark and placed on a secure hard drive. When the data collection is finished, the entire dataset will be reviewed in order to remove ineligible respondents, e.g. pulmonary trauma. Furthermore, the entire population of patients discharged from the Heart Centres during the data collection period will be drawn from the National Patient Register. This will be reviewed in order to remove irrelevant discharges, in accordance with the inclusion criteria.

Data monitoring

In order to monitor trial conduct, reports are continuously delivered from the scanning agency in order to identify the need for adjustments. A data file is delivered every two weeks during the first three months and every month thereafter throughout the entire data collection period. The data file includes a list of received questionnaires ranked by centre and unit, and information on whether the questionnaire has been completed on the front page. The numbers are compared to the number of patients discharged at unit level in the same period. Assessments of response rates are done and adjustments made if needed. Low response rates in a unit will lead to contact with the unit concerned to learn the reason

why and actions to increase them. Returned questionnaires will be screened for systematic errors.

Study size

The study size is not derived statistically, as it consists of the total population of patients discharged from the five Heart Centres in the project period. The five Heart Centres diagnose and treat about 45,000 patients per year. These patients are diagnosed with numerous diseases and conditions and the aim is to describe differences, not only among the most common diagnoses but also the infrequent ones. Thus, all patients discharged from national Heart Centres over one year are included in order to secure as high a level of specificity as possible. Furthermore, by including a large number of participants, a shorter follow-up time is needed. Besides the primary objectives, further ancillary and spin-off analyses will be prepared. Clearly, power calculations cannot be performed prospectively for all potential analyses based on data from the DenHeart study. Moreover, adverse outcomes have very different incidence rates.

Response rate

The final response rate is calculated based on discharge data from the National Patient Register. For calculating the actual number of eligible patients, the following are not included: patients without a Danish civil registration number, patients living in Greenland (no register follow-up possible), patients with two admissions within 24 hours, patients deceased in hospital and outpatient visits. Patients admitted for less than 24 hours without a procedure and readmitted with a procedure within one month are counted once.

Even though patients are encouraged to fill out the questionnaire within 3 days all questionnaires completed within 4 weeks of discharge are included in the analyses.

Patients who have filled out more than one questionnaire during the project period due to repeated hospitalizations will only be counted once (the first questionnaire returned) in the final count of the response rate. The repeated measurements may be included in sub-analyses.

Statistical methods

Objective 1: For each diagnostic group, age (mean), sex distribution and patient reported outcomes at hospital discharge distribution will be reported. Differences between groups will be tested by use of ANOVA tests for continuous variables and chi-squared tests for categorical variables. Multivariate logistic regression will be used to investigate the relationship between diagnostic group and patient reported outcomes when controlling for response date (number of days since hospital discharge), age, sex and other possible confounders, and in-hospital predicting factors (e.g. procedure, duration of index hospital admission, acute/elective admission, stay at intensive care unit, complications).

Objective 2a: For each diagnostic group, the crude associations between patient reported outcome measures at hospital discharge and all-cause and cardiac morbidity and all-cause and cardiac mortality after one year, will be described and assessed using ANOVA tests for continuous variables and chi-squared tests for categorical variables. In addition, multivariate Cox proportional hazards regression models, with age as the time scale, will be used to examine the associations between patient reported outcome measures at baseline and all-cause morbidity and mortality and cardiac morbidity and mortality when adjusting for response date, sex, co-morbidity and other potential confounding factors at baseline.

Objective 2b: For each diagnostic group, the crude associations between patient reported outcome measures at hospital discharge and labour market affiliation (employment status, sick leave, early retirement pension) after one year will be described and assessed using the ANOVA tests for continuous variables and chi-squared tests for categorical variables. Multivariate Cox proportional hazards regression models, with age as the time scale, will also be carried out to investigate the associations between patient reported outcome measures at baseline and labour market affiliation when adjusting for potential confounding factors (e.g. response date, sex, co-morbidity).

Objective 2c: For each diagnostic group, the crude associations between patient reported outcomes measures at hospital discharge and health care utilization (hospitalizations, contact with general practitioner, medical specialist, and physiotherapist) after one year, will be described and assessed using the ANOVA tests for continuous variables and chi-squared tests for categorical variables. Multivariate Cox proportional hazards regression models, with age as the time scale, will be used to analyse the association between patient reported outcome measures at baseline and health care utilization when adjusting for potential confounding variables (e.g. response date, sex, co-morbidity).

Weighting

It is possible to link both respondents and non-respondents in the survey on an individual level to different administrative registers. Thus, non-response weights will be computed based on register information (e.g. sex and age) in order to reduce non-response bias. Patients with a low probability of response will be given a higher weight in the analyses to represent the larger number of non-respondents with similar characteristics. Accordingly, patients more likely to respond will be given a lower weight.

Spin-off projects

Several spin-off analyses will be prepared. ~~and conducted, e.g. a three year follow up analysis on the primary outcomes, the association between patient reported outcomes at discharge and cardiac events over time, patient reported outcomes and medication compliance and patient reported outcomes as a screening tool in clinical practice. A follow-up survey after two to five years is being considered.~~

Ethics and dissemination

The study is conducted in accordance with the Declaration of Helsinki. According to Danish legislation, surveys should not be approved by an ethics committee system but only by the Danish Data Protection Agency, no. 2007-58-0015/30-0937. The DenHeart survey is approved by the Institutional Boards of the Heart Centres and registered at ClinicalTrials.gov (NCT01926145). Patients sign informed consent stating that participation is voluntary and that further information from patient records may be obtained.

The National Institute of Public Health stores data from the DenHeart survey. Access to data can only be provided to investigators after approval from the Publication Committee. All study results will be published in ~~international~~international research journals and conference presentations.

Discussion

Study population

The five Heart Centres treat the most critically ill cardiac patients in Denmark. Approximately 47 regional or local hospitals treat cardiac patients medically and care for terminally ill cardiac patients. These patients are underrepresented in the DenHeart study.

The patients in this study represent the patients with diagnoses where medical, invasive or surgical treatment is possible, and patients with rare conditions such as heart transplant and congenital heart disease. Furthermore, four of the five Heart Centres have a local hospital function treating all cardiac diagnoses. One surgical unit did not wish to participate in the study.

Patients who are hospitalised several times in the project period will be asked to fill out the questionnaire each time. Repeated measures will only be used in sub-analyses. For reporting of primary outcomes, patients will only be counted once (the first questionnaire returned).

Variables

The majority of the outcome measures included in the questionnaire is comprised of validated and standardised instruments to assess patient reported outcomes, which enhances the validity of the questionnaire. However, in the interpretation of the results, it must be taken into account that patients with different cardiac conditions differ regarding how much their health status has changed prior to admission to hospital, and that some of the instruments have long recall.

Confounding factors

From previous national health surveys, we know that age and socioeconomic position play a significant role for non-response. Also, regional differences of about 15 % in response rates have been documented.[29, 30] The patients treated at the Heart Centres are often aged and severely ill, which may be reflected in the response rates. This will be accounted for by reporting both actual responses as well as weighted data for the underrepresented groups in the analyses. However, several different initiatives are being conducted by the

centres to optimize response rates. Nurses are reminded to hand out the questionnaires at local meetings, by posters in the ward and logo-pens, and response rates are continuously shared with the ward nurses in order to secure motivation among the approximately 800 nurses involved in the distribution of questionnaires. Letters are sent to the local hospitals that receive patients from the Heart Centres asking to remind the patients to fill out the questionnaire at discharge to home. Some centres are mailing questionnaires to patients after discharge when they are not handed out in hospital. Mailed questionnaires are sent with overnight post service allowing the questionnaire to be filled out within the 3 days. As this is a national multicentre study, regional differences in ways to enhance the response rates may occur. All of these different strategies fall within the frame of the DenHeart study and timeframe for responding.

Contributorship

SKB conceived the study. SKB, AVC, MH, LT, BB, JS, AM, AL, AIC, KJ and OE initiated the study design and implementation. KJ, AIC and OE provided statistical expertise in the clinical trial design. All contributed to the refinement of the study protocol.

Funding

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Competing interest

No competing interests have been declared by the authors.

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