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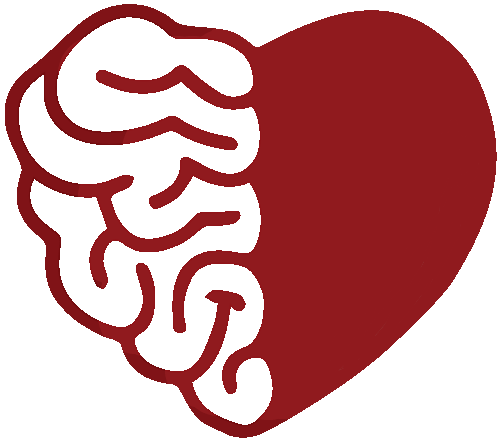

PhD Thesis

Annette Holdgaard

Anxiety and depression in patients with coronary artery disease

Development and effect of a group-based cognitive behavioural therapy intervention to reduce anxiety and depression in patients with heart disease and psychological distress

This thesis has been submitted to the Graduate School of Health and Medical Sciences, University of Copenhagen on 5 November 2023

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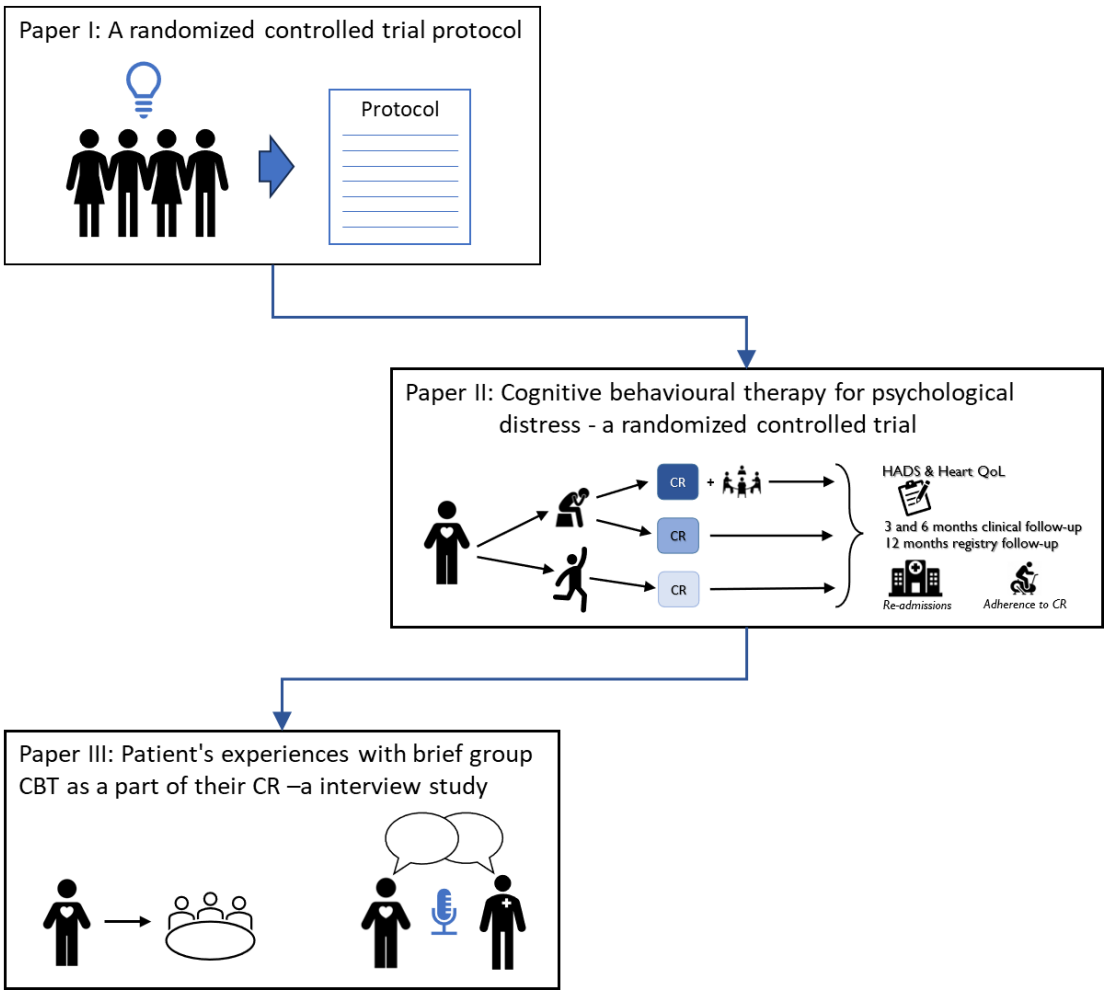

Paper I

Intensive group-based cognitive therapy in patients with cardiac disease and psychological distress-a randomized controlled trial protocol. Holdgaard A, Eckhardt-Hansen C, Lund T, Lassen CF, Sibiliz KL, Høfsten DE, Prescott E, Rasmusen HK. Trials. 2021 Jul 16;22(1):455. doi: 10.1186/s13063-021-05405-3. PMID: 34271952 Free PMC article.

Paper II

Cognitive-behavioural therapy reduces psychological distress in younger patients with cardiac disease: a randomized trial. Holdgaard A, Eckhardt-Hansen C, Lassen CF, Kjesbu IE, Dall CH, Michaelsen KL, Sibilitz KL, Prescott E, Rasmusen HK. Eur Heart J. 2023 Jan 18:ehac792. doi: 10.1093/eurheartj/ehac792. Online ahead of print. PMID: 36649937

Paper III

The experience of group cognitive behavioural therapy among patients with heart disease and psychological distress. Annette Holdgaard, Frey Toiberg, Eva Prescott, Hanne Kruuse Rasmusen, Bente Martinsen.

The papers are referred to in the text by their Roman numerals.

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Reflexivity

Reflexivity refers to the process of being a researcher and how your own role and notions of personal values and experiences may affect data collection and the interpretation of these data (1). As a cardiac nurse with a more than 20 years of experience from various hospitals and different departments of cardiology, entering the Rehabilitation Unit in this project was a familiar experience. Owing to my extensive clinical background, I am highly familiar with this context and understand how healthcare professional's work. Throughout the years, I have cared for a wide range of patients with all kinds of cardiac diseases who were passing through stable or unstable stages of their trajectory and being cared for in the outpatient clinic where rehabilitation takes place. In addition to my extensive knowledge, I have developed a special interest in the psychological aspect of having a heart disease. It has struck me as surprising that there has not been a stronger emphasis on the treatment of anxiety and depression, considering their common occurrence as reactions to having a life-threatening illness.

My reflections as a nurse needed to be transformed into the reflections of a researcher. I engaged in discussions with my supervisors to learn how to act as a researcher and how to initiate the project. During the implementation of the intervention at the other hospitals joining the project, I found it difficult not to act as a nurse, given all my knowledge and understanding of the challenges encountered in clinical practice. Being aware of my role as a researcher was very important throughout the process because many of the tasks for which I was responsible related to the practical implementation of the project. In the case study, where I had to provide the intervention, I pondered whether I should read the patients' electronic health record before the intervention or not. However, to avoid taking over the nursing role for patients, I refrained from doing so. If specific treatment questions were posed during the intervention, I urged patients to direct their questions at the nurses in the cardiac rehabilitation setting. To extend the overall perspective and prevent possible bias from my presence and control over the investigation and the research findings, we included patients from two other hospitals, and four other nurses from these hospitals conducted the intervention.

Abbreviations

ACE: Angiotensin-converting enzyme

ACS: Acute coronary syndrome

ACT: Acceptance and commitment therapy

AHA: American Heart Association

ANOVA: Analysis of variance

BDI: Beck Depression Inventory

BMI: Body Mass Index

BP: Blood Pressure

CABG: Coronary artery bypass graft

CAD: Coronary artery disease

CAQ: Cardiac Anxiety Questionnaire

CBT: Cognitive behavioural therapy

CCS: Canadian Cardiovascular Society grading of angina pectoris

CI: Confidence interval

CHD: Coronary heart disease

CONSORT: CONsolidated Standards of Reporting Trials

COPD: Chronic obstructive pulmonary disease

CR: Cardiac rehabilitation

ESC: European Society of Cardiology

GP: General practitioner

HADS: Hospital Anxiety and Depression Scale

HADS-A: HADS – anxiety subscale

HADS-D: HADS – depression subscale

HbA1: Glycated haemoglobin

HeartQol: Heart-related Quality of Life Questionnaire

HFA: Heart-focused anxiety

HR: Hazard ratio

iCBT: Internet- based cognitive behavioural therapy

IQR: interquartile range

LDL: low-density lipoprotein

MCID: Minimal clinically important difference

MI: myocardial infarction

NSTEMI: non- ST-elevation myocardial infarction

NYHA: New York Heart Association

LDL: Low-density lipoprotein

LVEF: left ventricular ejection fraction

PCI: percutaneous coronary intervention

PHQ-9: Patient Health Questionnaire

PROs: Patient-reported outcomes

PROMs: Patient-reported outcome measures

QUAL: Qualitative data

QUAN: Quantitative data

Qol: Quality of life

RCT: randomised controlled trial

SD: Standard deviation

Smartex-HF study: Controlled study of myocardial recovery after interval training in heart failure

STEMI: ST-elevation myocardial infarction

VHD: Valvular heart disease

UAP: Unstable angina pectoris

Summary

In Europe, 113 million people are living with heart disease. This imposes a great burden on individuals and society alike. Treatment of heart disease has improved profoundly over the past 30 years and mortality rates have therefore declined accordingly. Patients with recent heart disease often experience psychological distress in the form of anxiety and depression. Approximately 20% of patients with heart disease suffer from concomitant anxiety and depression, which is associated with poorer quality of life and increased morbidity and mortality. It is therefore crucial to identify and properly treat this vulnerable group of patients. International and national guidelines recommend screening and treatment, but evidence-based treatment options remain few. Treatment with cognitive behavioural therapy (CBT) has shown convincing effect in reducing anxiety and depression in this population. Treatment has often consisted of long-term individual interventions, which have been expensive and time-consuming. Adopting an individual approach is therefore hardly compatible with clinical practice. We hypothesised that an intervention with CBT, handled by an experienced nurse specialised in heart disease, could be implemented in existing rehabilitation, and would reduce psychological distress in patients with heart disease.

The overall objectives of this thesis were: 1) to evaluate the effect of an intervention with CBT to reduce anxiety and depression in patients with heart disease and 2) to describe the patients' experience of participating in group-based cognitive behavioural therapy.

A multicentre, randomized controlled trial was conducted to evaluate the effect of brief CBT given in addition to standard cardiac rehabilitation (CR) compared with CR alone (Article I + II). Furthermore, a qualitative interview study was conducted to describe the patients' experiences with brief group-based CBT as part of their cardiac rehabilitation (Paper III).

The main findings were that patients with heart disease who received CBT in addition to regular CR experienced significant improvement in anxiety and depression symptoms compared with patients with heart disease who received only regular CR. Participation in CR and heart quality of life also improved, whereas no improvement was seen in risk factors. The number of readmissions within the first year was significantly reduced for the group that received CBT. The CBT were provided by cardiac nurses and may be integrated with existing CR programmes.

Three themes were reflected the patients' experiences of participating in group-based CBT. **The significance of time**: Minimising the time between discharge and the first group session was critical for patients to avoid worsening anxiety and depression. **Mirroring as a way of normalising**: Sharing and reflecting with fellow patients helped to normalise feelings and underpinned their coping process. **Body and mind as a unity**: An essential aspect of the intervention was to understand the connection between body and mind. Developing this insight allowed patients to distinguish between anxiety-related symptoms and symptoms related to their heart disease.

Dansk resumé (Danish summary)

I Europa lever 113 millioner mennesker med hjertesygdom, hvilket er en stor byrde både for den enkelte og for samfundet. Behandlingen af hjertesygdom har ændret sig markant inden for de sidste 30 år, og tilsvarende er dødeligheden blevet væsentligt reduceret. Patienter med nylig opstået hjertesygdom oplever ofte psykisk belastning i form af angst og depression. Samtidig angst og depression forekommer blandt ca. 20% af patienter med hjertesygdom og er associeret med dårligere livskvalitet samt øget sygelighed og dødelighed. Det er derfor afgørende at identificere og behandle denne sårbare gruppe af hjertepatienter. Internationale og nationale retningslinjer anbefaler screening og behandling, men der er stadig kun meget få evidensbaserede behandlingstilbud. Behandling med kognitiv adfærdsterapi har vist overbevisende effekt i forhold til at reducere angst og depression hos patienter med hjertesygdom. Behandlingen er ofte blevet givet i langvarige individuelle interventioner, hvilket har været dyrt og tidskrævende. Denne tilgang er derfor uforenelig med implementering i klinisk praksis. Vores hypotese, var at en intervention med kognitiv adfærdsterapi, som kunne varetages af erfarne sygeplejersker med speciale i hjertesygdom, og som kunne implementeres i eksisterende rehabilitering, ville nedbringe den psykiske belastning hos patienter med hjertesygdom.

De overordnede mål for denne afhandling var: 1) at evaluere effekten af en intervention med kognitiv adfærdsterapi med hensyn til at reducere angst og depression hos patienter med hjertesygdom, og 2) at beskrive patienternes oplevelse af at deltage i forløbet med gruppebaseret kognitiv adfærdsterapi.

En multicenter randomiseret kontrolleret undersøgelse blev gennemført for at evaluere effekten af kort kognitiv adfærdsterapi givet i tillæg til vanlig hjerterehabilitering (CR) sammenlignet med hjerterehabilitering alene (Artikel I + II). Endvidere blev der gennemført en kvalitativ interviewundersøgelse for at beskrive patienters erfaringer med kort gruppebaseret kognitiv adfærdsterapi som en del af deres hjerterehabilitering (Paper III).

De vigtigste konklusioner

Patienter med hjertesygdom, som fik kognitiv adfærdsterapi i tillæg til vanlig CR, havde en signifikant forbedring i angst- og depressionssymptomer sammenlignet med patienter med hjertesygdom, som kun fik vanlig CR. Deltagelse i CR samt selvvurderet helbred blev også

forbedret, hvorimod man ikke så nogen forbedring i risikofaktorer. Antallet af genindlæggelser inden for det første år blev signifikant reduceret for den gruppe som fik kognitiv adfærdsterapi. CBT-interventionen blev varetaget af erfarne sygeplejersker med speciale i hjertesygdom og kan integreres med eksisterende CR-programmer.

Tre temaer afspejlede patienternes erfaringer/oplevelser (experiences) med at deltage i gruppebaseret kognitiv adfærdsterapi. **Betydning af tid**: Det var af afgørende betydning for patienterne at minimere tiden mellem udskrivelsen og den første gruppesession for at undgå forværring af angst og depression. **Spejling som en hjælp til normalisering**: At dele erfaringer og reflektere over deres situation sammen med medpatienter var med til at normalisere følelser og underbyggede patienternes mestringsproces. **Krop og sind som en helhed:** Et væsentligt aspekt af interventionen var at forstå sammenhængen mellem krop og sind. Udviklingen af denne indsigt gjorde det muligt for patienterne at skelne mellem angstrelaterede symptomer og de symptomer, der var relateret til deres hjertesygdom.

Background

Cardiac rehabilitation

Cardiovascular disease (CVD) remains the primary cause of global mortality, causing approximately 32% of all deaths and resulting in 18.6 million fatalities in 2019. Moreover, CVD significantly contributes to disability (2). In Europe, more than 113 million individuals are estimated to live with CVD, primarily because of population aging and improved treatment outcomes, leading to greater patient survival (3). This constitutes a substantial burden on the affected individuals who experience a diminished quality of life, and on society as a whole. The aetiology of CVD is multifaceted, encompassing genetic, biochemical, psycho-social and lifestyle factors (4). The risk of developing CVD arises from a complex interplay between genetics and lifestyle, with lifestyle factors accounting for approximately 50% of the overall risk (5). CDV prevention is a global priority given its high prevalence and incidence.

To mitigate the consequences of coronary artery disease (CAD), national guidelines on cardiac rehabilitation (CR) have been adopted worldwide. CR is a multidisciplinary and comprehensive intervention (listed below). Its primary objectives are to impede the progression of heart disease and enhance the physical, mental and social well-being (function) of patients (6). Both the European Society of Cardiology and the American Association of Cardiology endorse CR as a Class 1 A recommendation for treatment and secondary prevention of CVD (4,7).

Although CR programmes may exhibit some variability, they typically adopt a group-based approach and encompass the following components (7,8):

- Patient assessment
- Counselling on physical activity
- Exercise training
- Patient education on heart disease
- Management and control of cardiovascular risk factors
- Psycho-social support
- Dietary advice
- Up-titration of medication according to guidelines

In several studies, evidence-based CR programmes were shown to reduce morbidity and mortality alike while improving heart-related quality of life , reducing acute coronary revascularisations and acute and long-term pharmacotherapy (8,9). Although less extensively documented, CR is also recommended for patients with cardiac disease after valve surgery and

other conditions (10,11). Despite the recommendation of psycho-social support, including recognition and management of psychological distress, CR interventions have traditionally focused on physical exercise (4,12). In 2021, the American Heart Association stressed the importance of seeing the mind, heart and body as interconnected and interdependent and underlined the need to adopt a holistic view in the treatment of CAD (13).

Prevalence and implications of anxiety and depression in patients with cardiac disease

Anxiety and depression are prevalent among patients with cardiac disease and may significantly affect their physical and mental health outcomes (14). Studies have shown that approximately one third of all patients with cardiac disease experience symptoms of anxiety or depression. These symptoms may be related to the stress of coping with a chronic illness, the experience of a cardiac event or the presence of comorbid psychiatric disorders (15–17). Following an acute myocardial infarction (MI), 20-40% of patients have reported symptoms of anxiety or depression (18). The importance of psychological health for the subsequent risk of CVD has gained more attention in recent decades owing to emerging evidence of the association between psychological distress and CVD risk (19). In 2014, the American Heart Association officially acknowledged that depression was a factor contributing to adverse outcomes in individuals who were diagnosed with acute coronary syndrome (20). Additionally, mounting evidence suggests that anxiety is an independent predictor of poorer outcomes in patients with cardiac disease (21). Adverse outcomes arising from depression and anxiety can be ascribed to the intricate interplay of physiological and behavioural factors (22). Hence, evidence suggests a bidirectional connection between depression and ischaemic heart disease (IHD). This implies the existence of a link between IHD and a link between depression and IHD as well. The complex and potentially multifactorial underlying mechanisms are not fully understood (12,23). Moreover, psychological distress may also influence physiological processes directly, e.g. the autonomic nervous system (24) and endothelial function (25).

In general, 15-25% of patients with cardiac disease meet the criteria for major depression and an even higher proportion of patients experience clinically relevant levels of depression (14,26). For anxiety, the estimated prevalence of depression following a cardiac event is 30% (26,27). Anxiety and depression are not temporary conditions; thus, several studies have found persistent, high prevalences for both conditions at up to one year of follow-up (28,29). Furthermore,

depression and anxiety may present subsequently rather than at the time of the cardiac event (29,30).

The psychological impact of CAD is substantial, and it has been linked to impaired quality of life. In this context it is worth noticing that symptoms of anxiety may exacerbate subjective distress and reduce overall functioning (27). Additionally, depression and anxiety are associated with increased morbidity, cardiac events and all-cause mortality (31–33).

The association between mental health and cardiac disease also involves behavioural mechanisms. Patients with anxiety and depression are more likely to engage in unhealthy behaviours, including suboptimal dietary choices, smoking, drug and alcohol abuse, poor compliance with treatment regimens, poor sleep patterns and physical inactivity (22). Furthermore, anxiety and depression act as barriers to participation in and adherence to CR programmes (34). Managing these behavioural factors requires active behavioural changes, which may pose a considerable challenge, especially for patients grappling with anxiety and depression (35).

Predictors of anxiety and depression in patients with cardiac disease are numerous, comprising clinical and socio-demographic factors alike. Both anxiety and depression are associated with female gender, lower educational level, living alone, a high number of comorbidities and physical inactivity. Anxiety tends to be more common among individuals in younger age categories, whereas depression tends to rise as people get older. Furthermore, a connection has been established between depression and current smoking, central obesity and self-reported diabetes (36,37). Additionally, a history of depression and financial strain are predictive of anxiety or depression (26).

Psychological interventions for anxiety and depression

Given the significant impact of anxiety and depression on cardiac health outcomes, it is important for healthcare providers to screen patients with cardiac disease for these conditions and to provide appropriate treatment and support as needed. Treatment may include medications, psychotherapy, lifestyle changes or a combination of these approaches, depending on the individual patient's needs and preferences.

In 2020, the European Association of Preventive Cardiology published a position paper emphasising the importance of addressing psycho-social issues, such as anxiety and depression, as a core component of CR (7). Standardised questionnaires, such as the Hospital Anxiety and Depression Scale (HADS), are used to identify patients with these conditions (38,39). However, HADS primarily focuses on the psychic symptoms of mood disorders, omitting any physical

symptoms that may be mistaken for physical illness (40). Unfortunately, studies indicate that anxiety and depression are often underdiagnosed and undertreated in patients with cardiac disease (41), despite clear evidence of their association with cardiovascular health (13). Currently, treatment options are limited for patients with cardiac disease experiencing psychological distress, and it remains unclear which is the optimal treatment approach.
In 2017, a Cochrane review analysed 35 studies comprising 10,703 patients with CAD randomly assigned to multifactorial psychological interventions. The review concluded that such interventions may have a positive impact on cardiac mortality, anxiety and depression. However, the evidence suffers from some limitations as the included trials were very small and the participants included were both with and without psychological disorders. Further the interventions were multifactorial, indicating a need for further research on specific psychological interventions (42). Mindfulness has been used to address the psychological impact of CAD but has yielded mixed results in terms of effectiveness. While it has been shown to reduce symptoms of depression and stress, it has not been found to significantly impact symptoms of anxiety. Additionally, the positive effects of mindfulness have been observed only in the short term, and high-quality studies on its long-term impact are currently lacking (43,44).
As outlined in a review conducted by Reavell et al. (45), CBT has proven successful for addressing anxiety and depression in individuals with heart disease. Thus, in-person therapy sessions were pivotal in optimising treatment effectiveness, with a minimum of four sessions deemed necessary to yield positive results. Furthermore, a recent meta-analysis, encompassing 22 RCTs involving nearly 5,000 CAD patients, demonstrated that CBT significantly reduced anxiety and depression levels, while simultaneously improving HeartQoL (46). These interventions were administered in various ways; yet a majority were tailored to individual needs and comprised over ten sessions, spanning a duration of more than 12 weeks. Typically, these interventions were administered by a therapist or psychologist. However, these interventions are typically not accessible or standardised for implementation in a CR setting.

A more affordable and widely accessible variant of CBT is internet-based CBT (iCBT). In a comprehensive U-CARE study involving 239 participants, iCBT demonstrated no significant reduction in anxiety and depression compared with conventional care methods (47). A recent review delved into the effectiveness of internet-based psychological interventions, specifically focusing on iCBT for patients struggling with both cardiac disease and comorbid anxiety and depression (48). It is worth noting that the studies encompassed by this review exhibited notable variations in terms of sample size, study designs and intervention contents. This diversity

underscores the imperative need for more extensive research involving large-scale studies and interventions tailored to address specific needs. ICBT present several evident advantages, including allowing patients to engage with therapy conveniently from their own laptops or smartphones within the comfort of their own homes. This convenience may potentially enhance the integration of therapy into their daily lives. However, it is important to acknowledge that prior studies have reported challenges such as low treatment adherence and high participant drop-out rates. These factors may have contributed to the absence of a significant difference between the intervention and control groups. This phenomenon underscores the importance of ensuring that patients targeted for these interventions possess the requisite skills and competencies for effective participation, including proficiency in using computers and related technologies (48). Possessing skills and competences to participate in internet-based interventions is an eligibility criterion that may exclude certain patients, whereas others may require in-person interactions to derive maximum benefit from iCBT interventions.

A recent study conducted by Wells et al. (49) investigated the impact of an intervention with six group-based metacognitive therapy sessions. The sessions were delivered face-to-face by physiotherapists, CR nurses and occupational therapists trained to provide this therapy. The metacognitive therapy was given in addition to standard CR in 332 patients with cardiac disease exhibiting symptoms of anxiety or depression, defined as a HADS score of 8 or above. The intervention was conducted in a single-blind, parallel, controlled multicentre RCT. The primary outcome measured was change in HADS score after four months. The study found a significant improvement in the score, which was sustained at 12 months.

Summary and rationale for this thesis

As previously mentioned, anxiety and depression frequently manifest among individuals with cardiac diseases, and their impact on overall health may be substantial. Unfortunately, psychological distress often does not receive the same degree of attention as other preventive cardiology measures, such as physical activity. It is essential to recognise that anxiety and depression may impede patients' capacity to make positive behavioural changes and adhere to their CR programme. This may, in turn, result in a decline in the individual's quality of life, decreased ability to return to work and an elevated risk of recurrent cardiac events, morbidity and mortality.

Despite a wealth of evidence underpinning the efficacy of CBT in alleviating symptoms of anxiety and depression, it is frequently perceived as time intensive and incompatible with a

standard CR programme. Furthermore, it is worth noticing the conspicuous absence of well-structured RCTs assessing the effectiveness of concise, group-based CBT interventions delivered by skilled nurses as part of CR. This intervention targets patients newly diagnosed with CAD and/or those who have undergone surgical treatment for valvular heart disease (VHD) and are presenting with symptoms of anxiety and depression.

We hypothesised that integrating a group-based CBT intervention in the framework of CR significantly reduce psychological distress among patients with cardiac diseases.

Aims

Paper I

The study aimed to develop an efficient and feasible model using intensive group-based CBT to address psychological distress in patients recently diagnosed with CAD and/or those who had undergone surgical treatment for VHD and are concomitantly experiencing psychological distress.

Paper II

The main aim was to evaluate the effect of brief group-based CBT integrated with CR and delivered by nurses to reduce symptoms of anxiety, depression or both in patients recently diagnosed with a new CAD event and/or those who had undergone surgical treatment for VHD. The main secondary outcomes were adherence to CR, retention in the workforce and lower re-admission rates.

Paper III

The study aimed to describe patients' experiences with brief group-based CBT provided as part of their CR.

Methods and design

This section initially outlines the overall design, outcomes and data of the thesis. The more specific methods used in each study are described in separate sections.

A mixed methods, embedded experimental design was applied to evaluate the effect of brief group-based CBT integrated into CR and to describe patients' experiences with the intervention (Figure 1) (50,51). The premise of the mixed methods design is that a single data set may prove inadequate and that distinct research questions require diverse methodological approaches (52). In Study I, which was an RCT, we made use of patient-reported outcome measures (PROMs) to evaluate the effect of a change in psychological distress measured before and after group-based CBT. However, PROMs do not provide nuanced insight into patients' experiences of participating in group-based CBT interventions. Therefore, in Study II, we chose to conduct a qualitative study to facilitate the expression of patients' experience. The quantitative data from the HADS were used to answer the primary question. The qualitative data from the interview study were integrated following the intervention to elucidate the patients' experiences regarding participating in group-based CBT. Therefore, the design may be characterised as an embedded-design experimental model. The rationale for this approach was that the combination of the two data sets provides a more comprehensive understanding of the research question than would have been obtained with a single data set. Thus, the results from the analysis of the qualitative data (QUAL) nuance and explain the statistical results from the RCT (QUAN) (52).

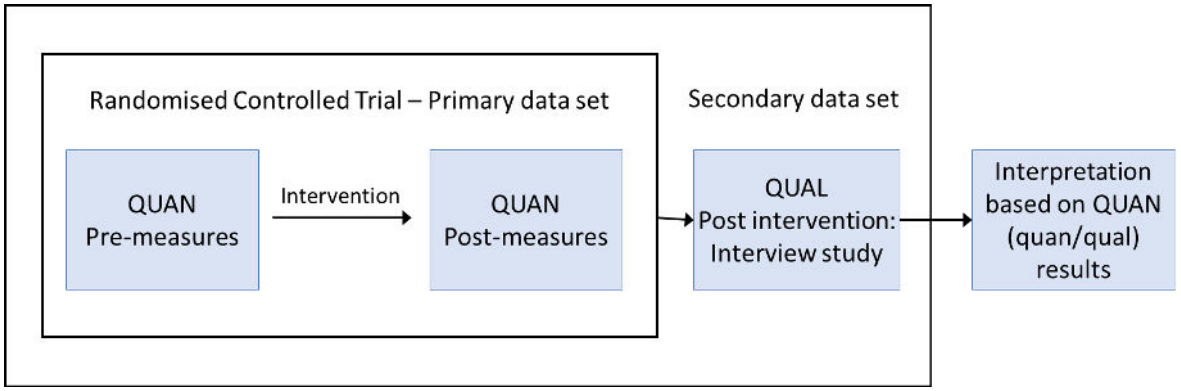

Figure 1: Outline of the study design illustrating the combined use of qualitative and quantitative data.

Quantitative data

The assessment of anxiety and depression symptoms in patients with cardiac diseases primarily relies on standardised questionnaires focused on patient-reported outcomes (PROs) (53). PROs are designed to explore patients' subjective perceptions of relevant phenomena, including disease-specific symptoms, such as anxiety and depression, and their HeartQoL (53). Typically, PROs are standardised self-administered questionnaires yielding numerical scores providing quantifiable results. When using PROMs, it is crucial to select instruments that have been demonstrated to produce valid and reliable results, ideally only PROMs that have been tested within the specific language and population for which they are intended. When employing Patient-Reported Outcome Measures (PROMs), it is essential to choose assessment tools that have been proven to yield accurate and consistent outcomes. Ideally, opt for PROMs that have undergone validation and testing within the particular language and demographic group for which they are intended (52).

The quality of a PROM is typically evaluated based on its validity, reliability and, if applicable, its responsiveness to changes over time. Validity pertains to whether the questionnaire effectively measures what it is intended to measure, whereas reliability addresses how reproducible the questionnaire data are (53).

In our RCT, we employed the PROM termed HADS, which was deemed suitable for routine CR screening for anxiety and depression by clinicians (39,40). HADS was chosen because of its documented validity and reliability, making it a robust tool for assessing these psychological aspects in patients with cardiac disease.

Qualitative data

Qualitative research is widely applied to access patients' views and experiences. In this study, a qualititative approach was deemed appropirate to gain insight into patients' experinces of participating in group-based CBT. We therefore interviewed 11 people who had participated in group-based CBT. The interviews were conducted by the second author (a reaserch nurse) experienced in working with individuals living with heart disease. The interview material was transcribed and interpreted using qualitative content analysis. We found that the qualitative content analysis was a suitable method to address the research question because of its utllity for exploring multifaceted, sensitive phenomena, which are often inherent in the field of nursing. Additionally, this method was chosen as no previous studies had explored this particular phenomenon (54). The specifics of our content analysis are further described on page 38. Briefly,

we used manifest content analysis, which provides a phenomenological description of the data (55).

Study I: Randomised clinical trial: Study design and outcome (Paper I+II)

Study design

As written in paper II study I was a multicentre, open-label, prospective, randomised trial with three and six months of clinical follow-up comparing group-based CBT in addition to usual CR to CR alone. The patients were recruited at three hospitals (Bispebjerg and Frederiksberg Hospital, Hvidovre and Amager Hospital, and North Zealand Hospital) in Denmark (56). The randomised controlled design was applied and reported according to the CONSORT guidelines for non-pharmacological trials (57).

Participants and data collection

Before this RCT, we conducted a pilot study in our CR unit with 232 consecutive patients. We screened the patients with HADS and found that the proportion of patients with a HADS score of 8 (for HADS-Anxiety (HADS-A) and/or HADS-Depression (HADS-D)) or above was highest (32%) in the group of patients below 65 years who were still working.

We screened consecutive patients with CAD and/or surgically treated VHD who had been referred to CR for eligibility to participate in the study at their first visit, using the following in- and exclusion criteria (56):

Inclusion criteria	Exclusion criteria
• Referred to CR and accepting CR, patients with a new CAD event [ST or non-ST-elevation MI and/or revascularised (percutaneous coronary intervention or coronary artery bypass graft)] within three months before their first visit at the CR and/or surgically treated VHD within three months before their first visit • A HADS score ≥8 for HADS-Anxiety (HADS-A) and/or HADS-Depression (HADS-D) • Age <65 years or, if >65 years who remain occupationally active • Able to speak and understand Danish	• Left ventricular ejection fraction <35% • Other serious comorbidities expected to have a serious impact on life expectancy • Known abuse of alcohol or euphoric drugs • Known more serious psychopathology such as schizophrenia, bipolar disorder, severe personality disorder and treatment with psychoactive drugs, including selective serotonin reuptake inhibitors

Recruitment, randomisation and blinding

Patients meeting the eligibility requirements and consenting to participate received comprehensive written and verbal information from a study nurse. Afterwards, they proceeded to sign an informed consent document before randomisation. To uphold objectivity, randomisation was conducted by an impartial researcher with no affiliation with the trial and no knowledge of the specific patient characteristics.

For the randomisation process, we used the STATA II software with the Ralloc programme. This programme employed permutation techniques, generating random block sizes of 2, 4 and 6 to ensure proper participant allocation to the study groups.

Method used to define psychological distress

The HADS is recommended for use in patients with cardiac disease for identification of psychological distress in the form of symptoms of anxiety and depression (11,32,58–60). HADS is a 14-item questionnaire designed to evaluate levels of anxiety and depression among patients who are not primarily diagnosed with psychiatric conditions but are struggling with medical illnesses. The 14 items are divided into two subscales, HADS-A and HADS-D, each consisting of seven questions assessing anxiety and depression, respectively (38). The scale primarily

targets psychological aspects of mood disorders and intentionally excludes physical symptoms that could be mistaken for physical illness. This characteristic is beneficial in populations affected by cardiac diseases as symptoms like heart palpitations, dizziness, or shortness of breath might be directly associated with the underlying cardiac condition rather than an underlying mood disorder (40). A threshold of ≥8 on each subscale was used to determine the presence of any mood disorders as it is considered to be the cut-off for mild clinical symptoms. Moreover, this cut-off yields the optimal sensitivity and specificity for both HADS-A and HADS-D for identifying clinical caseness (38). The validity, internal consistency and reliability of the scale are good (38). This was confirmed in a large sample of Danish patients with cardiac disease (40).

Health-related quality of life

Patients who experience psychological distress tend to have a lower quality of life. To monitor these patients' quality of life, a validated questionnaire coined the HeartQoL disease-specific questionnaire was used. This questionnaire measures the HeartQoL in patients with heart disease and consists of 14 items. The HeartQoL provides two subscales: a physical subscale with 10 items and an emotional subscale with four items. The subscales are scored from 0 to 3, with higher scores indicating a better quality of life (61,62).

Usual care

Participants followed our usual CR programme. The CR programs were slightly different (first visit lead by a nurse or a consultant cardiologist) across the three hospitals but all offered the below core components (see Table 1) further described in paper II (56).

Table 1: The cardiac rehabilitation programme at the three hospitals

Hospital	Bispebjerg/Frederiksberg Hospital	Hvidovre and Amager Hospital	North Zealand Hospital
First visit to CR	Physician	Nurse	Nurse
Group	• Training x 2 /week for 8 weeks • Education on heart disease, training, and risk factor management	• Training x 2 /week for 8 weeks • Education on heart disease, training, and risk factor management	• Training x 2 /week for 8 weeks • Education on heart disease, training, and risk factor management
Individual	• VO_2 peak • Session with a nurse and up-titration of medication • Session with dietician • Session with cardiologist	• VO_2 peak • Session with a nurse and up-titration of medication • Session with dietician • Session with cardiologist	• VO_2 peak • Session with a nurse and up-titration of medication • Session with dietician • Session with cardiologist

Vo2peak: Maximal Oxygen Consumption

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Intervention

CBT is a well-established, evidence-based psychotherapeutic approach drawing on clinical experience, theory, and research. It encompasses three distinct parts. The first part is rooted in behavioural therapy and focuses on modifying behavioural patterns. The second part centres on the relationship between thoughts and their impact on emotions, bodily sensations and actions, known as cognitive therapy. The third part of CBT emphasises the acceptance of thoughts and feelings (63). This part comprises acceptance and commitment therapy (ACT), metacognitive therapy and mindfulness-based therapy. In cognitive therapy, the emphasis is on identifying the patient's thoughts and behavioural patterns that contribute to current issues and impede functional well-being. By modifying these thoughts and behavioural patterns, positive changes in functioning and overall quality of life can be achieved (63,64). In ACT, the focus shifts towards accepting the present circumstances while committing to changing maladaptive behaviours. The purpose of thinking takes precedence to the specific content of thoughts.

CBT and ACT share common elements, such as their focus on the present moment and internal experiences. Both approaches equip patients with skills that may be applied across various contexts. Given these shared characteristics, integrating the two approaches may be beneficial. In

the present study, sessions 2, 3 and 5 were rooted in the concepts of changing thoughts and behaviours (CBT), whereas sessions 1 and 4 primarily incorporated ACT interventions (65).

Table 2: Overview of the psycho-educational group course

Session	Theme	Contents
1	Introduction to CBT and mapping of own values (individual values limited/affected by cardiac disease)	• A matrix (22) was used to clarify which values were important to the patient • Actions and barriers concerning alignment with values were identified
2	Anxiety and anxiety reduction techniques	• Psychoeducation focusing on anxiety and its physiology, especially the role of the sympathetic nervous system • The anxiety circle was reviewed • Introduction to exposure and various types of strategies to cope with anxiety
3	Behavioural analysis (awareness of consequences of own behaviour)	• Dealt with the analysis and consequences of current inappropriate behaviours in the short and long term
4	Concerns and strategies for dealing with concerns	• Recognising one's own thinking including worries and their influence on behaviour. • Explaining strategies including acceptance and diffusion to achieve change
5	How to cope with future psychological distress by using CBT strategies	• Balancing demands and strengths with an emphasis on committing to nourishing and long-term strategies.

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As described in paper I (66) the course was facilitated by an experienced cardiac nurse and imparted as a single weekly scheduled 2h session. Each group consisted of three to four patients. The group-based CBT intervention followed a structured manual for each session with integrated homework assignments and a feedback session for participants. Moreover, the nurses

administering the intervention received feedback from the psychologist. The nurses had undergone CBT training conducted by a specialised CBT psychologist, followed by supervised training to deliver the intervention to an initial test group. They also had access to ongoing supervision from a psychologist throughout the trial. In this trial, the primary goal of group-based CBT was to provide support to patients, enabling them to effectively manage their heart disease.

First session

Experiencing a severe illness frequently triggers deep reflections on life, mortality and the intrinsic value of certain aspects. Consequently, the initial session aimed to elucidate the patient's values and actions that resonated with those values. It also analysed the challenges that impeded the patient from behaving in accordance with his or her values and established how their actions aligned with their core priorities.

For instance, a patient with a cardiac disease may prioritise their health as a core value, which translates into adhering to the dietary recommendations provided by a dietitian and maintaining an exercise regimen. Their difficulties may arise from the fear of experiencing another heart attack, which may potentially lead to a lack of physical activity. As part of the session, patients were assigned homework, which involved completing a matrix (see Figure 2) (67) to further explore these aspects.

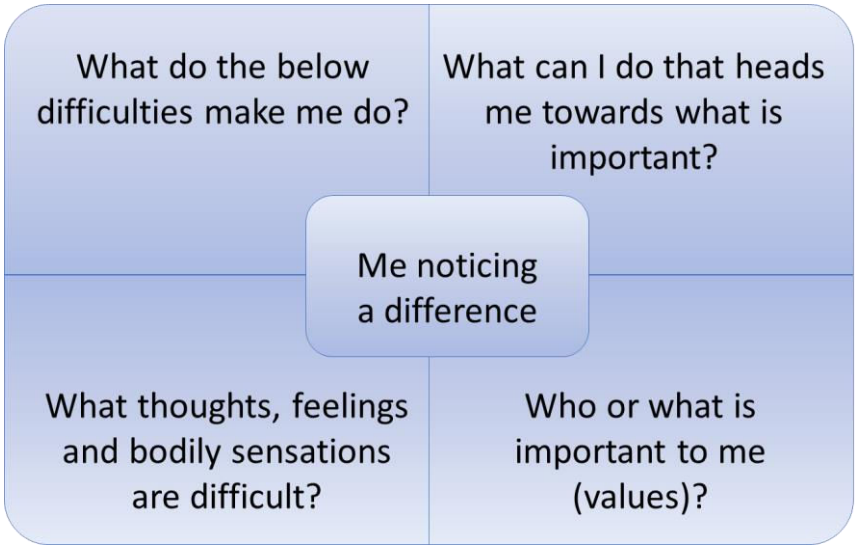

Figure 2: The matrix shows the significance of discovering one´s values to overcome difficulties Reprint from Holdgaard et al. 2021 (66) with permission from Springer Nature

Second session

Following a heart attack, patients commonly experience apprehension regarding the risk of suffering another cardiac event. Hence, the focus of the second session revolved around addressing anxiety. Initially, it is crucial to emphasise that anxiety is a natural emotion and a normal response to perceived threats. However, it becomes problematic when anxiety is associated with an "imagined" danger or escalates into an "excessive" fear.

The session delved into a comprehensive exploration of the physiology of anxiety. This enabled patients to recognise the physical manifestations of anxiety and differentiate these manifestations from symptoms of a heart attack. By understanding the underlying principles, the session proceeded to examine the concept of the anxiety circle. The anxiety circle illustrates how perceived threats may trigger physical reactions and catastrophic thoughts, often leading to avoidance behaviours or engaging in safety precautions.

While avoiding anxiety-inducing situations may temporarily alleviate anxiety, it ultimately reinforces the expectation of anxiety and instils fear of encountering similar situations in the future (see Figure 3). Thus, to conclude this session, various strategies were introduced highlighting the importance of gradually exposing oneself to challenging situations to effectively manage anxiety levels. As a homework assignment, patients were encouraged to initiate a process of gradual exposure and apply the learned strategies to their everyday lives (68).

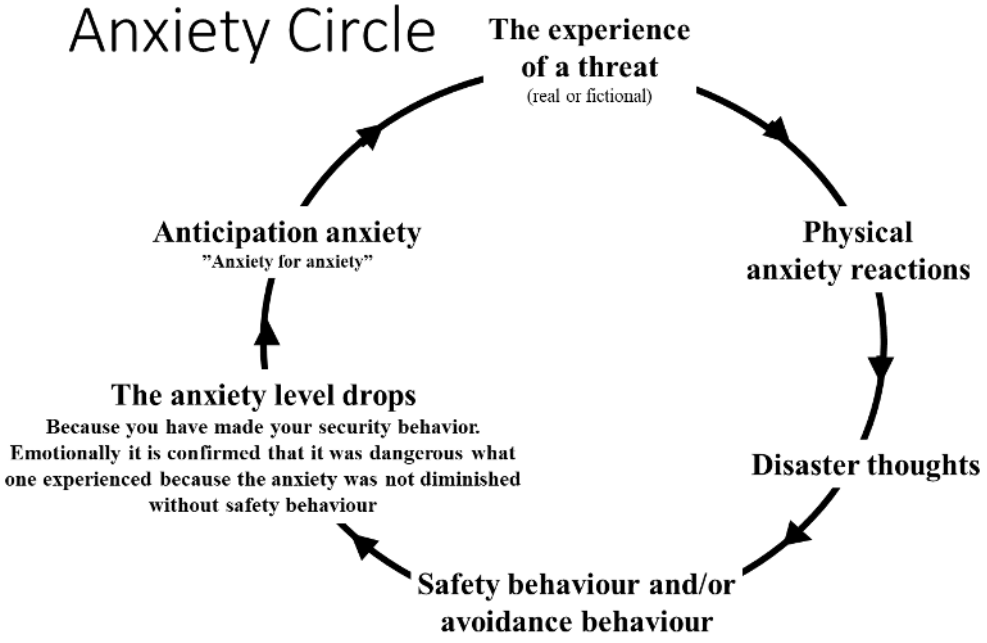

Figure 3: The circle of anxiety demonstrates the correlation between thoughts, feelings and behaviour. Inspired by Esben Hougaard. Reprint from Holdgaard et al. 2021 (66) with permission from Springer Nature

Third session

After being diagnosed with CAD and undergoing surgical treatment for VHD, several lifestyle adjustments are typically recommended, including dietary modifications and initially reducing work hours for a certain period of time. However, adopting and integrating these new habits into daily life can be challenging. Hence, the focus of the third session revolved around analysing current behaviours and understanding their consequences.

For instance, consider a patient who derives satisfaction from their work, leading them to dedicate 50 hours per week to their job. While this may bring them short-term contentment and happiness, it could also hinder their ability to allocate sufficient time for recovering from their illness. This lack of rehabilitation may have significant long-term implications for their health.

As part of the session, patients were assigned homework in the form of completing a "behavioural analysis" form (see Figure 4). This activity encourages individuals to reflect on their behaviours, examine their consequences and gain insights into how their choices may impact their well-being in the short and long term.

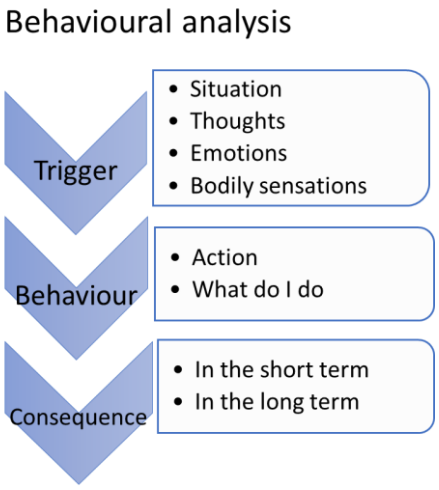

Figure 4: Behavioural analysis demonstrating the consequences of behaviour and showing what leads to the behaviour. Reprint from Holdgaard et al. 2021 (66) with permission from Springer Nature

Forth session

CAD and VHD often trigger various concerns that may potentially restrict patients. Worrying is a cognitive process that can be constructive for problem-solving, but it may also cause excessive rumination. Therefore, the fourth session focused on fostering an understanding of one's own thinking patterns and the impact they have on behaviour in order to cultivate more constructive

behaviours. During this session, patients were provided with a comprehensive explanation of several strategies, including acceptance and diffusion techniques, that involve distancing themselves from distressing thoughts. These strategies aim to allow individuals to recognise their own thinking patterns and gain control over them, thereby facilitating a shift towards more constructive behaviours.

As a homework assignment, patients were encouraged to be mindful of instances when they find themselves pondering or worrying. If such instances occurred, they were advised to apply some of the strategies discussed during the session (69).

Fifth session

The final session concentrated on exploring the patient's strengths to their fullest potential. It highlighted the importance of striking a balance between the demands they face and the strengths they possess. In this endeavour, the significance of committing to sustainable and nourishing strategies is emphasised, e.g., employing techniques like breaking down a large task into smaller, manageable steps.

In the latter part of this session, the matrix introduced in the first session was revisited and explored in greater depth. This served to assess whether the participants had modified their strategies and gained new comprehension since the beginning of the programme. The session concluded with valuable feedback on the entire process, which contributed to a more comprehensive understanding of the entire process for both participants and facilitators (70,71).

Outcomes

The primary outcome was change in psychological distress measured by the HADS total score from baseline to a three-month follow up in the intervention group compared with the usual care group.

Secondary outcomes were measured at the three- and six-month follow-ups: HADS-A, HADS-D, adherence to CR, return to work, HeartQoL and risk-factor management which are described in detail in paper II (56).

We evaluated instances of readmission due to cardiac issues, overall mortality, both fatal and non-fatal MI and coronary artery revascularisation procedures occurring within 12 months following randomization. This is described in detail in Paper II (56). We conducted an evaluation on several aspects relevant to heart-related outcomes occurring within a year after randomisation. These included cardiac readmissions, all-cause mortality, fatal and non-fatal MI, and coronary artery revascularisation procedures.

Cardiac readmissions encompassed any subsequent visits to the emergency department or cardiac departments due to cardiac symptoms. It is important to note that readmissions to other departments for somatic diseases were not considered in this assessment. However, admissions to psychiatric departments were evaluated separately.

To ensure accuracy and impartiality, cardiac readmissions were identified by analysing electronic health records. Additionally, an independent cardiologist, who was unaware of the treatment intervention, reviewed and verified these readmissions.

Sample size and power calculations

The primary focus of this study was to assess change in HADS scores after three months. A significant and meaningful difference between the groups would be a decrease in the overall score of minimum 2 points. In a previous study (72), it was observed that the changes in HADS scores within each group followed a normal distribution pattern, with a standard deviation (SD) of 2.5. Another study estimated a minimal clinically important difference (MCID) of change in HADS to be 1.7 points, which may serve as an indicator of treatment success (73). However, for this study, we opted for a more conservative estimate and used an SD of 4. Based on these assumptions and aiming for a type 1 error risk of 0.05 and a statistical power of 0.8, a total of 64 patients were enrolled in each group. By employing an SD of 4, we achieved 80% power to detect a difference in the change of HADS score (delta HADS) of 2.3 or higher between the two groups (66). Considering the possibility of patient dropouts, which is common in this kind of trial, we increased the total number of patients by 15%, resulting in a final sample size of 148 patients as described in the previously published protocol (66).

Furthermore, as described in Study I, we assembled a non-randomised group of consecutive patients who met the inclusion and exclusion criteria. Importantly, these patients displayed no indications of psychological distress, as indicated by HADS-A and HADS-D scores of less than 8. These patients formed a background group, receiving usual CR with re-evaluation after three and six months. The purpose of including this group was to follow the natural course, including any subsequent development in psychological distress during the follow-up period (66).

Statistical analysis

We employed descriptive statistics to compare baseline data between the intervention group and the control group, and between the group with psychological distress and the group without. We rigorously assessed the normal distribution of all continuous variables, utilising both visual examination and the Shapiro-Wilk test. Variables conforming to a normal distribution were

subjected to comparison through the t-test or ANOVA. The results were presented as mean ± SD. Data not following a normal distribution were presented as medians (interquartile range (IQR)), using the Kruskal-Wallis test. Categorical variables were compared using Pearson's chi-squared test. We used linear regression mixed models, adjusting for the baseline HADS value, to analyse the main outcome, i.e. the change in total HADS from baseline to three months. We also included the centre (three sites), testing for treatment-centre interaction.

Secondary outcomes, including HeartQol and other continuous measures, were also analysed in this way. Dichotomised secondary outcomes (e.g., adherence to CR, return to work) were assessed using logistic regression while considering the treatment centre.

We used Kaplan Meier curves and time-to-event analyses (Cox regression), while adjusting for centre, to compare clinical events (number of re-admissions within 12 months from randomisation) between groups.

The study followed the intention-to-treat principle. Sensitivity analyses encompassed data from all time points for patients lost to follow-up. A per-protocol analysis was planned but not needed. Missing data for the primary outcome were minimal, and imputation methods were used when necessary. Additional analyses were conducted after excluding patients with missing data. Stata SE 17 v17.0.116. (StataCorp LP) was used for all analyses. The level of significance was set at $p < 0.005$.

Ethical considerations

The trial was conducted in accordance with the Declaration of Helsinki (74). Each patient provided informed consent after they had received written and oral information. Before trial commencement, approval was obtained from the Danish Data Protection Agency and the regional ethics committee (H-16042832). The trial is registered with www.ClinicalTrials.gov (NCT04254315).

Study II: Qualitative interview study (Paper III)

Study design

The study "The experience of group CBT among patients with heart disease and psychological distress" was a qualitative interview study. The patients had participated in a large RCT, which compared usual out-patient CR with CR supplemented by brief nurse-led group-based CBT. This study was based on semi-structured interviews with 11 patients who had participated in the group-based CBT intervention (56).

Participants

To gain a broad understanding of the experience of participating in group-based CBT, a purposive sample (75) of 20 patients who had completed the intervention were invited to participate. The nurses who facilitated the group therapy helped the researcher identify relevant patients. Variation was sought in terms of age, gender, marital status, education, geography and heart diagnosis (see Table 3). The interview was conducted within a month after the patients' group-based CBT had concluded. After 11 interviews, an appropriate amount of data had been obtained to answer the research question (75).

Table 3: Patient characteristics

Patient no.	Gender	Age	Married/ Cohabiting	Diagnosis
1	Male	59	-	STEMI + PCI
2	Female	58	+	NSTEMI + PCI
3	Male	61	-	NSTEMI + PCI
4	Female	52	+	STEMI + PCI
5	Female	39	-	NSTEMI + PCI
6	Male	56	+	NSTEMI + PCI
7	Male	56	-	STEMI + PCI
8	Male	55	-	NSTEMI + PCI
9	Male	40	+	NSTEMI + PCI
10	Male	64	-	STEMI + PCI
11	Male	41	+	Heart valve disease

Abbreviations: NSTEMI: non- ST-elevation myocardial infarction. PCI: percutaneous coronary intervention. STEMI: ST-elevation myocardial infarction

Data collection

Following an interview guide with open-ended questions (Appendix IV) (75), we conducted the interviews to offer participants an opportunity to express their experience of participating in group-based CBT. The gold standard for conducting an interview is in-person interviews, where body language, facial expressions and other non-verbal social signals may be observed by the interviewer (76). Furthermore, a physical meeting may enhance the possibility of creating a safe and comfortable environment that helps the participant to share views and experiences relating to the research topic. However, due to Covid-19 restrictions, it was not possible to conduct the semi-structured interviews in person. Instead, the interviews were conducted using videoconferencing by Facetime and Skype, which made it possible to see each other despite physical distance. Use of video-conferencing is considered a valid and trustworthy alternative to traditional face-to-face interviews (76). The interviews were audio recorded and transcribed verbatim.

Qualitative content analysis

Content analysis is a widely recognised research method in the field of nursing (77–80). It is a highly adaptable technique that is sensitive to the content being analysed. The goal of content analysis is to provide a concise and extensive description of a particular phenomenon. The result

of the analysis consists of categories that describe the studied phenomenon (54). When conducting qualitative data analysis, Graneheim and Lundman (81) suggested that researchers may choose to focus on either the manifest content or the latent content of the written text. When focusing on the manifest content, researchers identify the visible and readily apparent components of the text to maintain a distance and describe only what is actually present in the data material. Since this approach is useful for evaluation of a particular intervention, we conducted a manifest content analysis in Study II (82).

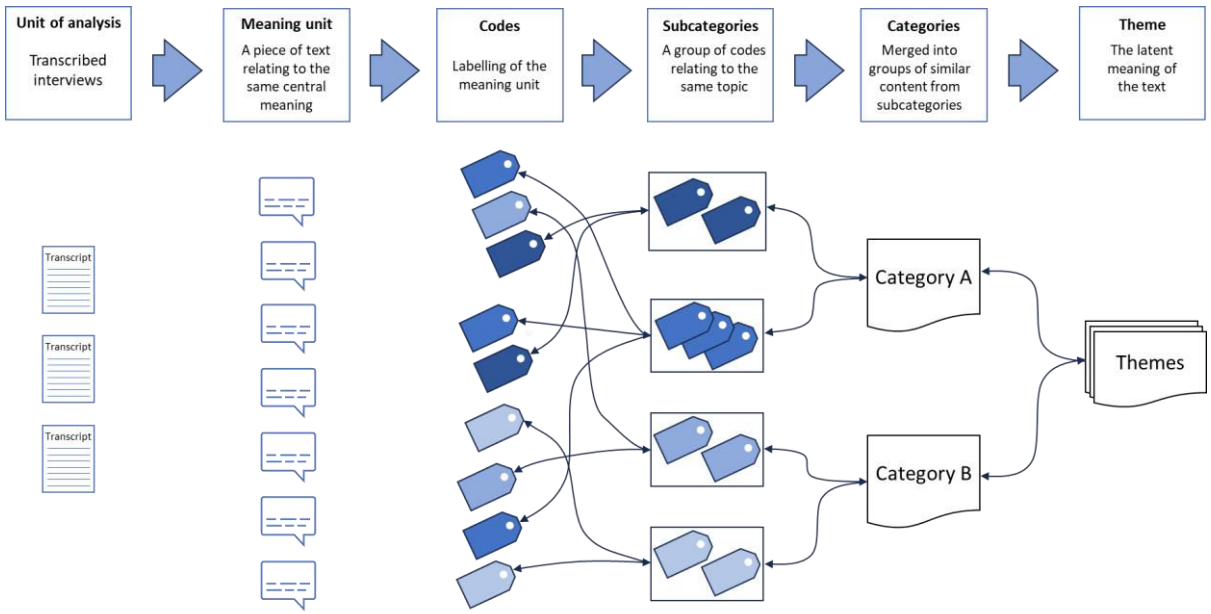

Figure 5: Illustration of qualitative content analysis inspired by Graneheim and Lundman (81). The figure is inspired by Lotte Helmark.

To initiate the analysis process, we thoroughly read the eleven transcribed interviews multiple times to become familiar with the data and form a general understanding of how patients experienced participating in intensive group-based CBT. Next, we divided each transcript into smaller segments of meaning, known as meaning units. The meaning units were condensed, while still retaining the essence of their content. Finally, we assigned each condensed meaning unit a code that represented a higher level of abstraction, allowing us to identify ´What the text says´.

The research team compared the codes to identify similarities and differences in patients' experiences. The codes helped structure the text into categories and sub-categories based on shared content. The next step involved uncovering the latent and interpretive content to determine ´What the text talks about´, with a focus on identifying themes that covered the

categories. Finally, the researchers interpreted the meanings and synthesised them into a cohesive whole. Throughout the process, the three authors (AH, FT and BM) discussed the emerging patterns and aimed to establish themes that fully represented patients' experiences of participating in the intervention. Furthermore, the team used quotes from the transcribed material to provide additional context for their findings.

Ethical considerations

Study approval was obtained from the Regional Research Ethics Committee (file number H-16042832) and the Danish Data Protection Agency. We followed the ethical principles of the Declaration of Helsinki (74). All study participants received written and verbal information about the study and gave informed consent. Participants were made aware that their personal details, including their names, would be anonymised to safeguard confidentiality. They were also informed of their right to withdraw from the study at any point without any impact on their subsequent treatment.

Results

In the following, a summary of the primary results from both studies is presented. The full text of the articles, providing additional detail, is enclosed in the appendices.

Results from study I: RCT study (Paper I and II)

The consort diagram of patient numbers and their flow is depicted in **Fejl! Henvisningskilde ikke fundet.**. Among the 1,532 patients with newly diagnosed CAD and/or surgically treated heart valve disease who were screened, 176 were eligible and were invited to participate in the RCT. Out of the individuals who displayed elevated depression scores and underwent assessment by a psychiatrist, eight individuals (constituting 25% of this group) were subsequently enrolled in the research. The remaining 57 patients with a HADS-D score of ≥11 and a Beck Depression Inventory (BDI) score of >17 was excluded for various reasons (see Figure 6). Additionally, a background group of 41 consecutive patients was recruited from the pool of 318 non-distressed patients to serve as a reference group during a shorter period (see Figure 6).

After randomisation, eight patients (12%) in the intervention group were excluded due to the COVID-19 lockdown (four patients) or loss to follow-up as they did not wish to continue in the trial or participate in follow-ups (four patients). Out of the total, 66 patients (89%) completed the intervention defined as attending four or all five sessions. During the three-month follow-up, two patients in the control group were lost to follow-up. At the six-month follow-up, three patients (5%) in the intervention group, four patients (6%) in the control group and none in the background group were lost to follow-up.

As written in paper II (56) the two groups with psychological distress, exhibited similar clinical and demographic characteristics, except for a significantly higher number of control group patients who underwent coronary artery bypass grafting (CABG) (see Table 4). The mean age of the participants was 54 years ± 8 years, with 67% being male and 92% having CAD as their primary event. The characteristics of the background group without psychological distress were similar to those of the groups with psychological distress, except for a higher proportion of male participants (85% versus 67%, $p = 0.03$), older age (57 ± 7 years versus 54 ± 6 years) and a higher percentage of patients who were employed before their event (98% versus 78%).

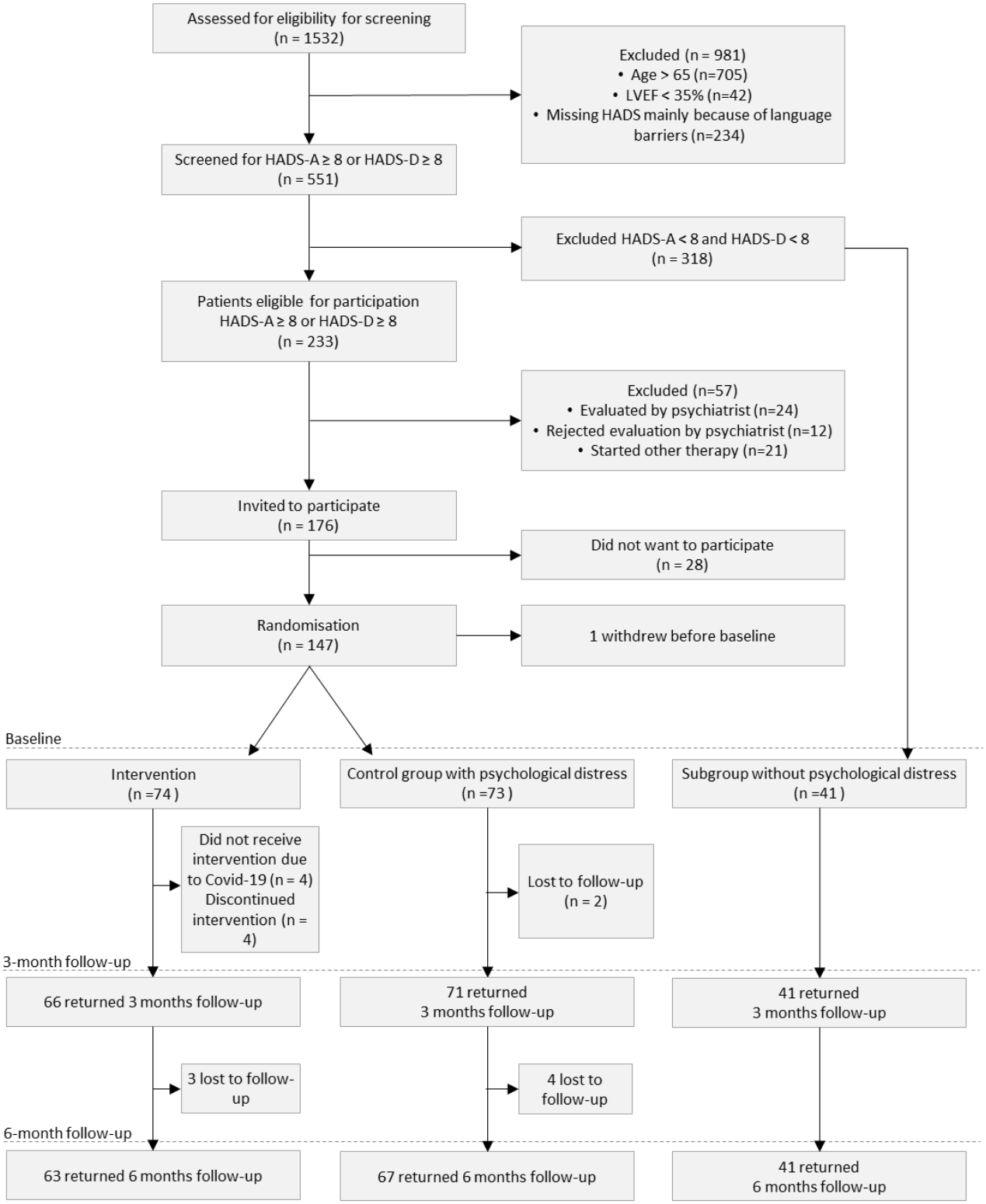

Figure 6: Patient recruitment, randomisation and follow-up in the study (Adapted from Paper II)

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Table 4: Demographic and clinical characteristics of the three groups at baseline

	With psychological distress		p-value	Without psychological distress
	Intervention (n = 74)	Control (n = 73)	Intervention/ Control group	(n = 41)
Male	45 (61%)	54 (74%)	0.079	35 (85%)
Age (years), mean (SD)	54 (8)	55 (7)	0.51	57 (6)*
BMI, mean (SD)	28,2 (5,2)	27.1 (5.0)	0.23	27.2 (4.8)
Living alone	24 (34%)	31 (43%)	0.26	9 (23%)
Education			0.43	
No education	6 (9%)	13 (18%)		7 (17%)
Short-term education	25 (37%)	22 (31%)		13 (32%)
Medium-term education	20 (29%)	19 (27%)		11 (27%)
Higher education	17 (25%)	17 (24%)		10 (24%)
Working status at event			0.077	
Working	60 (86%)	51 (71%)		40 (98%) *
Unemployed	8 (11%)	14 (19%)		1 (2%)
Sick leave	2 (3%)	7 (10%)		0 (0%)
LVEF	55 (50-60)	50 (50-60)	0.41	60 (50-60)
LVEF ≤ 40%	8 (11%)	7 (9%)	0.79	4 (10%)
Index event			0.069	
STEMI	25 (34%)	31 (42%)		13 (32%)
NSTEMI	29 (39%)	16 (22%)		9 (22%)
UAP	9 (12%)	8 (11%)		6 (15%)
Stable angina pectoris	4 (5%)	13 (18%)		12 (29%)
Heart valve disease	6 (8%)	6 (8%)		1 (2%)
Aorta aneurism	1 (1%)	0 (0%)		0 (0%)
PCI	52 (74%)	46 (63%)	0.15	30 (73%)
CABG	5 (7%)	14 (19%)	0.034	7 (17%)
Heart valve replacement				
Aorta	3 (4%)	3 (4%)	0.99	3 (7%)
Mitral	4 (5%)	3 (4%)	0.71	0 (0%)
NYHA				
≥ NYHA II	16 (23%)	8(11%)	0.057	6 (15%)
CCS				

CCS I	64 (93%)	66 (92%)	0.81	41 (100%)
Cardiac history prior to index event	6 (9%)	7 (10%)	0.77	3 (7%)
COPD	3 (4%)	0 (0%)	0.080	3 (7%)
Kidney disease	2 (3%)	4 (6%)	0.40	4 (10%)
Hypertension	31 (44%)	33 (46%)	0.85	22 (54%)
Dyslipidaemia	42 (59%)	43 (60%)	0.94	30 (73%)
Diabetes mellitus	10 (14%)	9 (13%)	0.78	6 (15%)
Family history	34 (50%)	32 (47%)	0.73	18 (45%)
Current smoker	12 (17%)	13 (18%)	0.76	5 (13%)
Medication				
Other antiplatelet medication	52 (75%)	51 (71%)	0.54	31 (76%)
Statin	61 (87%)	65 (90%)	0.55	38 (93%)
Beta blocker	35 (50%)	34 (49%)	0.87	15 (37%)
ACE inhibitor	28 (40%)	31 (44%)	0.66	12 (30%)
Diabetes medication	5 (7%)	8 (11%)	0.41	13 (33%)
VO_2peak (ml/kg/min), mean (SD)	23.0 (6.4)	23.9 (6.4)	0.44	25.9 (6.3)*
Physical activity (>30 min pr day)	2 (0 – 5)	2 (0 – 5)	0.33	3 (0 – 5)
HADS total, median[IQR]	17[14-21]	17[13-21)	0,86	5[3-7] *
HADS anxiety, median[IQR]	10[8-12]	10[8-13]	0,98	3[2-5] *
HADS depression, median[IQR]	7[5-10]	8[5-10]	0,76	1[1-3] *

Abbreviations: ACE: Angiotensin-converting enzyme. BMI: Body Mass Index. CABG: Coronary artery bypass grafting. CCS: Canadian Cardiovascular Society Angina Classification. COPD: Chronic obstructive pulmonary disease. HADS: Hospital Anxiety and Depression Scale. LVEF: left ventricular ejection fraction. NSTEMI: non- ST-elevation myocardial infarction. NYHA: New York Heart Association Functional Classification. PCI: percutaneous coronary intervention. SD: Standard deviation. STEMI: ST-elevation myocardial infarction UAP: Unstable angina pectoris.

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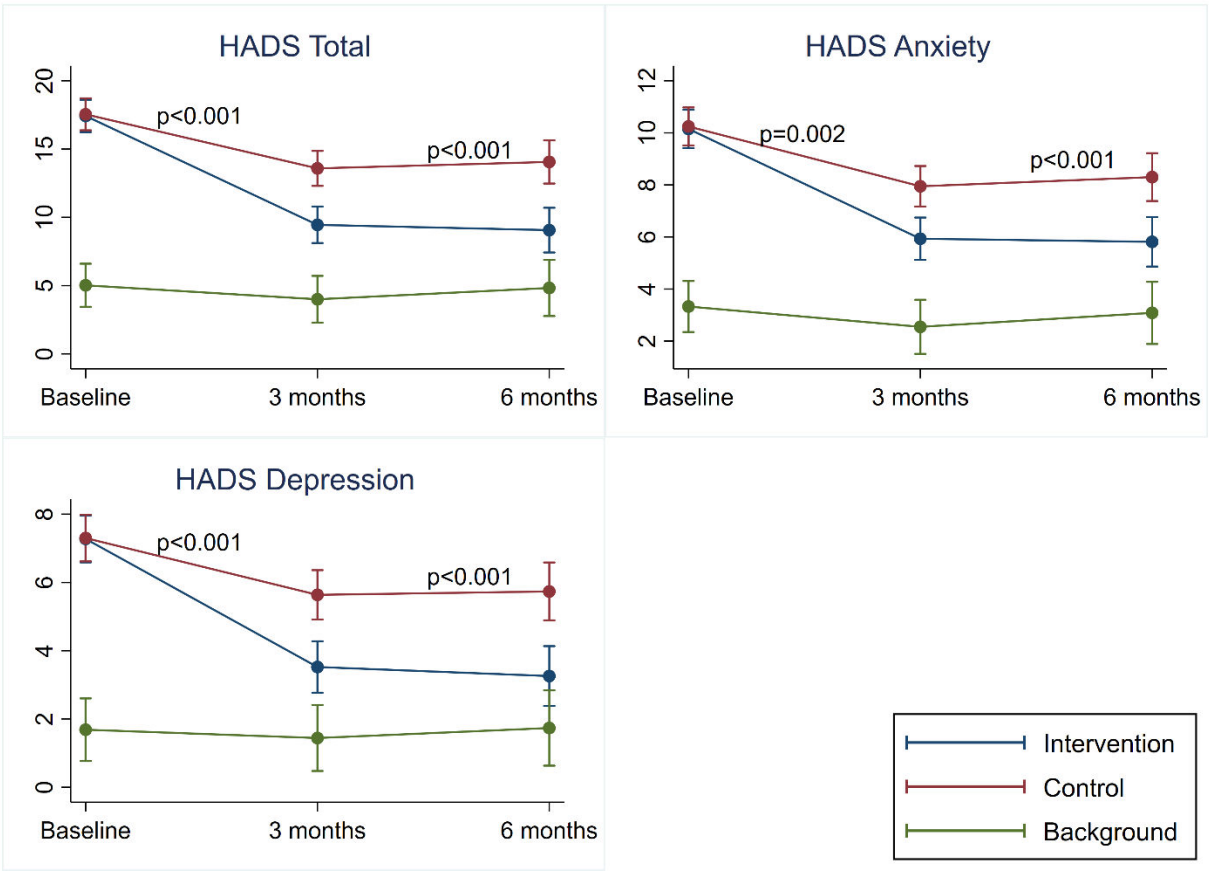

Abbreviations: HADS: Hospital Anxiety and Depression Scale

Figure 7: Change in hospital anxiety and depression scale score in the intervention, control, and background groups. Estimated total hospital anxiety and depression scale score, subscore on depression, and subscore on anxiety at baseline, and after three and six months for the three groups from mixed models adjusting for centre. P-values denote comparison of Δ hospital anxiety and depression scale between the intervention and control groups.

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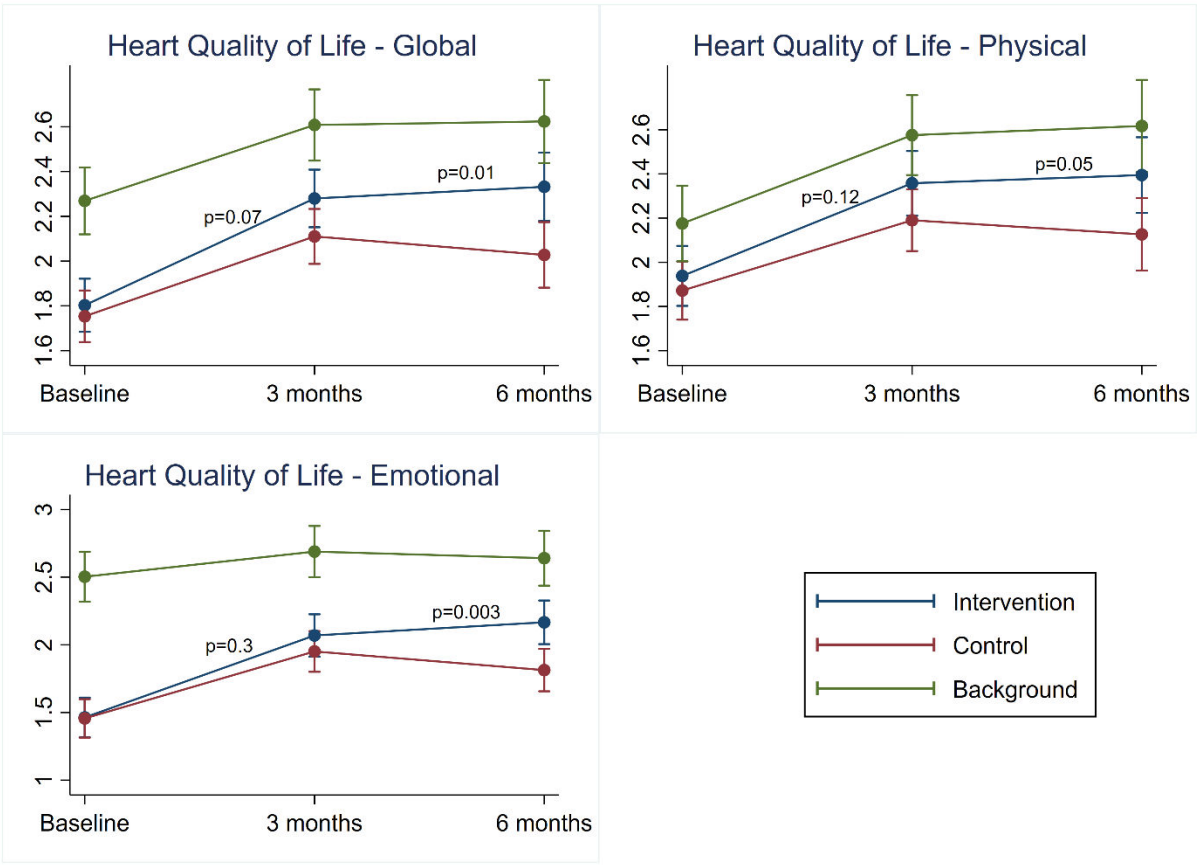

Abbreviations: HeartQol: Heart-related Quality of Life Questionnaire

Figure 8: Change in HeartQoL score in the intervention, control and background group. HeartQoL-global score, subscore on HeartQol-physical and subscore on HeartQol-emotional at baseline, and after three and six months for the three groups. P-values denote comparison of ΔHeartQoL between the intervention and control groups from mixed models adjusted for centre effect.

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Table 5: Change in risk factors in the intervention and the control group

	Baseline			3-month follow-up			6-month follow-up		
	Intervention n = 74	**Control n = 73**	**p-value**	**Intervention n = 66**	**Control n = 71**	**p-value**	**Intervention n = 66**	**Control n = 71**	**p-value**
HbA1c < 48 mmol/mol	52 (76%)	65 (93%)	0.007	54 (86%)	65 (92%)	0.28	56 (88%)	57 (90%)	0.59
BP < 135/85 mmHg	42 (61%)	44 (61%)	0.98	42 (65%)	47 (67%)	0.76	33 (52%)	40 (62%)	0.30
LDL < 1.4 mmol/l*	21 (30%)	25 (35%)	0.59	27 (42%)	30 (43%)	0.82	26 (41%)	30 (46%)	0.53
BMI	56(76%)	50(68%)	0.27	48(72%)	49(69%)	0.75	43(68%)	47(70%)	0.92
Current smoker	12 (17%)	13 (18%)	0.92	10 (15%)	8 (11%)	0.52	7 (11%)	8 (12%)	0.83
Physical activity 30 min > 4 days/week	23 (31%)	25 (34%)	0.68	34 (46%)	42 (58%)	0.16	42 (57%)	43 (59%)	0.79
Rehabilitation completed (training sessions > 80%)				51 (77%)	40 (56%)	0.010			

Abbreviations: BMI: Body Mass Index. BP: blood pressure. LDL: low-density lipoprotein.

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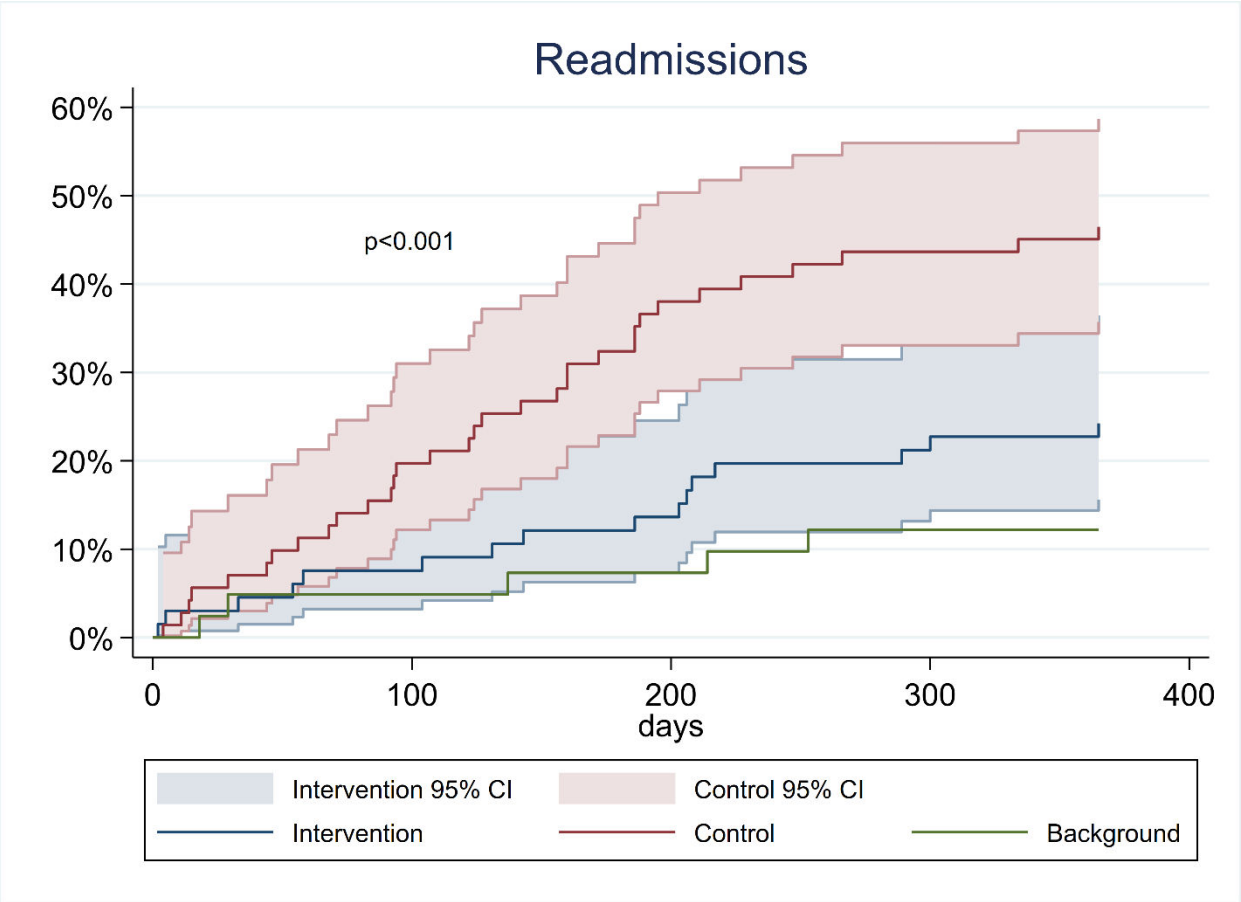
Outcomes

As written in paper II the average total HADS score at three months had improved by 8.0 (SD 5.6) in the intervention group compared with 4.1 (SD 7.8) in the control group (p for difference < 0.001). The anxiety and depression subscales also improved significantly more in the intervention group than in the control group (see Figure 7). These differences persisted at the six-month follow-up. We observed no differences in treatment effects between the three sites (no treatment centre interaction), between genders or between patients with CAD and VHD. However, the statistical power to detect these interactions was limited. The background group with no psychological distress experienced no significant changes in total HADS score at the three- and six-month follow-up. Comparable findings were obtained when analyzing data for patients lost to follow-up (56).

The HeartQol showed significant improvement in all three groups with no significant difference observed between the intervention group and the control group in terms of the global score or the physical/emotional sub scores at the three-month follow-up (see Figure 8). As described in Paper II a significant difference was found at the six-month follow-up in favour of the intervention group for the total and emotional scores but not for the physical score (p = 0.05). The background group had a significantly higher baseline HeartQol (p < 0.001), which remained higher than in the groups with psychological distress at both the three- and six-month follow-up. In regard to risk factor management, no significant differences were found between the intervention and control groups (see Table 3). However, we did find in favour a significant

difference in adherence to the physical training sessions and educational sessions of the intervention group (p = 0.02). Among the distressed patients, 78% in the intervention group and 67% in the control group had returned to work at the six-month follow-up (p = 0.11)(56).



Abbreviations: CI: confidence interval

Figure 9: Time-to-event curves for cardiac readmission in the intervention group compared with the control group at the 12-month follow-up change in hospital anxiety and depression scale score points. CI, confidence interval.

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At the 12-month mark, one patient in the intervention group had unfortunately passed away due to cancer. Among the patients in the intervention group, 16 individuals (25%) experienced one or more readmissions for cardiovascular issues. In the control group, the corresponding number was higher with 33 patients (49%) experiencing one or more readmissions (see Figure 9). When adjusting for centre, the hazard ratio for hospital admission in the intervention group compared with the control group was 0.43 (95% CI: 0.24-0.80), indicating a lower risk of hospitalisation in the intervention group. The between-group difference was driven primarily by a higher rate of emergency room visits, hospital admissions for angina and angiography in the control group.

However, no significant differences were seen in terms of MI or revascularisation. Furthermore, no significant interaction was found between treatment and gender. In the background group, only five patients experienced one or more cardiovascular readmissions. No fatal MIs were recorded, but two non-fatal MIs occurred (one in the control group and one in the background group). Other causes of readmission is showed in Table 6 below.

Table 6: Causes of readmissions

	Patients with distress		Patients without distress
Causes of acute cardiac readmissions	**Intervention group**	**Control group**	**Background group**
Acute coronary syndrome			
STEMI	0	0	0
NSTEMI		1	1
UAP	10	19	5
Subacute CAG	7	12	4
Revascularisation (PCI)	2	2	1
Emergency room only due to chest discomfort	15	22	4
Atrial fibrillation	1	2	0
Infections	0	1	0
A complication to CAG (Pseudoaneurysm)	0	1	0
Endocarditis	0	1	0
Psychological admissions	1	0	0

Causes of readmissions for the three groups at 12 months: Number of readmissions among the three different groups devided into different causes.

STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non-ST-segment elevation myocardial infarction, UAP: Unstable angina pectoris, CAG: coronary angiography, PCI: percutaneous coronary intervention

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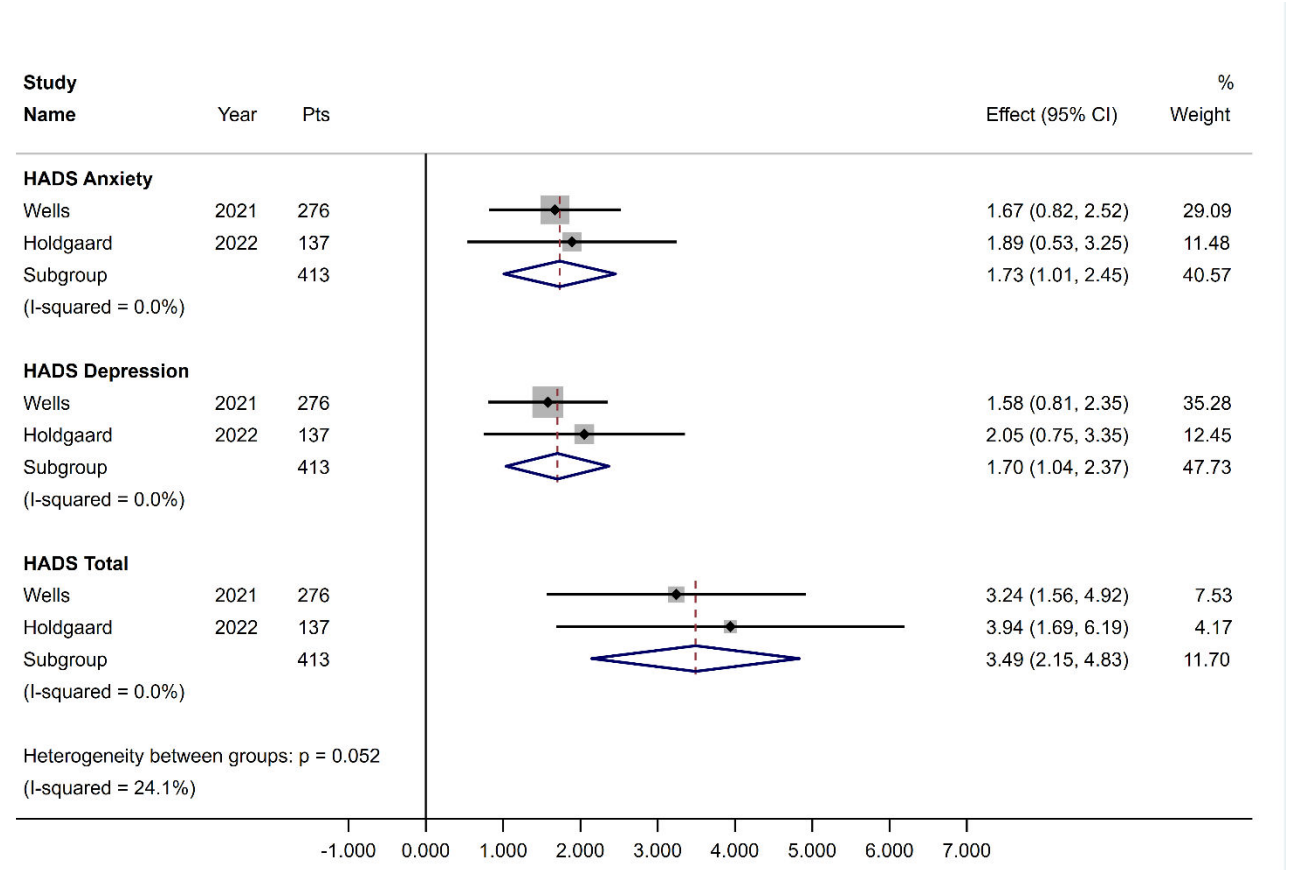
Results from a meta-analysis summarising the results from the current trial and a very similar, newly published multicentre RCT from the UK (n = 332) (49,56) are provided in Figure 10.



Abbreviations: CR: cardiac rehabilitation. HADS: Hospital Anxiety and Depression Scale

Figure 10: Forest plot of metacognitive therapy + CR/ CBT + effect of CR on anxiety and depression.

Findings from Study II: Qualitative interview study (Paper III)

Overall, the patients were very positive about participating in the group course. Three main themes emerged from the analysis, highlighting key aspects of the patients' experiences of participating in brief group-based CBT. The three themes are described in detail in Paper III and presented in brief below.

The significance of time

Upon revising the interviews and categories, we learned that the patients were profoundly impacted by their heart disease and the sudden frailty they experienced. They expressed ambivalence towards their experience. On one hand, they were grateful for their rapid treatment and quick discharge from hospital. On the other hand, they felt isolated and insecure in their new situation. The period between discharge and their first visit to the CR unit was described as agonisingly long. Despite looking forward to returning home, patients experienced great uncertainty upon being alone and having to carry the responsibility of monitoring their

symptoms and general condition. They reported an increased awareness of their body after being discharged, characterised by various worries and anxieties that made them feel vulnerable and caused them to avoid certain activities. Some patients experienced symptoms of dizziness and breathlessness, which prevented them from going out. They considered their bodies unreliable, and some felt that time was slipping away and that they were forced to assume a more passive role.

Joining the group therapy was perceived as a way to move forward and return to a sense of normality. Patients also described group therapy as a valuable aid for personal development which allowed them to progress safely. However, the duration of the group therapy was challenging for some patients, particularly those who experienced a high degree of anxiety and lived alone. These patients found that group therapy was very supportive, and they expressed a need for more sessions to work with the tools to reduce anxiety and be supported by their fellow patients. During the course, they had come to realise that their heart disease was life-changing and that returning to their pre-disease life was no longer an option. They understood that cognitive tools needed to be integrated into their lives and they expressed a desire to follow their fellow patients for an indefinite period of time.

The information provided to patients prior to discharge regarding their expected full recovery did not align with the actual experiences of the patients in the present study. They were initially informed that they could anticipate complete recovery within a 14-day timeframe. However, the findings of our study revealed a notable disparity in the expected recovery time. This inconsistency in the projected recovery period prompted significant distress among the patients, who began to question their well-being when they were unable to resume work within the originally indicated 14-day timeframe.

Certain patients found that their rehabilitation period was highly stressful as they grappled with the perception of limited time and the difficulty of managing heart disease alongside tending to family and work responsibilities. The intervention proved particularly beneficial to those who felt overwhelmed by the demands of rehabilitation, work and family commitments. The intervention equipped these patients with strategies to lighten their workload, foster open discussions about the stress they were experiencing and gain awareness of the importance of setting realistic boundaries for themselves and others.

Mirroring as a way of normalising

Patients in this study reported feeling a sense of relief and comfort in forming part of a group with others who were going through similar experiences. The group provided a safe space for

them to express their worries and compare symptoms and trajectories. They felt that they were understood by both healthcare professionals and fellow patients, making the group a special place. Meeting patients in similar situations was especially valuable as it helped them gain insights into their own new situation. By hearing about fellow patients' struggles with anxiety and dark thoughts, patients realised that their own reactions were normal.

The small-group setting allowed for open sharing and interaction among patients, leading to improved adaptation to their situation and, for some, faster rehabilitation. Patients often felt embarrassed by their emotional instability, particularly in relation to their family members. However, the group allowed them to discuss all kinds of reactions without feeling judged. Healthcare professionals were attentive listeners and offered professional knowledge to supplement the discussion.

Patients were also able to voice existential thoughts about life and death in the group setting. Moreover, the matrix introduced in the first session was a helpful tool for reconsidering which values they wanted to prioritise in the future. Participants inspired each other in the process of accepting their new life situation and learned to use cognitive tools to manage worries. Overall, the group experience was beneficial for patients in this study, providing a supportive environment where they could share their experiences and receive valuable feedback and support.

Body and mind as a unity

Throughout all interviews, it became apparent that the heart condition had heightened patients' awareness of their bodies. In some patients, symptoms from the chest region triggered anxiety and fear of another heart attack. Group therapy helped patients understand the connection between their body and mind, leading some patients to recognise that they suffered from anxiety. Psychoeducation proved particularly effective in this regard because it provided patients with relief as they learned breathing exercises to calm their agitated nervous system. For some patients, the increased awareness of all symptoms from the heart made them perceive that their body was unreliable. A simple extra heartbeat was interpreted as potentially dangerous, which led to even more heart symptoms. The physical CR exercises addressed this issue by providing a secure environment for patients to test their heart rate. Patients talked about the importance of training with confidence, knowing how the nervous system works and being aware of its interactions with the mind. Some patients felt that it was crucial that nurses with comprehensive knowledge of their specific heart disease delivered CBT in the context of CR.

Discussion

Main findings

In the RCT (Papers I and II), we found that supplementing CR with five group-based CBT sessions significantly reduced anxiety and depression levels compared with CR alone among patients with psychological distress. These improvements were sustained during the six-month follow-up period. At six months, noteworthy enhancements were also observed in HeartQol. Moreover, adherence to the physical training sessions improved significantly in the intervention group. However, other secondary outcomes related to risk factors did not improve significantly. Moreover, after 12 months, we observed a significant decrease in cardiac readmissions within the intervention group compared with the control group (56).

In the interview study (Paper III), we found that the patients were overall positive about participating in the group course and experienced relief from forming part of a group with other patients in a similar situation. Through sharing and reflecting with fellow patients, they were able to normalise their emotions and come to terms with their current circumstances. An essential aspect of the intervention was developing a profound understanding of the deep connection between body and mind. This newfound insight allowed patients to differentiate between anxiety-related symptoms and those stemming from their heart condition.

Evidence-based treatment of psychological distress in patients with cardiac disease

Traditionally, CR has predominantly focused on addressing physical well-being in relation to heart disease and has devoted only relatively little attention to psychological health. However, there is a growing recognition of the profound influence of psychological well-being on cardiovascular health. Both the American Heart Association and the European Association of Cardiovascular Prevention and Rehabilitation now acknowledge the crucial significance of integrating treatment of the heart and the mind in their guidelines (7,13). In 2013, the Danish Health Authority included screening for symptoms of depression and anxiety using the HADS in the national clinical guidelines on CR (83). Patients who screen positive for anxiety and depression are recommended treatment (84). However, the CR setting offers no evidence-based treatment, with the primary recourse being referring patients to their general practitioner (GP). A growing number of studies have tested various types of interventions for anxiety and depression and obtained diverse outcomes. CBT was found to be an efficient treatment (45,46). However, it is also expensive, time consuming and therefore not feasible in the context of a standard CR programme. Furthermore, it is often provided by psychologists who hold no knowledge of heart

disease and are not usually part of the rehabilitation staff. This thesis tested an intervention that addresses some of the above-mentioned barriers to implementation. The brief, group-based CBT delivered by CR nurses and integrated into usual CR provided significant reductions in anxiety and depression levels. To our knowledge, the present study is the first to test CBT in a brief intervention given as an add-on to CR. The most relevant comparable study is a recent multicentre RCT in which 332 patients with cardiac diseases in the UK were included (49). This study was the first to test metacognitive therapy in relation to CR. Remarkably, this study observed outcomes similar to those of our own research, where a concise, group-oriented metacognitive therapy intervention was administered by CR professionals, including cardiac nurses, comprising six sessions. Both studies align closely in terms of the primary outcome, specifically the HADS scores, within a 3-4 month period. When integrating the two datasets (Figure 10), the CBT intervention yielded a notable between-group difference in HADS score of 3.49 (2.15-4.83). This effect size is considerably greater than reported in previous studies using individual or group-based CBT as reported in the meta-analyses (46).

The patients who participated in the intervention with metacognitive therapy expressed how being a part of a group and interacting with the other patients had helped them adapt to their new situation (85). This is in line with the qualitative findings from our interview study. Additionally, the CBT intervention aimed to support patients in coping with their cardiac disease using a method comprising interaction between thoughts, emotions, body and behaviour (64). This method helped the patient understand the connection between body and mind and allowed them better able to distinguish between symptoms of anxiety and symptoms originating from the heart.

Time and resource consumption for the treatment of psychological distress

In the context of addressing psychological distress in individuals with CVD, CBT emerges as the predominant approach. Moreover, interventions grounded in CBT principles appear to yield the most favourable outcomes in mitigating symptoms of depression and anxiety (42,45,86). In a comprehensive meta-analysis conducted by Reavell et al. (45), the effectiveness of CBT in CVD patients was examined, and it was suggested that longer-duration CBT interventions offered superior, sustained benefits over time.

A more recent meta-analysis considered a wide range of CBT trials exhibiting considerable diversity in their delivery methods. However, a common feature of these trials was inclusion of individualised sessions and treatment courses lasting longer than 12 weeks and involving more than ten sessions (46). Consequently, it is worth noting that many of these interventions may

pose challenges for practical clinical implementation due to their significant time and resource requirements.

Furthermore, in the meta-analysis, the duration of the treatment course was not predictive of the effect of the intervention (46). In the present study, the duration of the treatment course was five weeks and in the comparable study by Wells et al. (49), the treatment duration was six weeks. The feasibility of both courses in terms of introduction into clinical practice is heightened by the duration of the courses and the fact that nurses and other healthcare professionals provided the interventions. We only followed the patients with clinical control for six months, whereas the study by Wells et al. followed their patients for one year and found that the improvement in anxiety and depression was maintained (49). Our qualitative findings revealed that most of the patients found that the length of the course was sufficient to improve their mental well-being. Even so, for some patients, the length of the group therapy was challenging as they felt pressured to recover within the five-week period. Especially patients who experienced a high degree of anxiety and lived alone found that group therapy was very supportive. In addition, they expressed a need for more sessions to work with the tools provided, to reduce their anxiety and receive support from their fellow patients.

CBT and depression

Depression is a frequently observed comorbidity in individuals diagnosed with coronary heart disease (CHD). It stands as an independent risk factor linked to increased cardiovascular morbidity and mortality, along with a decreased quality of life (QoL) (20,32,87). Evidence-based treatment for reducing symptoms of depression in patients with cardiac disease includes antidepressant medications, psychological interventions and exercise-based CR (12,45,87). Treatment options depend on the severity of the depression and the patient's preferences.

In this study, we identified a significant reduction in the depression subscale in the group that received the brief CBT intervention compared with the control group at both the three- and the six-month follow-up. This was also found in other studies using face-to-face CBT and providing a minimum of five hours of therapy. Reductions in depression were greatest at the short-term follow-up. This suggests that longer CBT courses may be required to maintain psychological well-being after the intervention (45). We followed the patients for only six months after the intervention with HADS and are therefore unable to establish if the reduction in depressive symptoms was maintained for a longer period of time. A recent review suggested that CBT interventions may be more effective for depression in patients with CHD when delivered as an individual treatment and employing psycho-education, behavioural and cognitive strategies as

the main approaches (46). In the present study, we used group CBT, which also yielded positive results in terms of reduction of depressive symptoms. Further findings from the qualitative part of the study underlined the positive experience of forming part of a group. The group provided a safe space for the patients to express their worries and compare symptoms and trajectories. The use of psychoeducation to improve the patients' knowledge about CHD and the corresponding cognitive and behavioral techniques was also considered useful by the patients.

Patients with CVD may have difficulties in identifying depressive symptoms because their symptoms may overlap with somatic symptoms from the heart (88). In line with other studies (46), we found that the use of psychoeducation helped patients to distinguish between the symptoms of depression and the symptoms of heart disease, and to accept their reactions to the experienced symptoms.

In the qualitative part of this study, we found that the patients felt ashamed of being emotionally unstable and experiencing depressive symptoms such as dark thoughts and feelings of hopelessness for the future. In the group, however, it was acceptable to talk about all kinds of reactions. This helped the patients to recognise that their own reactions to having a life-threatening disease were expected and therefore normal.

The findings from our study are comparable to those of a recent qualitative study from Sweden which also found that patients expressed that their depressive symptoms were difficult to handle. Furthermore, the patients with cardiac disease perceived that the healthcare professionals overlooked depressive symptoms and focused only on the somatic aspects of heart disease (89). Integrating the CBT intervention with CR may help patients and healthcare professionals to also address depressive symptoms in the context of the cardiac disease course.

Anxiety

Anxiety is often viewed as an expected, universal emotion to a cardiac event. However, when it increases or persists, anxiety potentially has serious consequences. This response is triggered by the perception of potential threats, which can originate from both internal or external factors, and may manifest as actual or perceived dangers (90). This understanding is crucial for effective treatment of anxiety. Regrettably, anxiety is frequently overlooked by healthcare providers. This is likely due to a combination of insufficient knowledge and limited treatment options (90). A recent review(27) assessing the efficacy of psychological interventions in addressing anxiety found that interventions that had anxiety as their primary intervention focus yielded the most favourable outcomes. Additionally, research with more extended follow-up durations (27) demonstrates that the beneficial impacts of these psychological interventions on anxiety can

persist in the long term. In the present study, we found that the intervention produced a significant reduction in anxiety compared with the control group at the 3- and 6-month follow-up. The impact of anxiety has been found to be independent of depression; moreover, therapeutically addressing anxiety and its consequences often requires a different approach. The included interventions varied in length, intensity, facilitation and format - but they were all provided in the early stages following a cardiac event, suggesting that this may be the appropriate time to offer help (27). Results from the qualitative findings supported that the patients wanted the interval from their cardiac event to the first group session to be as short as possible. A short interval was perceived as important because the period between discharge from the hospital and the first visit to the CR unit was experienced as extremely long and challenging. In this period, the patients lacked the necessary support to manage their emotional distress and prevent the progression of anxiety. Some patients highlighted the importance of a comprehensive exploration of the physiological aspects of anxiety as it contributed to reducing their anxiety levels. Furthermore, our findings indicated that nurses' specific knowledge of cardiology was much appreciated as patients lacked knowledge about their own body. This knowledge gap is crucial because of the overlapping symptoms between heart disease, anxiety and depression, emphasising the need for a comprehensive understanding of how mental and physical symptoms intersect and interact. In line with these findings, McPhillips et al. (85) emphasised the importance of CR staff expertise in cardiology and their delivery of treatment, an element which was also highlighted by our patients.

Adherence to CR and risk-factor management

Anxiety and depression have been demonstrated to have a detrimental impact on the management of risk factors and adherence to CR programmes, as indicated by previous studies (14,91). Concerning health-seeking behaviour, anxiety may exhibit a protective influence by prompting individuals to undergo more frequent check-ups and actively engage in preventive healthcare strategies. Nevertheless, anxiety can also manifest adverse effects by fostering social inhibition and encouraging negative coping mechanisms (91). Our investigation revealed no discernible disparity between the groups in terms of the enhancement of cardiovascular risk factors. Nonetheless, risk factor management exhibited a high degree of effectiveness in both the intervention and the control group, leaving minimal opportunity for enhancement. It is well known that patients with psychological distress tend to have poorer CR adherence (92,93). We found that the patients in the intervention group were significantly more adherent to the training sessions than the patients in the control group were. In the qualitative findings, the patients

expressed a new awareness of their body. Furthermore, for some of the patients, any symptoms from the chest region caused anxiety and worries about a new heart attack. Some patients mentioned that when their heart rate increased, they felt insecure and therefore reduced their training intensity, and some even stopped training. This was also found in a recent study of heart-focused anxiety (HFA). HFA was found to be related to avoidance of psychical activity because the body sensations induced by physical activity - e.g., a faster heartbeat - triggered anxiety (94). Induced exposure is an effective intervention in the treatment of HFA, which can be used in psychical rehabilitation (94). Exposure was also induced in the present study in conjunction with psychoeducation describing how the nervous system worked. The patients expressed that the new knowledge and treatment for anxiety allowed them to train with greater confidence. These factors may potentially have contributed to the higher adherence rate seen in the intervention group.

Work retention

Numerous studies have underpinned the adverse effects of untreated anxiety and depression on a patient's ability to retain employment (95–97). The work retention process is influenced by a combination of individual factors, including the fear of work-related stress and work-related factors such as high job demands and low control, which significantly reduce retention (98,99). Conversely, support and understanding from the employer and the possibility of a gradual return to work have shown a positive effect on retention (100). Our qualitative findings indicated that patients expressed a sense of pressure to resume work as quickly as possible, leading to feelings of unease and concern about how a stressful work life would affect their heart condition. This pressure posed a substantial threat that could not be alleviated by discussing it with fellow patients in their group. In our research, the majority of patients had resumed work by the six-month follow-up, and no notable distinction was observed between the intervention and control groups (78% versus 67%, $p = 0.11$). This return-to-work rate was comparable to the findings from the EUROASPIRE IV study (101), where 76% of patients had returned to work within a timeframe ranging from six months to three years. Importantly, we only tracked patients' employment status for a six-month period(56). Recent research shows that a proportion of patients feel pressure to return to work before they feel physically or mentally ready. This might make it difficult to sustain employment after initial return and may cause drop out at a later point (102).

Readmission

Readmissions are common after a cardiac event for both cardiac and non-cardiac causes. Studies have shown that most readmissions occur within a month from discharge. One of the most common diagnoses for readmission is chest pain(103,104). A robust correlation exists between psychological distress and recurrent hospitalizations stemming from cardiac events. (105,106). Our research was not originally intended to present morbidity and mortality as its primary focus. Furthermore, the study's size and duration were insufficient to provide these measures. Nonetheless, we did uncover notably elevated readmission rates among individuals grappling with psychological distress compared with the background group without psychological distress. Additionally, we observed a 57% reduction in readmission risk within the initial 12 months following randomization for the intervention group. There were no disparities in the incidence of MI or revascularization procedures. This implies that the prompt identification and management of psychological distress following a cardiac event could potentially prevent a significant number of avoidable readmissions. Our research findings are consistent with another study, which reported that individuals experiencing psychological distress have a higher probability of both encountering and reporting chest pain. This suggests that they may have a lower threshold for seeking emergency care and, consequently, an increased risk of readmissions (107).

In a recent study, chest pain was found to be the second most common reason for emergency department visits, and only 5–6% of patients visiting the emergency department for this symptom were diagnosed with AMI (108). Results from the UK study UPBEAT showed that an elevated anxiety score was strongly associated with an increased short-term risk of recurrent cardiac events. The study showed a need to focus on specific treatment for management of fear, worry and panic symptoms (91). Another study also found that body sensations, depressive symptoms and cardiac anxiety are strongly related to each other and that cardiac anxiety in particular influences health seeking behaviour such as emergency visits (109). In the present study, the circle of anxiety (66) was used to understand the underlying principles of anxiety and how anxiety may escalate into fear and panic. Psychoeducation allowed the patients to understand the connection between body and mind, and some became aware that they suffered from anxiety. Patients suffering from anxiety learned how to handle their anxiety and gained awareness that anxiety attacks are of limited duration. Another study, which employed routine psychological screening with the HADS in the emergency room found a high number of patients with panic attacks. The same study also found an association between a certain type of personality (type D personality) and readmissions, which we did not test for (110).

Methodological considerations

Mixed methods research is becoming widely used as research approach in mental health and psychiatric nursing (111). In this thesis, we adopted an embedded design in which quantitative data from the RCT study were supported by qualitative data from the interviews, thereby enhancing our understanding of the results from scales by adding the participants' views (51,112). The results of the present study should be interpreted with the following limitations in mind.

We aimed to study the effect of CBT in patients with cardiac disease participating in CR. The majority of patients participating in CR are patients with CAD or VHD. However, structural changes in CR limited our access to the group of patients with VHD. Therefore, we tested for statistical interaction between the effects of intervention and CAD versus VHD (and gender) and found no interactions. Another limitation is that the patients were highly selected as we recruited patients only from hospitals in the Capital Region of Denmark. An attempt to include patients from a broader geographical area in Denmark failed due to excessive patient transportation time. We chose the younger segment among patients with cardiac disease as this group suffers the most. Before this RCT, we conducted a pilot study in our CR with 232 consecutive patients. We screened the patients with HADS and found that the proportion of patients with a HADS score of 8 or above was highest (32%) in the group of patients below 65 years who were still working. This was confirmed in several other studies, indicating a need to focus on this group (26).

One of the strengths of our study is that cardiac nurses already working in the CR provided the intervention. They had an in-depth understanding of how mental and somatic symptoms from the heart overlap and interact. It may raise concern that patients with a psychiatric diagnosis or treatment were excluded from the study. However, cardiac nurses are not trained to care for patients with psychiatric diagnoses and the patients would not have benefitted from this intervention. The nurses were trained in CBT and employed a standardised manual for each session. This approach allows us to generalise the intervention to other CR settings in comparable communities and hospitals in the Western world.

The natural course of anxiety and depression following an acute event must also be considered in both the qualitative and quantitative part of the study. A reduction in symptoms of anxiety and depression was seen in both the intervention group and the control group. This indicates that the natural course of psychological distress following a cardiac event is that time itself provides relief. This 'natural' relief may possibly be reinforced by CR and other factors, which likely vary from one patient to another (113).

Other limitations are that we did not compare the effectiveness of CBT treatment to a so-called 'sham intervention', which would have improved the credibility of our findings. The primary purpose of a sham intervention is to serve as a control group, in this case helping to assess the specific effects of the CBT intervention while controlling for factors such as placebo effects, therapist-patient interactions and participant expectations (114). In our context, a sham intervention could have comprised educational components about mental health or the participants' specific condition, ensuring that the sessions would be relevant and informative. We used the HADS. It may be argued that the use of a more specific questionnaire for anxiety and depression would potentially have captured more patients with psychological distress. The Cardiac Anxiety Questionnaire (CAQ) is more sensitive to detecting cardiac-specific anxiety symptoms. Moreover, patients with cardiac disease may find the CAQ more understandable and engaging because it directly addresses their concerns (115,116). Another option would be the Patient Health Questionnaire (PHQ-9), which is primarily designed to assess depression and has been validated in patients with heart disease. The PHQ-9 provides a more precise assessment and assesses the severity of depressive symptoms, which also is relevant in clinical practice (60). However, the HADS is validated and widely used in patients with cardiac disease (40). Furthermore, it is the questionnaire used to systematically screen Danish patients in CR according to the Danish national clinical guideline (83).

Conclusion

Based on the objectives of the thesis, the following conclusions may be drawn from the two studies:

Study I: In the RCT, brief CBT delivered by cardiac nurses in the context of CR for patients with cardiac disease and psychological distress had a clinically relevant effect on anxiety and depression and improved HeartQoL at six months. Moreover, intervention group patients were significantly more adherent to CR and had fewer cardiovascular readmissions. The CBT programme is simple, brief and feasible and practicable when integrated into existing CR.

Study II: From the qualitative interview study, three themes emerged reflecting the patients' experience of participation in the group-based CBT intervention. Our research findings highlighted the positive impact of CBT on patients suffering from heart disease and concurrent psychological distress. Those who underwent CBT reported significant alleviation of their anxiety and depressive symptoms. Collectively, this enhanced progress in their rehabilitation process. Moreover, we identified a notable challenge during the passive waiting period after hospital discharge in the period leading up to the first group session. Patients experienced a sense of isolation as they were grappling with their cardiac symptoms and concerns and struggling to cope with the psychological distress they were facing. However, participation in the intervention group provided much-needed relief. Through sharing and reflection with fellow patients, they were able to normalise their emotions and come to terms with their current circumstances. An essential aspect of the intervention was developing a profound understanding of the deep connection between body and mind. This newfound insight enabled patients to differentiate between anxiety-related symptoms and those originating from their heart condition.

Based on the findings from both studies, our conclusion is that integrating CBT as an essential part of usual CR may ensure that heart and mind are treated equally, which will decrease symptoms of anxiety and depression, ease patients' suffering and therefore reduce the number of readmissions. In addition, the time from discharge to the first visit in the group must be as short as possible to prevent progression of anxiety and depression.

Future perspectives

Clinical implications

This PhD thesis adds important findings to current evidence on interventions for patients with heart disease and psychological distress. We found that the CBT intervention had a clinically relevant effect on anxiety and depression. Overall, the patients were positive about participating in the group course. The CBT intervention was simple, brief and feasible in conjunction with existing CR programmes. Experienced cardiac nurses working in CR provided the CBT intervention after a short training programme and with supervision from a psychologist. Furthermore, the intervention was well described and therefore relatively easy to implement in practice.

Since June 2022, the intervention has been an option for patients referred to CR with a HADS score ≥ 8 for HADS-A and/or HADS-D at our cardiac department at Bispebjerg and Frederiksberg Hospital in Denmark. The nurses have received the same training programme as the study nurses, and supervision by a psychologist also forms part of clinical practice to ensure the quality of the intervention and to maintain the cognitive approach. The cardiac nurses were very positive about the cognitive tools they learned because they were easy to use together with their cardiac knowledge. Hopefully, their experience will expand to other departments nationally and internationally.

Future research

Nevertheless, further research is needed to explore the psychological needs of the broad range of patients enrolled in CR. It would be interesting to establish whether similar effects may be achieved in other patients with cardiac disease with psychological distress and whether the effects are maintained throughout longer follow-up periods. Some CR patients may be unable or unwilling to attend face-to-face treatment or may be returning to work or have difficulties in leaving their home. For this group, an eHealth solution may potentially be a relevant alternative (117). Patients targeted for these interventions must possess the necessary skills and competences allowing them engage in the intervention, including being able to use computers and related technologies (118).

Some patients will benefit from being part of a group, whereas others need individual therapy. Hopefully, in the future, it will be possible to offer differentiated modes of delivery thereby giving patients a choice and potentially enhancing adherence.

Other questions that warrant further research include how we may reach patients with psychological distress who do not participate in CR and patients who are not referred in the first place (34).

References

1. Polit F D and Beck T C. Essentials of Nursing Research: Appraising Evidence for Nursing Practice. Ninth Edition. Wolters Kluwer;

2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, m.fl. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. J Am Coll Cardiol. 22. december 2020;76(25):2982–3021.

3. Timmis A, Vardas P, Townsend N, Torbica A, Katus H, De Smedt D, m.fl. European Society of Cardiology: cardiovascular disease statistics 2021. Eur Heart J. 21. februar 2022;43(8):716–99.

4. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, m.fl. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur J Prev Cardiol. 19. februar 2022;29(1):5–115.

5. Khera AV, Kathiresan S. Genetics of coronary artery disease: discovery, biology and clinical translation. Nat Rev Genet. juni 2017;18(6):331–44.

6. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, m.fl. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 1. august 2016;37(29):2315–81.

7. Ambrosetti M, Abreu A, Corrà U, Davos CH, Hansen D, Frederix I, m.fl. Secondary prevention through comprehensive cardiovascular rehabilitation: From knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. Eur J Prev Cardiol. 30. marts 2020;2047487320913379.

8. Dibben G, Faulkner J, Oldridge N, Rees K, Thompson DR, Zwisler AD, m.fl. Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database Syst Rev. 6. november 2021;2021(11):CD001800.

9. Salzwedel A, Jensen K, Rauch B, Doherty P, Metzendorf MI, Hackbusch M, m.fl. Effectiveness of comprehensive cardiac rehabilitation in coronary artery disease patients treated according to contemporary evidence based medicine: Update of the Cardiac Rehabilitation Outcome Study (CROS-II). Eur J Prev Cardiol. november 2020;27(16):1756–74.

10. Taylor RS, Dalal HM, McDonagh STJ. The role of cardiac rehabilitation in improving cardiovascular outcomes. Nat Rev Cardiol. 2022;19(3):180–94.

11. Borregaard B, Ekholm O, Riber L, Sørensen J, Møller JE, Thrysoe L, m.fl. Patient-reported outcomes after aortic and mitral valve surgery – results from the DenHeart Study. Eur J Cardiovasc Nurs. 1. marts 2018;17(3):246–54.

12. Vaccarino V, Badimon L, Bremner JD, Cenko E, Cubedo J, Dorobantu M, m.fl. Depression and coronary heart disease: 2018 position paper of the ESC working group on coronary pathophysiology and microcirculation. Eur Heart J. 1. maj 2020;41(17):1687–96.

13. Levine GN, Cohen BE, Commodore-Mensah Y, Fleury J, Huffman JC, Khalid U, m.fl. Psychological Health, Well-Being, and the Mind-Heart-Body Connection: A Scientific Statement From the American Heart Association. Circulation. 9. marts 2021;143(10):e763–83.

14. Pogosova N, Saner H, Pedersen SS, Cupples ME, McGee H, Höfer S, m.fl. Psychosocial aspects in cardiac rehabilitation: From theory to practice. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation of the European Society of Cardiology. Eur J Prev Cardiol. 1. oktober 2015;22(10):1290–306.

15. Tully PJ, Harrison NJ, Cheung P, Cosh S. Anxiety and Cardiovascular Disease Risk: a Review. Curr Cardiol Rep. december 2016;18(12):120.

16. Thombs BD, Bass EB, Ford DE, Stewart KJ, Tsilidis KK, Patel U, m.fl. Prevalence of Depression in Survivors of Acute Myocardial Infarction. J Gen Intern Med. januar 2006;21(1):30–8.

17. Berg SK, Rasmussen TB, Thrysoee L, Lauberg A, Borregaard B, Christensen AV, m.fl. DenHeart: Differences in physical and mental health across cardiac diagnoses at hospital discharge. J Psychosom Res. 1. marts 2017;94:1–9.

18. Flygare O, Boberg J, Rück C, Hofmann R, Leosdottir M, Mataix-Cols D, m.fl. Association of anxiety or depression with risk of recurrent cardiovascular events and death after myocardial infarction: A nationwide registry study. Int J Cardiol [Internet]. 18. april 2023 [henvist 24. april 2023]; Tilgængelig hos: https://www.sciencedirect.com/science/article/pii/S0167527323005764

19. Cohen BE, Edmondson D, Kronish IM. State of the Art Review: Depression, Stress, Anxiety, and Cardiovascular Disease. Am J Hypertens. november 2015;28(11):1295–302.

20. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, m.fl. Depression as a Risk Factor for Poor Prognosis Among Patients With Acute Coronary Syndrome: Systematic Review and Recommendations: A Scientific Statement From the American Heart Association. Circulation. 25. marts 2014;129(12):1350–69.

21. Deter HC, Albert W, Weber C, Merswolken M, Orth-Gomér K, Herrmann-Lingen C, m.fl. Does Anxiety Affect Survival in Patients with Coronary Heart Disease? J Clin Med. 7. marts 2023;12(6):2098.

22. Berg SK, Rasmussen TB, Thrysoee L, Thorup CB, Borregaard B, Christensen AV, m.fl. Mental health is a risk factor for poor outcomes in cardiac patients: Findings from the national DenHeart survey. J Psychosom Res. 2018;112:66–72.

23. Wium-Andersen MK, Wium-Andersen IK, Prescott EIB, Overvad K, Jørgensen MB, Osler M. An attempt to explain the bidirectional association between ischaemic heart disease, stroke and depression: a cohort and meta-analytic approach. Br J Psychiatry. august 2020;217(2):434–41.

24. Carney RM, Blumenthal JA, Stein PK, Watkins L, Catellier D, Berkman LF, m.fl. Depression, Heart Rate Variability, and Acute Myocardial Infarction. Circulation. 23. oktober 2001;104(17):2024–8.

25. Sherwood A, Hinderliter AL, Watkins LL, Waugh RA, Blumenthal JA. Impaired Endothelial Function in Coronary Heart Disease Patients With Depressive Symptomatology. J Am Coll Cardiol. august 2005;46(4):656–9.

26. Murphy B, Le Grande M, Alvarenga M, Worcester M, Jackson A. Anxiety and Depression After a Cardiac Event: Prevalence and Predictors. Front Psychol [Internet]. 2020 [henvist 23. marts 2020];10. Tilgængelig hos: https://www.frontiersin.org/articles/10.3389/fpsyg.2019.03010/full

27. Ryan EM, Creaven AM, Ní Néill E, O'Súilleabháin PS. Anxiety following myocardial infarction: A systematic review of psychological interventions. Health Psychol Off J Div Health Psychol Am Psychol Assoc. september 2022;41(9):599–610.

28. Rao A, Zecchin R, Newton P, Phillips J, DiGiacomo M, Denniss A, m.fl. The prevalence and impact of depression and anxiety in cardiac rehabilitation: A longitudinal cohort study. Eur J Prev Cardiol. 1. marts 2020;27(5):478–89.

29. Murphy BM, Elliott PC, Worcester MUC, Higgins RO, Le Grande MR, Roberts SB, m.fl. Trajectories and predictors of anxiety and depression in women during the 12 months following an acute cardiac event. Br J Health Psychol. 2008;13(1):135–53.

30. Pedersen SS, Nielsen JC, Wehberg S, Jørgensen OD, Riahi S, Haarbo J, m.fl. New onset anxiety and depression in patients with an implantable cardioverter defibrillator during 24 months of follow-up (data from the national DEFIB-WOMEN study). Gen Hosp Psychiatry. september 2021;72:59–65.

31. Norlund F, Lissåker C, Wallert J, Held C, Olsson EM. Factors associated with emotional distress in patients with myocardial infarction: Results from the SWEDEHEART registry. Eur J Prev Cardiol. juni 2018;25(9):910–20.

32. Lichtman Judith H., Bigger J. Thomas, Blumenthal James A., Frasure-Smith Nancy, Kaufmann Peter G., Lespérance François, m.fl. Depression and Coronary Heart Disease. Circulation. 21. oktober 2008;118(17):1768–75.

33. Palacios J, Khondoker M, Mann A, Tylee A, Hotopf M. Depression and anxiety symptom trajectories in coronary heart disease: Associations with measures of disability and impact on 3-year health care costs. J Psychosom Res. januar 2018;104:1–8.

34. Resurrección DM, Moreno-Peral P, Gómez-Herranz M, Rubio-Valera M, Pastor L, Caldas de Almeida JM, m.fl. Factors associated with non-participation in and dropout from cardiac rehabilitation programmes: a systematic review of prospective cohort studies. Eur J Cardiovasc Nurs. 1. januar 2019;18(1):38–47.

35. Pedretti RFE, Hansen D, Ambrosetti M, Back M, Berger T, Ferreira MC, m.fl. How to optimize the adherence to a guideline-directed medical therapy in the secondary prevention of cardiovascular diseases: a clinical consensus statement from the European Association of Preventive Cardiology. Eur J Prev Cardiol. 1. februar 2023;30(2):149–66.

36. Pogosova N, Kotseva K, De Bacquer D, von Känel R, De Smedt D, Bruthans J, m.fl. Psychosocial risk factors in relation to other cardiovascular risk factors in coronary heart disease: Results from the EUROASPIRE IV survey. A registry from the European Society of Cardiology. Eur J Prev Cardiol. september 2017;24(13):1371–80.

37. Sever S, Golder S, Doherty P. Factors associated with acute depressive symptoms in patients with comorbid depression attending cardiac rehabilitation. BMC Cardiovasc Disord. 10. december 2018;18:230.

38. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: An updated literature review. J Psychosom Res. 1. februar 2002;52(2):69–77.

39. Pedersen SS, von Känel R, Tully PJ, Denollet J. Psychosocial perspectives in cardiovascular disease. Eur J Prev Cardiol. 1. juni 2017;24(3_suppl):108–15.

40. Christensen AV, Dixon JK, Juel K, Ekholm O, Rasmussen TB, Borregaard B, m.fl. Psychometric properties of the Danish Hospital Anxiety and Depression Scale in patients with cardiac disease: results from the DenHeart survey. Health Qual Life Outcomes. 7. januar 2020;18(1):9.

41. Pogosova N, Kotseva K, De Bacquer D, von Känel R, De Smedt D, Bruthans J, m.fl. Psychosocial risk factors in relation to other cardiovascular risk factors in coronary heart disease: Results from the EUROASPIRE IV survey. A registry from the European Society of Cardiology. Eur J Prev Cardiol. september 2017;24(13):1371–80.

42. Richards SH, Anderson L, Jenkinson CE, Whalley B, Rees K, Davies P, m.fl. Psychological interventions for coronary heart disease. Cochrane Database Syst Rev [Internet]. 2017 [henvist 18. februar 2020];(4). Tilgængelig hos: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002902.pub4/full

43. Scott-Sheldon LAJ, Gathright EC, Donahue ML, Balletto B, Feulner MM, DeCosta J, m.fl. Mindfulness-Based Interventions for Adults with Cardiovascular Disease: A Systematic Review and Meta-Analysis. Ann Behav Med Publ Soc Behav Med. 5. juni 2019;54(1):67–73.

44. Zou H, Cao X, Chair SY. A systematic review and meta-analysis of mindfulness-based interventions for patients with coronary heart disease. J Adv Nurs. maj 2021;77(5):2197–213.

45. Reavell J, Hopkinson M, Clarkesmith D, Lane DA. Effectiveness of Cognitive Behavioral Therapy for Depression and Anxiety in Patients With Cardiovascular Disease: A Systematic Review and Meta-Analysis. Psychosom Med. oktober 2018;80(8):742–53.

46. Li YN, Buys N, Ferguson S, Li ZJ, Sun J. Effectiveness of cognitive behavioral therapy-based interventions on health outcomes in patients with coronary heart disease: A meta-analysis. World J Psychiatry. 19. november 2021;11(11):1147–66.

47. Norlund F, Wallin E, Olsson EMG, Wallert J, Burell G, von Essen L, m.fl. Internet-Based Cognitive Behavioral Therapy for Symptoms of Depression and Anxiety Among Patients With a Recent Myocardial Infarction: The U-CARE Heart Randomized Controlled Trial. J Med Internet Res. 8. marts 2018;20(3):e88.

48. Pedersen SS, Andersen CM, Ahm R, Skovbakke SJ, Kok R, Helmark C, m.fl. Efficacy and cost-effectiveness of a therapist-assisted web-based intervention for depression and anxiety in patients with ischemic heart disease attending cardiac rehabilitation [eMindYourHeart

trial]: a randomised controlled trial protocol. BMC Cardiovasc Disord. 7. januar 2021;21:20.

49. Wells A, Reeves D, Capobianco L, Heal C, Davies L, Heagerty A, m.fl. Improving the Effectiveness of Psychological Interventions for Depression and Anxiety in Cardiac Rehabilitation: PATHWAY—A Single-Blind, Parallel, Randomized, Controlled Trial of Group Metacognitive Therapy. Circulation. 6. juli 2021;144(1):23–33.

50. Creswell JW. A Concise Introduction to Mixed Methods Research. United states of America: Sage Publications Ltd.; 2015.

51. Creswell JW, Creswell JD JW. Research design Qualitative, Quantitative, and Mixed Methods Approaches. Sixth Edition. Bd. 2023. Thousand Oaks, Calif: SAGE Publications;

52. Creswell JW, Plano Clark VL. Designing and conducting mixed methods research. Bd. 2007:xviii. Thousand Oaks, Calif: SAGE Publications;

53. David L. Streiner. Geoffrey R. Norman, John Cairney. health measurement scales a practical guide to their development and use. Fifth edition. Bd. 2015. Oxford university press;

54. Elo S, Kyngäs H. The qualitative content analysis process. J Adv Nurs. 2008;62(1):107–15.

55. Graneheim UH, Lindgren BM, Lundman B. Methodological challenges in qualitative content analysis: A discussion paper. Nurse Educ Today. september 2017;56:29–34.

56. Holdgaard A, Eckhardt-Hansen C, Lassen CF, Kjesbu IE, Dall CH, Michaelsen KL, m.fl. Cognitive-behavioural therapy reduces psychological distress in younger patients with cardiac disease: a randomized trial. Eur Heart J. 18. januar 2023;ehac792.

57. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, for the CONSORT Group. Extending the CONSORT Statement to Randomized Trials of Nonpharmacologic Treatment: Explanation and Elaboration. Ann Intern Med. 19. februar 2008;148(4):295.

58. Bambauer KZ, Locke SE, Aupont O, Mullan MG, McLaughlin TJ. Using the Hospital Anxiety and Depression Scale to screen for depression in cardiac patients. Gen Hosp Psychiatry. juli 2005;27(4):275–84.

59. Scherer M, Himmel W, Stanske B, Scherer F, Koschack J, Kochen MM, m.fl. Psychological distress in primary care patients with heart failure: a longitudinal study. Br J Gen Pract. 1. oktober 2007;57(543):801–7.

60. Haddad M, Walters P, Phillips R, Tsakok J, Williams P, Mann A, m.fl. Detecting Depression in Patients with Coronary Heart Disease: a Diagnostic Evaluation of the PHQ-9 and HADS-D in Primary Care, Findings From the UPBEAT-UK Study. Shimizu E, redaktør. PLoS ONE. 10. oktober 2013;8(10):e78493.

61. Oldridge N, Höfer S, McGee H, Conroy R, Doyle F, Saner H. The HeartQoL: Part I. Development of a new core health-related quality of life questionnaire for patients with ischemic heart disease. Eur J Prev Cardiol. 1. januar 2014;21(1):90–7.

62. Oldridge N, Höfer S, McGee H, Conroy R, Doyle F, Saner H. The HeartQoL: Part II. Validation of a new core health-related quality of life questionnaire for patients with ischemic heart disease. Eur J Prev Cardiol. 1. januar 2014;21(1):98–106.

63. Arendt M. Kognitiv terapi: nyeste udvikling. 2012.

64. Beck JS, Beck JS. Cognitive behavior therapy: basics and beyond. 2nd ed. New York: Guilford Press; 2011. 391 s.

65. Hallis L, Cameli L, Bekkouche NS, Knäuper B. Combining Cognitive Therapy With Acceptance and Commitment Therapy for Depression: A Group Therapy Feasibility Study. J Cogn Psychother. 2017;31(3):171–90.

66. Holdgaard A, Eckhardt-Hansen C, Lund T, Lassen CF, Sibiliz KL, Høfsten DE, m.fl. Intensive group-based cognitive therapy in patients with cardiac disease and psychological distress—a randomized controlled trial protocol. Trials. 16. juli 2021;22(1):455.

67. Polk KL, Schoendorff B, redaktører. The ACT matrix: a new approach to building psychological flexibility across settings & populations. Oakland, CA: Context Press, an imprint of New Harbinger Publications, Inc; 2014. 266 s.

68. Hougaard E, Hougaard E, Rosenberg NK. Kognitiv behandling af panikangst og socialfobi: en vejledning for klienter og behandlere. Kbh.: Dansk Psykologisk Forlag; 2007.

69. Harris R, Aisbett B. Lykkefælden: illustreret guide til, hvordan du stopper kampen og lever livet. Virum: Dansk Psykologisk Forlag; 2013.

70. Due Madsen J. Kognitiv adfærdsterapi ved depression: manual til gruppebehandling. Virum: Dansk psykologisk Forlag; 2008.

71. Martell CR, Dimidjian S, Herman-Dunn R. Adfærdsaktivering ved depression: en klinisk guide. Kbh.: Dansk psykologisk Forlag; 2012.

72. Karlsen T, Videm V, Halle M, Ellingsen Ø, Støylen A, Dalen H, m.fl. Baseline and Exercise Predictors of V˙O2peak in Systolic Heart Failure Patients: Results from SMARTEX-HF. Med Sci Sports Exerc. april 2020;52(4):810–9.

73. Lemay KR, Tulloch HE, Pipe AL, Reed JL. Establishing the Minimal Clinically Important Difference for the Hospital Anxiety and Depression Scale in Patients With Cardiovascular Disease. J Cardiopulm Rehabil Prev. november 2019;39(6):E6–11.

74. World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. JAMA. 27. november 2013;310(20):2191–4.

75. Kvale S, Brinkmann S. Interviews : learning the craft of qualitative research interviewing. 3. edition. Thousand Oaks, Calif.: Sage Publications; 2014. xviii, 405 sider s.

76. Saarijärvi M, Bratt EL. When face-to-face interviews are not possible: tips and tricks for video, telephone, online chat, and email interviews in qualitative research. Eur J Cardiovasc Nurs. 24. april 2021;zvab038.

77. Helmark C, Egholm CL, Rottmann N, Skovbakke SJ, Andersen CM, Johansen JB, m.fl. A web-based intervention for patients with an implantable cardioverter defibrillator – A qualitative study of nurses' experiences (Data from the ACQUIRE-ICD study). PEC Innov. 28. november 2022;2:100110.

78. Rosenstrøm S, Chou WX, Brødsgaard A. How Family Members Experienced a Family-Focused Atrial Fibrillation Intervention in an Outpatient Setting—A Qualitative Study. SAGE Open Nurs. 2. august 2022;8:23779608221114264.

79. Sanaie N, Kakhki AD, Ahmadi F. Exploring the consequences of patient commitment to cardiac rehabilitation program: A qualitative study. J Educ Health Promot. 28. januar 2021;10:30.

80. Mäenpää S, Ekstrand E, Petersson C, Nymark C. Patients' experiences when afflicted by takotsubo syndrome – is it time for guidelines? Scand J Caring Sci. 2021;35(3):824–32.

81. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today. februar 2004;24(2):105–12.

82. Kleinheksel AJ, Rockich-Winston N, Tawfik H, Wyatt TR. Demystifying Content Analysis. Am J Pharm Educ. januar 2020;84(1):7113.

83. Sundhedssstyrelsen. National Klinisk Retningslinje for Hjerterehabilitering - 2013. https://www.sst.dk/da/udgivelser/2015/~/media/401919781C 684EE9AAE544EB5E76847B.ashx. 2015.

84. Forløbsprogram for rehabilitering af hjertesygdomme.

85. McPhillips R, Capobianco L, Cooper BG, Husain Z, Wells A. Cardiac rehabilitation patients experiences and understanding of group metacognitive therapy: a qualitative study. Open Heart. 1. juli 2021;8(2):e001708.

86. Dickens C, Cherrington A, Adeyemi I, Roughley K, Bower P, Garrett C, m.fl. Characteristics of Psychological Interventions That Improve Depression in People With Coronary Heart Disease: A Systematic Review and Meta-Regression. Psychosom Med. marts 2013;75(2):211.

87. Wang L, Sun Y, Zhan J, Wu Z, Zhang P, Wen X, m.fl. Effects of Exercise Therapy on Anxiety and Depression in Patients With Coronary Heart Disease: A Meta-Analysis of a Randomized Controlled Study. Front Cardiovasc Med. 11. oktober 2021;8:730155.

88. Alderson SL, Foy R, Glidewell L, McLintock K, House A. How patients understand depression associated with chronic physical disease – a systematic review. BMC Fam Pract. 28. maj 2012;13:41.

89. Westas M, Lundgren J, Mourad G, Neher M, Johansson P. How Healthcare Professionals in Cardiac Care Address Depressive Symptoms. J Cardiovasc Nurs. 2021;36(4):340–8.

90. Moser DK. "The Rust of Life": Impact of Anxiety on Cardiac Patients. Am J Crit Care Off Publ Am Assoc Crit-Care Nurses. juli 2007;16(4):361–9.

91. Norton J, Pastore M, Hotopf M, Tylee A, Mann A, Ancelin ML, m.fl. Time-dependent depression and anxiety symptoms as risk factors for recurrent cardiac events: findings from the UPBEAT-UK study. Psychol Med. november 2022;52(15):3442–50.

92. McGrady A, McGinnis R, Badenhop D, Bentle M, Rajput M. Effects of depression and anxiety on adherence to cardiac rehabilitation. J Cardiopulm Rehabil Prev. december 2009;29(6):358–64.

93. Edwards BL, Sydeman SJ. Depression Is Associated With Reduced Outpatient Cardiac Rehabilitation Completion Rates: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS. J Cardiopulm Rehabil Prev. november 2019;39(6):365–72.

94. Schmitz C, Wedegärtner SM, Langheim E, Kleinschmidt J, Köllner V. Heart-Focused Anxiety Affects Behavioral Cardiac Risk Factors and Quality of Life: A Follow-Up Study Using a Psycho-Cardiological Rehabilitation Concept. Front Psychiatry. 9. maj 2022;13:836750.

95. Smedegaard L, Numé A, Charlot M, Kragholm K, Gislason G, Hansen PR. Return to Work and Risk of Subsequent Detachment From Employment After Myocardial Infarction: Insights From Danish Nationwide Registries. J Am Heart Assoc [Internet]. 11. oktober 2017 [henvist 31. august 2020];6(10). Tilgængelig hos: https://www.ahajournals.org/doi/10.1161/JAHA.117.006486

96. Stendardo M, Bonci M, Casillo V, Miglio R, Giovannini G, Nardini M, m.fl. Predicting return to work after acute myocardial infarction: Socio-occupational factors overcome clinical conditions. Lazzeri C, redaktør. PLOS ONE. 13. december 2018;13(12):e0208842.

97. de Jonge P, Zuidersma M, Bültmann U. The presence of a depressive episode predicts lower return to work rate after myocardial infarction. Gen Hosp Psychiatry. 1. juli 2014;36(4):363–7.

98. Andersen EB, Kristiansen M, Bernt Jørgensen SM. Barriers and facilitators to return to work following cardiovascular disease: a systematic review and meta-synthesis of qualitative research. BMJ Open. 27. januar 2023;13(1):e069091.

99. Sadeghi M, Rahiminam H, Amerizadeh A, Masoumi G, Heidari R, Shahabi J, m.fl. Prevalence of Return to Work in Cardiovascular Patients After Cardiac Rehabilitation: A Systematic Review and Meta-analysis. Curr Probl Cardiol. 1. juli 2022;47(7):100876.

100. Reibis R, Salzwedel A, Abreu A, Corra U, Davos C, Doehner W, m.fl. The importance of return to work: How to achieve optimal reintegration in ACS patients. Eur J Prev Cardiol. 1. september 2019;26(13):1358–69.

101. Cauter JV de, Bacquer DD, Clays E, Smedt DD, Kotseva K, Braeckman L. Return to work and associations with psychosocial well-being and health-related quality of life in coronary heart disease patients: Results from EUROASPIRE IV. Eur J Prev Cardiol. 1. september 2019;26(13):1386–95.

102. Bernt Jørgensen SM, Johnsen NF, Gerds TA, Brøndum S, Maribo T, Gislason G, m.fl. Perceived return-to-work pressure following cardiovascular disease is associated with age, sex, and diagnosis: a nationwide combined survey- and register-based cohort study. BMC Public Health. 27. maj 2022;22:1059.

103. Kwok CS, Shah B, Al-Suwaidi J, Fischman DL, Holmvang L, Alraies C, m.fl. Timing and Causes of Unplanned Readmissions After Percutaneous Coronary Intervention. JACC Cardiovasc Interv. 22. april 2019;12(8):734–48.

104. Hansen K, Bendix K, Antonsen L, Veien K, Maeng M, Junker A, m.fl. One-year rehospitalisation after percutaneous coronary intervention: a retrospective analysis. EuroIntervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol. 23. januar 2018;14.

105. Lauzon C, Beck CA, Huynh T, Dion D, Racine N, Carignan S, m.fl. Depression and prognosis following hospital admission because of acute myocardial infarction. CMAJ Can Med Assoc J. 4. marts 2003;168(5):547–52.

106. Nguyen MT, Ali A, Ngo L, Ellis C, Psaltis PJ, Ranasinghe I. Thirty-Day Unplanned Readmissions Following Elective and Acute Percutaneous Coronary Intervention. Heart Lung Circ. 1. maj 2023;32(5):619–28.

107. Mayou RA, Gill D, Thompson DR, Day A, Hicks N, Volmink J, m.fl. Depression and Anxiety As Predictors of Outcome After Myocardial Infarction. Psychosom Med. april 2000;62(2):212–9.

108. Holzmann MJ, Andersson T, Doemland ML, Roux S. Recurrent myocardial infarction and emergency department visits: a retrospective study on the Stockholm Area Chest Pain Cohort. Open Heart. juni 2023;10(1):e002206.

109. Mourad G, Strömberg A, Johansson P, Jaarsma T. Depressive Symptoms, Cardiac Anxiety, and Fear of Body Sensations in Patients with Non-Cardiac Chest Pain, and Their Relation to Healthcare-Seeking Behavior: A Cross-Sectional Study. Patient - Patient-Centered Outcomes Res. 1. februar 2016;9(1):69–77.

110. Kuijpers PM, Denollet J, Wellens HJ, Crijns HM, Honig A. Noncardiac chest pain in the emergency department: the role of cardiac history, anxiety or depression and Type D personality. Eur J Cardiovasc Prev Rehabil. 1. april 2007;14(2):273–9.

111. Kettles AM, Creswell JW, Zhang W. Mixed methods research in mental health nursing. J Psychiatr Ment Health Nurs. 2011;18(6):535–42.

112. Östlund U, Kidd L, Wengström Y, Rowa-Dewar N. Combining qualitative and quantitative research within mixed method research designs: A methodological review. Int J Nurs Stud. 1. marts 2011;48(3):369–83.

113. Zheng X, Zheng Y, Ma J, Zhang M, Zhang Y, Liu X, m.fl. Effect of exercise-based cardiac rehabilitation on anxiety and depression in patients with myocardial infarction: A systematic review and meta-analysis. Heart Lung. januar 2019;48(1):1–7.

114. Finsrud I, Nissen-Lie HA, Vrabel K, Høstmælingen A, Wampold BE, Ulvenes PG. It's the therapist and the treatment: The structure of common therapeutic relationship factors. Psychother Res J Soc Psychother Res. februar 2022;32(2):139–50.

115. Eifert GH, Thompson RN, Zvolensky MJ, Edwards K, Frazer NL, Haddad JW, m.fl. The Cardiac Anxiety Questionnaire: development and preliminary validity. Behav Res Ther. 1. oktober 2000;38(10):1039–53.

116. Leissner P, Held C, Rondung E, Olsson EMG. The factor structure of the cardiac anxiety questionnaire, and validation in a post-MI population. BMC Med Res Methodol. 29. december 2022;22(1):338.

117. Johansson P, Westas M, Andersson G, Alehagen U, Broström A, Jaarsma T, m.fl. An Internet-Based Cognitive Behavioral Therapy Program Adapted to Patients With Cardiovascular Disease and Depression: Randomized Controlled Trial. JMIR Ment Health. 3. oktober 2019;6(10):e14648.

118. Pedersen SS, Skovbakke SJ, Skov O, Carlbring P, Burg MM, Habibović M, m.fl. Internet-Delivered, Therapist-Assisted Treatment for Anxiety and Depression in Patients with Cardiovascular Disease: Evidence-Base and Challenges. Curr Cardiol Rep. 1. juni 2023;25(6):443–53.

Interview guide

Research questions	**Interview questions**
What kind of psychological reaction do the patients describe before starting the group course (Must be described if the patient does not quite know what is meant by psychological reaction, anxiety, depression, sadness, stress, difficulty concentrating)	Try to tell me a little about your life now? What psychological reactions did you experience after you were diagnosed with heart disease? What made you want to participate? What expectations did you have for the course?
What significance does heart disease have on the patients' lives	In what areas have changes occurred in your life after you have had a heart condition? (Support questions if necessary: How did it affect the relationship with your loved ones? Friends? Leisure activities? How did it affect your work?) What reprioritisations has the disease given rise to? What thoughts do you have about the future?
The cognitive tools promote a processing of the stress reaction, including symptoms of anxiety and depression, and can be used in the future • Content of intervention:	How did you experience being in a group? How have you used the cognitive tools? Do you feel that there is a connection between body and soul? Possibly. how?

• Matrix mapping of values • The circle of anxiety, exposure • Behaviour analysis • Strategies for worries • To create balance, things that charge or drain	How has heart disease changed your psychological reactions? What suggestions do you have for improving the process?
Does the group process promote a reduction in stress response?	How did you experience participating in the group course? How has it changed your mental well-being? What role has the course played in your way of handling your situation?

Appendices

Papers 1-3

Appendix I

Paper I

Intensive group-based cognitive therapy in patients with cardiac disease and psychological distress-a randomized controlled trial protocol. Holdgaard A, Eckhardt-Hansen C, Lund T, Lassen CF, Sibiliz KL, Høfsten DE, Prescott E, Rasmusen HK. Trials. 2021 Jul 16;22(1):455. doi: 10.1186/s13063-021-05405-3. PMID: 34271952 Free PMC article.

Holdgaard et al. Trials (2021) 22:455
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Trials

STUDY PROTOCOL Open Access

Intensive group-based cognitive therapy in patients with cardiac disease and psychological distress—a randomized controlled trial protocol

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Abstract

Background: Many patients with coronary artery disease (CAD) and valvular heart disease (VHD) suffer from psychological distress. Such stress is associated with increased morbidity, reduced quality of life and delayed return to work. European guidelines emphasize recognition and intervention, but evidence-based treatment options are limited and perceived as costly. The present study will test the effect of brief, group-based cognitive therapy as an adjunct to usual cardiac rehabilitation in a randomized design.

Methods: A total of 148 patients with CAD and/or VHD after surgical intervention and concomitant psychological distress (defined as HADS anxiety (A) or depression (D) score ≥8) will be randomized to either usual out-patient cardiac rehabilitation (CR) comprising an 8-week multidisciplinary programme or usual care supplemented by five group-based cognitive therapy sessions performed by trained CR nurses. A structured, standardized treatment manual will be used. Patients will be randomized 1:1 at three different sites. Additionally, a non-randomized sub-group of 40 matched patients without signs of psychological distress will be followed to investigate spontaneous variation in HADS. The primary outcome is Hospital Anxiety and Depression Score (HADS). Secondary outcomes are adherence to cardiac rehabilitation (CR), health-related quality of life measured by HeartQoL, time to return to work, adherence to lifestyle interventions and cardiovascular readmissions. Patients are followed up for 12 months.

Discussion: To our knowledge, this is the first randomized controlled trial (RCT) on patients with cardiac disease with an intensive group-based programme of cognitive therapy performed by CR nurses, which makes it affordable and widely implementable. The outcome will elucidate the feasibility and effect of cognitive therapy as an adjunct to CR in patients with post-surgery CAD and/or VHD and psychological distress and could possibly benefit patients with other heart conditions as well. The clinical trial complies with the Declaration of Helsinki. The trial has been approved by The Regional Research Ethics Committee (file number H-16042832) and The Danish Data Protection Agency. The results will be disseminated as original research in peer-reviewed manuscripts.

Trial registration: www.clinicaltrials.gov NCT04254315. Retrospectively registered on 30 January 2020.

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Keywords: Coronary heart disease, Cardiac rehabilitation, HADS, Depression, Anxiety, Psychological distress, Cognitive therapy

Background

Psychological distress in the form of anxiety and depression is a common but often unrecognized problem in many cardiac patients. Up to 38% report psychological distress at 2 months and 33% at 12 months after myocardial infarction (MI) [1, 2]. The importance of recognizing this condition is underlined by studies that find that psychological distress not only impairs quality of life (QoL) but is also associated with increased rates of cardiac and all-cause mortality [3, 4]. Data from the national SWEDEHEART registry show that patients with persistent emotional distress following acute coronary syndrome (ACS) were more likely to die from cardiovascular and non-cardiovascular causes than those with no distress [5]. Patients undergoing valvular heart surgery have received less attention in current research, but one study has indicated that after aortic valve surgery female patients have anxiety symptoms at a level equal to that of patients with coronary artery disease (CAD) [6].

Untreated emotional distress may worsen cardiac prognosis because of behavioural mechanisms such as unhealthy lifestyle, reduced success of risk factor modification and less adherence to cardiac rehabilitation (CR) and medical treatment [7]. In one study of 5908 patients with heart disease and moderate depression, those with anxiety or stress symptoms were significantly less likely to adhere to CR than those with normal-to-mild symptoms [8]. Psychological distress may also have a direct impact on pathophysiological mechanisms such as the autonomic nervous system [9] and endothelial dysfunction [10]. Psychological distress has an impact by retaining patients with cardiac disease from returning to working. Among 20,415 patients who returned to work after MI, a quarter were no longer in employment after 1 year but were instead being supported by social benefits [11]. Important risk factors of unemployment are depression and low socioeconomic status [11, 12].

The best treatment for cardiac patients with psychological distress is uncertain, but cognitive behavioural therapy (CBT) may be an effective option. A recent systematic review and meta-analysis [13] concluded that CBT significantly reduced both depression and anxiety and improved QoL compared with controls. Group-based cognitive therapy may be a cost-effective option that can be delivered by specially trained nurses as part of a CR programme. A few studies have reported the effect of group-based CBT on psychological distress in patients with cardiac disease. In a multi-centre RCT [14], 151 unselected patients with cardiac disease received cognitively based group therapy for 12 weeks and obtained a significant additive effect on top of standard CR on a combined endpoint of stress management, cardiac biomarkers and physical activity compared with standard CR alone. Another trial with a 20-week intervention found a similar effect [15]. However, although CBT seems effective, it is still not widely implemented in CR. A main barrier is the perceived need for a comprehensive, time-consuming intervention, which is not possible in the context of a standard CR programme. Therefore, the aim of this trial is to investigate whether brief, group-based CBT integrated in CR and delivered by cardiac nurses can reduce the level of psychological distress in patients with cardiac disease.

Methods

Aim

The aim of the study is to develop an efficient and cost-effective model for the use of intensive group-based cognitive therapy to address psychological distress in patients with newly diagnosed CAD and/or surgically treated valvular heart disease (VHD) and concomitant psychological distress.

Design

The study is a multi-centre, prospective, randomized clinical trial in patients with newly diagnosed CAD and/or surgically treated VHD and concomitant psychological distress defined as HADS (HADS A (Anxiety) or D (Depression) ≥ 8) and part of the work force. Patients with HADS D ≥ 11 and Beck Depression Inventory (BDI) > 17 are evaluated by a psychiatrist to ensure that patients with severe depression or other psychiatric diagnoses are not included in the study. Additionally, 40 patients with HADS score < 8 at their first visit to CR will be followed for spontaneous variation in HADS score at 3 and 6 months to determine whether screening at the first visit to CR is the optimal time at which to identify patients with psychological distress.

Participants

The trial is a multi-centre trial planned to include 188 patients from three departments of cardiology. The main trial includes 148 randomized patients. We will also include a non-randomized subgroup of 40 matched patients (relative to inclusion and exclusion criteria) without signs of psychological distress to investigate spontaneous variation in HADS scores over time.

Inclusion criteria are:

- Referred to CR and accepting CR
- Patients with newly diagnosed CAD and/ or surgically treated VHD
- HADS score > 8 for HADS-A and/or HADS-D
- Age < 65 years
- Able to speak and understand Danish

Exclusion criteria are:

- EF < 35%
- Other serious comorbidity expected to have a serious impact on life expectancy
- Known abuse of alcohol or euphoric drugs
- Known more serious psychopathology such as schizophrenia, bipolar disorder, severe personality disorder and treatment with psychoactive drugs

Trial procedure and randomization

Consecutive patients discharged from the hospital with newly diagnosed ischaemic heart disease and/or surgically treated VHD will be screened with HADS at their first visit to CR.

If a patient decides to participate in the study after having received written and verbal information from a research nurse, an informed consent form is signed and the patient is randomized to either (1) CR and intervention consisting of five sessions of CBT or (2) CR alone (Fig. 1).

Randomization is performed by an independent researcher, and the randomization programme is kept in a secured, logged hard disk. STATA II, the Ralloc programme, permuting random block sizes of 2, 4 and 6, respectively, is used for randomization. Before randomization, baseline data are collected (see Table 1).

Both the intervention and the control group will receive usual care in interdisciplinary CR.

As our patients are still part of the work force, the follow-up visit must fit with their working schedule to reduce potential loss to follow-up. We therefore accept considerable flexibility in the scheduling of follow-up appointments. The patients receive an email or SMS as a reminder before their appointments. If they do not meet for the scheduled appointment, they will be contacted by telephone.

SPIRIT trial schedule

This paper presents the detailed protocol for the trial "Intensive group-based cognitive therapy in patients with cardiac disease and psychological distress". The trial is described in accordance with the current SPIRIT guidelines (Standard Protocol Items: Recommendations for Interventional Trials [16]. Results will be reported following the CONSORT (CONsolidated Standards Of Reporting Trials) guidelines for non-pharmacological interventions [17].

Method to define psychological distress

Psychological distress in patients with cardiac disease has formerly been identified by symptoms of anxiety and depression and identified with HADS [18–23]. HADS is a 14-item questionnaire that assesses anxiety and depression levels in medically ill persons who are not admitted to psychiatric wards. The scale has two scores, HADS-A and HADS-D, and consists of seven questions to assess anxiety and seven questions to assess depression [24]. The scale is focused on psychological symptoms of mood disorders, leaving out physical symptoms that can be confused with physical illness. This is an advantage in populations with cardiac disease where symptoms such as dizziness, dyspnoea or palpitations might be related to the underlying cardiac disease and not to a potential mood disorder [25].

Psychological distress is associated with reduced QoL. Therefore, these patients' QoL is monitored by a validated questionnaire, the HeartQoL disease-specific questionnaire. The HeartQoL measures health-related QoL in patients with heart disease. It consists of 14 items and provides two subscales: a 10-item physical subscale and a 4-item emotional subscale, which are scored from 0 to 3. Higher scores indicating better QoL [26, 27].

Usual care

Our usual CR programme consists of a supervised 8-week outpatient exercise intervention at the hospital with 2 weekly sessions of 1.5 h with high-intensity intervals (80% of peak oxygen uptake) and resistance training. The programme is complemented with a weekly session of group-based patient education for 1.5 hours on heart disease, psychological issues and diet counselling. When needed, patients also have one or more individual sessions with a cardiologist, dietician or a nurse.

Intervention

In addition to our usual CR programme, the intervention group will receive CBT as described below.

Cognitive behavioural therapy (CBT) background

CBT is an established and recognized evidence-based psychotherapeutic method based on clinical experience, theory and research. Three categories of CBT exist. The first originates from behavioural therapy; the second rests on theories about thoughts and their influence on the body, emotions and actions (cognitive therapy), while the third CBT category (such as acceptance and commitment therapy (ACT), metacognitive therapy and mindfulness-based therapy) is based on acceptance of one's thoughts and feelings. In cognitive therapy, focus is

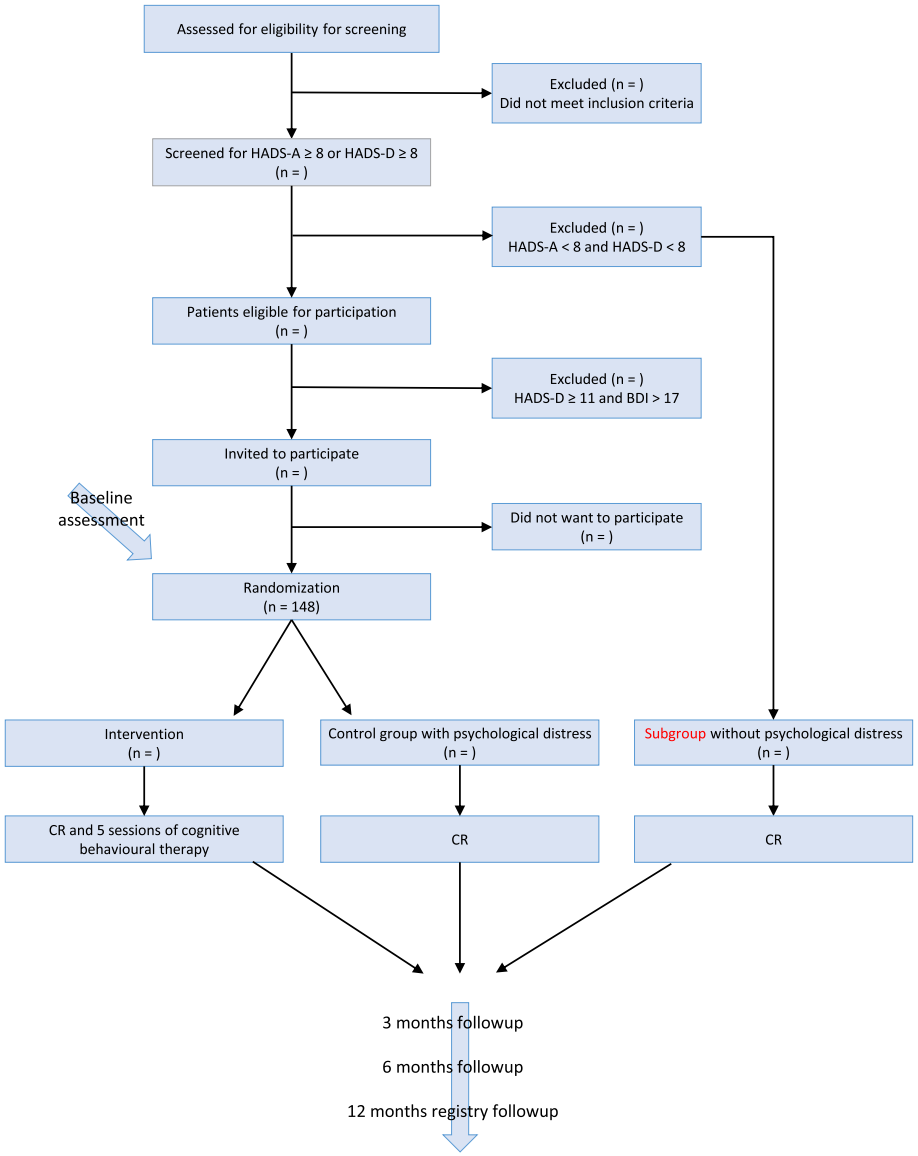

Fig. 1 The trial diagram. Flow of patients. Participants in the intervention group follow CR and five sessions of CBT therapy and the control group follow standard CR

on which of the patient's thoughts and behavioural patterns may create and maintain current problems and influence functional levels. By changing thoughts and patterns of behaviour, the level of functioning and/or QoL may also be changed [28, 29]. In ACT, the focus is rather on accepting the current situation combined with a commitment to change inappropriate behaviour. In this context, focus is given to the purpose of one's thinking rather than to the contents of a given thought. CBT and ACT have much in common; they both focus on the present and private internal experiences, and they both present the patient with skills that can be applied in different contexts. Because they share these characteristics, it is possible and even helpful to integrate the two approaches. In the present study, sessions 2, 3, and 5 are based on concepts of changing thoughts and behaviours (CBT), and sessions 1 and 4 are primarily based on ACT interventions [30].

CBT intervention

The CBT intervention is a psycho-educational group course conducted as five sessions led by an experienced nurse under the supervision of a psychologist who is a specialist in CBT. There will be 3–4 patients in each group for the therapy sessions. Each session will last 2 h and has a set structure, with the use of homework and always ending with the opportunity to give feedback [28].

Table 1 Schedule of enrolment, intervention and assessments

	Study period (months)								
	Baseline	Intervention (allocation) Group-based therapy (5 weeks)					Post-allocation (months)		Close-out
Timepoint	0	0	1 week	2 weeks	3 weeks	4 weeks	3 months	6 months	12 months
Enrolment									
Eligibility screen	x								
Informed consent	x								
Allocation of patients	x								
Intervention		x	x	x	x	x	x	x	
Control							x	x	
Follow-up visit							x	x	
Assessments									
Background									
Cohabitant	x						x	x	
Level of education	x								
Employment status	x						x	x	
Sick leave	x						x	x	
Return to work	x						x	x	
Index event	x								
Clinical measurements									
Weight	x						x	x	
Heart rate	x						x	x	
Blood pressure	x						x	x	
ECG	x						x	x	
Biochemical screening	x						x	x	
NYHA classification	x						x	x	
CCS classification	x						x	x	
Medication	x						x	x	
Comorbidity									
History of heart disease	x								
Chronic obstructive pulmonary disease	x								
Kidney disease	x								
Depression	x								
Risk factors									
Hypertension	x								
Dyslipidaemia	x								
Diabetes mellitus	x						x	x	
Family history	x								
Smoking	x						x	x	
Physical activity	x						x	x	
Rehabilitation received							x	x	
Questionnaires									
HADS	x						x	x	
HeartQol	x						x	x	
Psychosocial status	x						x	x	
Cardiovascular readmission									x

The five sessions contain:

1) Introduction to CBT and mapping of own values
2) Anxiety and anxiety reduction techniques
3) Functional analysis (awareness of consequences of own behaviour)
4) Concerns and strategies for dealing with concerns
5) Balance between requirements and forces as well as conclusion

First session

The experience of having a severe illness sets in motion a variety of existential thoughts about life and death and about what is important in life. Thus, the first session seeks to clarify which values the patient has and which actions bring him/her into alignment with these values. It also reveals which difficulties prevent him from acting the way he really wants to act and how a given behaviour is related to what is important to him. For example, a heart patient may have a value linked to health and the associated behaviour might be to follow the dietician's advice and to continue exercising. His difficulties might be associated with fear of having another heart attack, which could lead to inactivity. The assigned homework in this session is completing a matrix (see Fig. 2) [31].

Second session

After a heart attack, patients commonly fear another attack. The second session is thus based on anxiety. Initially, it is emphasized that anxiety is a normal feeling and a natural reaction to danger. Anxiety becomes inconvenient when connected to an "imagined" danger and/or takes on the character of an "excessive" danger. The physiology of anxiety is thoroughly reviewed, so that the patient will be able to recognize its physical components and thus distinguish between a regular heart attack and anxiety symptoms. When the basic conditions are explained in this way, the anxiety circle is reviewed; the anxiety circle describes how an experienced threat can cause physical reactions and catastrophizing thoughts. This often leads to avoidance behaviour and/or safety behaviour. Of course, when anxiety-filled situations are avoided, anxiety diminishes, but the expectation of anxiety rises, and the person may begin to fear a similar situation in the future (see Fig. 3). This session ends with the introduction of various types of strategies as well as explanations of why it is important gradually to expose oneself to situations in which it is difficult to keep anxiety at a low level. The homework for this session is to begin gradual exposure and to apply the strategies in everyday life [32].

Third session

After CAD and surgically treated VHD, several lifestyle changes are recommended, such as a change of diet and initial part-time sick leave. It can be difficult to change lifestyle and incorporate new habits. Therefore, the third session deals with the analysis and consequences of current behaviour. For example, a patient is satisfied with his work, wherefore he works 50 h per week. The consequence of this is that in the short term he is satisfied and happy while not having time to recover from his illness, which can have serious implications in the

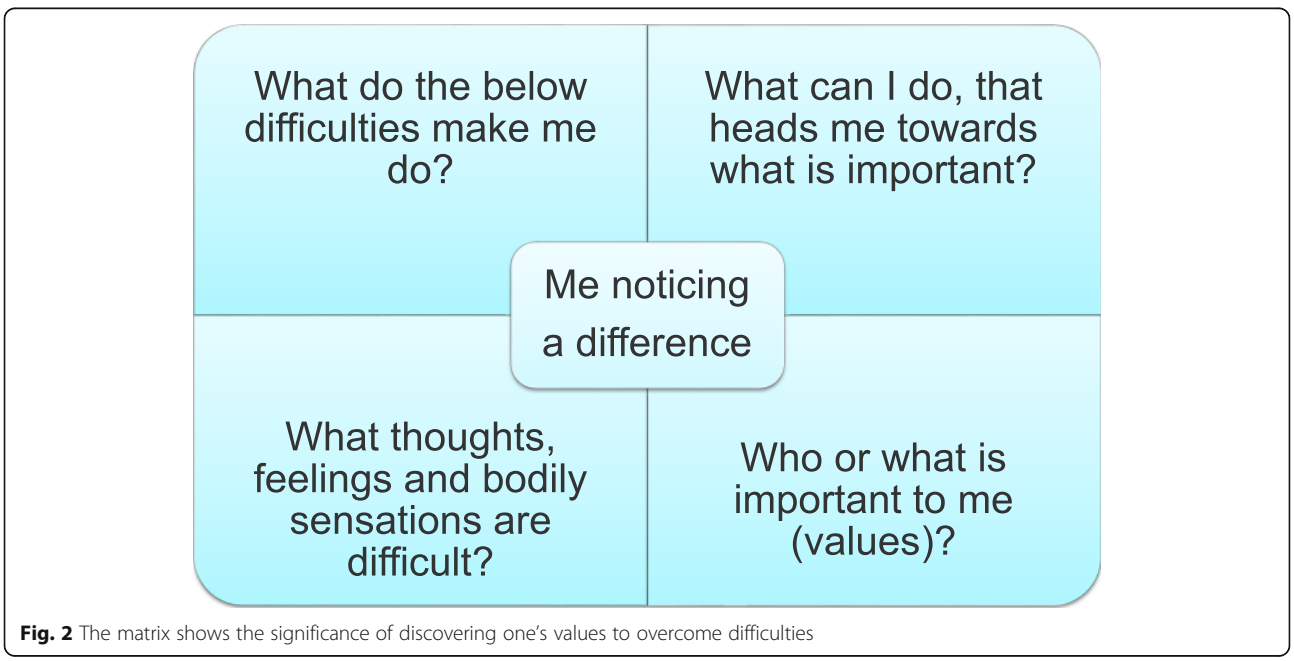

Fig. 2 The matrix shows the significance of discovering one's values to overcome difficulties

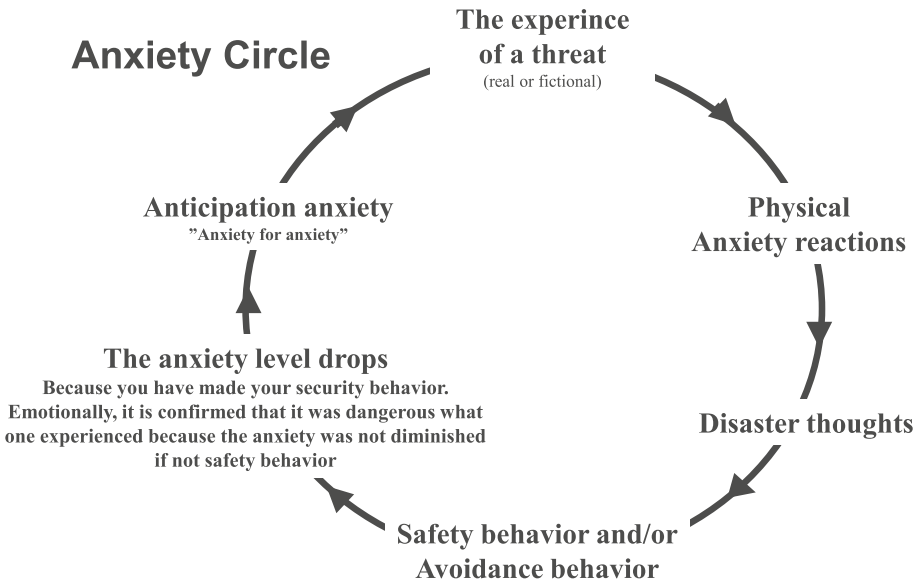

Fig. 3 Circle of anxiety demonstrates a correlation between thoughts, feelings and behaviour. The anxiety circle is inspired by Esben Hougaard

longer term. Homework in this session is the completion of a "behavioural analysis" form (see Fig. 4).

Fourth session

CAD and VHD give rise to many concerns that potentially limit the patient. Worry is a way of thinking that can lead to problem-solving, but it can also lead to pondering. Therefore, the fourth session is about recognizing one's own thinking and the influence it has on one's behaviour in order to move towards a more constructive behaviour. The session broadly explains several strategies including acceptance and diffusion (creating distance to thought). Homework is to recognize if/when one ponders/worries and if so, to possibly apply some of the strategies [33].

Fifth session

The last session focuses on how to make optimal use of the strengths the patient possesses. It illustrates how to balance demands and strengths with an emphasis on committing to nourishing and long-term strategies. It can for example be helpful to apply new strategies such as breaking up a larger task into smaller steps. In the latter half of this session, the matrix from the first session is explained and included more explicitly to examine whether the participants may have changed their strategies and comprehension in comparison with the beginning of the course. The session is concluded with feedback on the entire process [34, 35].

Primary outcome

The primary outcome is mean (method of aggregation) change (metric) in psychological distress (domain) measured by HADS total score (specific measurement) from baseline to three months (time) in the intervention group compared with the usual care group. This outcome may be subject to ascertainment bias when blinding is not possible, e.g. social desirability bias causing participants to respond more favourably. We have attempted to limit this by administering the paper questionnaires to be filled in unsupervised. Furthermore, since both the intervention and the control group receive usual CR in the same cardiac settings, both groups may be subject to similar social desirability bias. At the 6-month follow-up, we anticipate that this bias will be reduced.

Secondary outcomes

Secondary outcomes are adherence to CR defined as > 80% participation in planned training sessions (used as a secondary outcome under the hypothesis that participation in group-based therapy will improve CR adherence), health-related QoL measured by the questionnaire HeartQoL, return to work, marital status, adherence to medication and lifestyle interventions for CVD risk factor goals defined as four separate outcomes: HbA1c < 48, BP < 135/85 mmHg, BMI < 30 and LDL < 1.4 mmol/l, physical activity (days per week with ≥ 30 min of moderate physical activity) and cardiovascular readmissions at 12 months.

Sample size and power calculation

The primary outcome is a change in HADS score at 3 months. A clinically relevant difference between groups would be a reduction in the total sum score of 2. In a previous study [36], the change within each group was

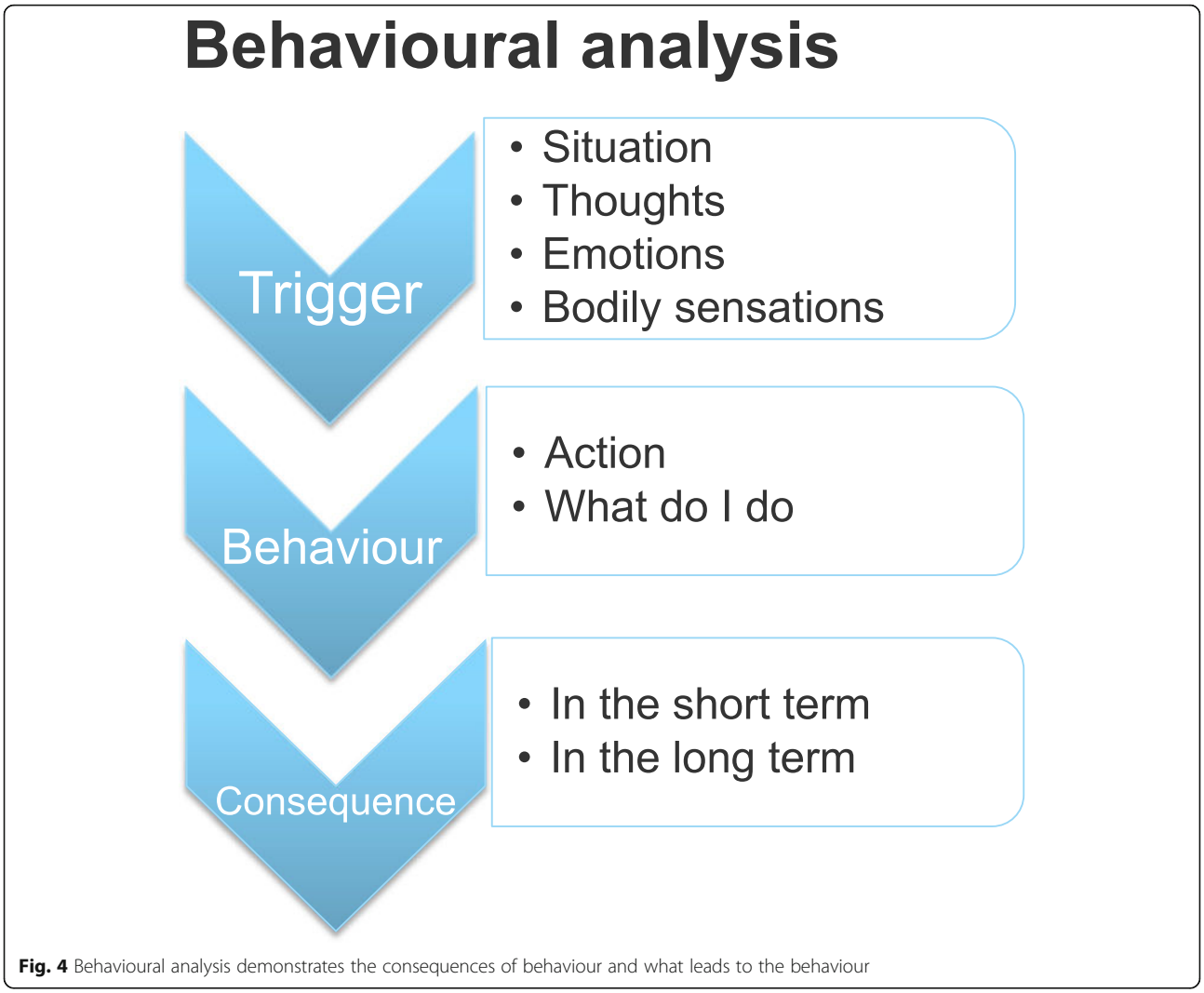

Fig. 4 Behavioural analysis demonstrates the consequences of behaviour and what leads to the behaviour

normally distributed with a standard deviation (SD) of 2.5. We have here used a more conservative estimate with an SD of 4. Under these assumptions with a risk of type 1 error of 0.05 and a power of 0.8, 64 patients should be included in each group. Due to the risk of dropout of patients included in this type of trial, the total number of patients included is increased by 15% to 148 patients

STATA II, the Ralloc programme is used for randomization, permuting random block sizes of 2,4 and 6.

To assess the spontaneous variation in HADS scores over time, we will investigate a non-randomized group of 40 matched patients (relative to inclusion and exclusion criteria) without signs of psychological distress (i.e. HADS A < 8 and HADS D < 8) at first measurement with re-evaluation after 3 and 6 months. With 64 patients in the usual care arm and assuming a SD of 4 as above, we will have 80% power to detect a difference in change in HADS score (delta HADS) of 2.3 or more between these two groups.

Data management

Data will be collected at baseline and follow-up visits. Questionnaire responses (all on paper) will be entered into electronic form in REDCap immediately after the assessment. Data from patient records (all electronic) will also be entered into REDCap. All participants will be identified by unique study identification numbers that will be included in a password-protected file. Data will be stored in accordance with the rules of the Danish Data Protection Agency. REDCap meets all criteria for the handling of patient data in accordance with the laws on the processing of personal data. The principal investigator HR, AH and EP will have unlimited access to the final trial dataset.

Statistical analysis

The primary analysis will be a comparison of the intervention and control group in mixed-models linear regression with robust standard errors with 3-month

values as outcome, and baseline and 6 months values will be used as adjustment variables. Analyses will also be adjusted for the centre and tested for treatment-centre interaction. For the analysis of the secondary outcomes return to work (yes/no), HbA1c< 48, BP< 135/85 mmHg, BMI< 30, LDL< 1.4 mmol/l and physical activity, we will also apply repeated measures regression. For adherence to CR (> 80%), we will compare groups by logistic regression adjusting for the centre. For the outcome of readmission at 12 months, we will compare outcomes across groups with Kaplan-Meier curves and time-to-event analyses (Cox regression) adjusting for age, left ventricular ejection fraction, co-morbidities and risk factors as described above. A two-sided $P < 0.05$ will be considered statistically significant, and all primary outcome analyses will be performed without knowledge of group allocation.

We will compare the primary outcome in intervention and control groups with the spontaneous variation in the non-distressed subgroup of 40 participants by separate mixed-models linear regression adjusting for baseline values and centre.

The primary reported analyses will be carried out as a modified intention-to-treat as participants with missing data on a primary or secondary outcome will be excluded from the corresponding analyses. The analysis is supplemented with per-protocol analyses defined by participation in ≥ 4 of the 5 group-based sessions. Missing information on other co-variates will be permuted if there is < 20% missing data for the co-variate in question.

Discussion

Psychological distress is often an overseen problem in patients with cardiac disease receiving CR the consequences of which are increased morbidity and mortality. If supported, our intervention will be a cost-effective and accessible way to improve QoL and reduce morbidity in these patients, and it might impact daily clinical practice. It is expected that results from the study will contribute to fill an important gap in our knowledge of how to address the physical and psychological needs of patients having undergone heart surgery.

Trial status

The study is currently enrolling patients and was planned to complete patient enrolment in 2021. However, due to the COVID-19 pandemic, the study is now expected to be extended until 2022. Due to the lockdown in Denmark, it was not possible to include patients from 11 March 2020 until 1 June 2020. The patients randomized immediately before this period had to be excluded as the time until start of the intervention was too long.

Abbreviations

ACS: Acute coronary syndrome; ACT: Acceptance and commitment therapy; AHA: American Heart Association; BDI: Beck Depression Inventory; BMI: Body mass index; BP: Blood pressure; CBT: Cognitive behavioural therapy; CCS: Canadian Cardiovascular Society grading of angina pectoris; CI: Confidence interval; CONSORT: CONsolidated Standards of Reporting Trials; CR: Cardiac rehabilitation; ECG: Electrocardiogram; ESC: European Society of Cardiology; HADS: Hospital Anxiety and Depression Scale; HbA1: Glycated haemoglobin; HeartQol: Heart-related quality of life; HR: Hazard ratio; LDL: Low-density lipoprotein; NYHA: New York Heart Association; ICBT: Internet-based cognitive behavioural therapy; PCI: Percutaneous coronary intervention; Qol: Quality of life; RCT: Randomized controlled trial; SD: Standard deviation; Smartex-HF study: Controlled study of myocardial recovery after interval training in heart failure; VHD: Valvular heart disease

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Authors' contributions

Authors HR, EP and AH conceived and designed the study, acquired data and drafted the manuscript. CEH, HR and AH conceived the intervention. HR and EP performed the statistical analysis and drafted the statistical analysis plan. KLM and CFL made substantial contributions and revisions to the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Danish legislation does not allow us to share data even if anonymized. The data will be made available in aggregated form from the authors upon request.

Declarations

Ethics approval and consent to participate

The Ethics Committee for the Capital Region of Denmark (file number H-16042832) and the Danish Data Protection Agency have approved the trail, and the study is registered at http://www.ClinicalTrials.gov (NCT04254315) The study is performed in accordance with the Declaration of Helsinki in its latest form. Participants can withdraw from the study at any time without any explanation or consequences. The regional ethics committee will be asked for permission in the case of protocol amendments.
A patient from the control group and the intervention group can follow the same group at the usual CR to make sure that the treatment will not be delayed.

Consent for publication

No consent for publication is required.

Competing interests

The authors declare that they have no competing interests.

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References

1. Norlund F, Lissåker C, Wallert J, Held C, Olsson EM. Factors associated with emotional distress in patients with myocardial infarction: results from the

SWEDEHEART registry. Eur J Prev Cardiol. 2018;25(9):910–20. https://doi.org/10.1177/2047487318770510.
2. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, et al. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. Circulation. 2014;129(12):1350–69.
3. Murphy B, Le Grande M, Alvarenga M, Worcester M, Jackson A. Anxiety and depression after a cardiac event: prevalence and predictors. Front Psychol. 2020;10 Tilgængelig hos: https://www.frontiersin.org/articles/10.3389/fpsyg.2019.03010/full. [henvist 23. marts 2020].
4. van Dijk MR, Utens EM, Dulfer K, Al-Qezweny MN, van Geuns R-J, Daemen J, et al. Depression and anxiety symptoms as predictors of mortality in PCI patients at 10 years of follow-up. Eur J Prev Cardiol. 2016;23(5):552–8.
5. Lissåker CT, Norlund F, Wallert J, Held C, Olsson EM. Persistent emotional distress after a first-time myocardial infarction and its association to late cardiovascular and non-cardiovascular mortality. Eur J Prev Cardiol. 2019;26(14):1510–8. https://doi.org/10.1177/2047487319841475.
6. Borregaard B, Ekholm O, Riber L, Sørensen J, Møller JE, Thrysoe L, et al. Patient-reported outcomes after aortic and mitral valve surgery – results from the DenHeart study. Eur J Cardiovasc Nurs. 2018;17(3):246–54.
7. Berg SK, Rasmussen TB, Thrysoee L, Thorup CB, Borregaard B, Christensen AV, et al. Mental health is a risk factor for poor outcomes in patients with cardiac disease: findings from the national DenHeart survey. J Psychosom Res. 2018;112:66–72. https://doi.org/10.1016/j.jpsychores.2018.07.002.
8. Rao A, Zecchin R, Newton P, Phillips J, DiGiacomo M, Denniss A, et al. The prevalence and impact of depression and anxiety in cardiac rehabilitation: a longitudinal cohort study. Eur J Prev Cardiol. 2020;27(5):478-89. https://doi.org/10.1177/2047487319871716. Epub 2019 Oct 9.
9. Carney RM, Blumenthal JA, Stein PK, Watkins L, Catellier D, Berkman LF, et al. Depression, heart rate variability, and acute myocardial infarction. Circulation. 2001;104(17):2024–8.
10. Sherwood A, Hinderliter AL, Watkins LL, Waugh RA, Blumenthal JA. Impaired endothelial function in coronary heart disease patients with depressive symptomatology. J Am Coll Cardiol. 2005;46(4):656–9. https://doi.org/10.1016/j.jacc.2005.05.041.
11. Smedegaard L, Numé A, Charlot M, Kragholm K, Gislason G, Hansen PR. Return to work and risk of subsequent detachment from employment after myocardial infarction: insights from Danish Nationwide Registries. JAHA. 2017;6(10) Tilgængelig hos: https://www.ahajournals.org/doi/10.1161/JAHA.117.006486. [henvist 31. august 2020].
12. Stendardo M, Bonci M, Casillo V, Miglio R, Giovannini G, Nardini M, et al. Predicting return to work after acute myocardial infarction: socio-occupational factors overcome clinical conditions. Lazzeri C, redaktør. PLoS ONE. 2018;13(12):e0208842.
13. Reavell J, Hopkinson M, Clarkesmith D, Lane DA. Effectiveness of cognitive behavioral therapy for depression and anxiety in patients with cardiovascular disease: a systematic review and meta-analysis. Psychosom Med. 2018;80(8):742–53. https://doi.org/10.1097/PSY.0000000000000626.
14. Blumenthal James A, Andrew S, Smith Patrick J, Lana W, Stephanie M, Kraus William E, et al. Enhancing cardiac rehabilitation with stress management training. Circulation. 2016;133(14):1341–50.
15. Gullikkson M, Burell G, Vessby B, Lundin L, Toss H, Svärdsudd K. Randomized controlled trial of cognitive behavioral therapy vs standard treatment to prevent recurrent cardiovascular events in patients with coronary heart disease: Secondary Prevention in Uppsala Primary Health Care project (SUPRIM). Arch Intern Med. 2011;171(2):134–40.
16. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200.
17. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, for the CONSORT Group. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. Ann Intern Med. 2008;148(4):295.
18. Bambauer KZ, Locke SE, Aupont O, Mullan MG, McLaughlin TJ. Using the Hospital Anxiety and Depression Scale to screen for depression in patients with cardiac disease. Gen Hosp Psychiatry. 2005;27(4):275–84. https://doi.org/10.1016/j.genhosppsych.2005.03.002.
19. Scherer M, Himmel W, Stanske B, Scherer F, Koschack J, Kochen MM, et al. Psychological distress in primary care patients with heart failure: a longitudinal study. Br J Gen Pract. 2007;57(543):801–7.
20. Haddad M, Walters P, Phillips R, Tsakok J, Williams P, Mann A, et al. Detecting depression in patients with coronary heart disease: a diagnostic evaluation of the PHQ-9 and HADS-D in primary care, findings from the UPBEAT-UK Study. Shimizu E, redaktør. PLoS ONE. 2013;8(10):e78493.
21. Lie I, Arnesen H, Sandvik L, Hamilton G, Bunch HE. Effects of a home-based intervention program on anxiety and depression 6 months after coronary artery bypass grafting: a randomized controlled trial. J Psychosom Res. 2007;62(4):411–8.
22. Lichtman JH, Thomas BJ, Blumenthal James A, Nancy F-S, Kaufmann Peter G, François L, et al. Depression and coronary heart disease. Circulation. 2008;118(17):1768–75.
23. Berg SK, Thorup CB, Borregaard B, Christensen AV, Thrysoee L, Rasmussen TB, et al. Patient-reported outcomes are independent predictors of one-year mortality and cardiac events across cardiac diagnoses: findings from the national DenHeart survey. Eur J Prev Cardiol. 2019;26(6):624–37.
24. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale an updated literature review. J Psychosom Res. 2002;52(2):69-77. https://doi.org/10.1016/s0022-3999(01)00296-3.
25. Christensen AV, Dixon JK, Juel K, Ekholm O, Rasmussen TB, Borregaard B, et al. Psychometric properties of the Danish Hospital Anxiety and Depression Scale in patients with cardiac disease: results from the DenHeart survey. Health Qual Life Outcomes. 2020;18 Tilgængelig hos: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6947856/. [henvist 24. september 2020].
26. Oldridge N, Höfer S, McGee H, Conroy R, Doyle F, Saner H. The HeartQoL: Part I. Development of a new core health-related quality of life questionnaire for patients with ischemic heart disease. Eur J Prev Cardiol. 2014;21(1):90–7.
27. Oldridge N, Höfer S, McGee H, Conroy R, Doyle F, Saner H. The HeartQoL: Part II. Validation of a new core health-related quality of life questionnaire for patients with ischemic heart disease. Eur J Prev Cardiol. 2014;21(1):98–106.
28. Beck JS, Beck JS. Cognitive behavior therapy: basics and beyond. 2nd ed. New York: Guilford Press; 2011. p. 391 s.
29. Arendt M. Cognitive therapy: recent development; 2012.
30. Hallis L, Cameli L, Bekkouche NS, Knäuper B. Combining cognitive therapy with acceptance and commitment therapy for depression: a group therapy feasibility study. J Cogn Psychother. 2017;31(3):171–90. https://doi.org/10.1891/0889-8391.31.3.171.
31. Polk KL, Schoendorff B, redaktører. The ACT matrix: a new approach to building psychological flexibility across settings & populations. Oakland: Context Press, an imprint of New Harbinger Publications, Inc; 2014. p. 266 s.
32. Hougaard E, Hougaard E, Rosenberg NK. Cognitive treatment of panic disorder and social phobia: a guide for clients and therapists. Kbh: Danish psychological publishers; 2007.
33. Harris R, Aisbett B. Lykkefælden: Illustrated guide on how to stop the fight and live life. Virum: Danish Psychological publishers; 2013.
34. Due MJ. Cognitive behavioral therapy for depression: manual for group therapy. Virum: Danish psychological publishers; 2008.
35. Martell CR, Dimidjian S, Herman-Dunn R. A behavioral activation in depression: a clinical guide. Kbh: Danish psychological publishers; 2012.
36. Karlsen T, Videm V, Halle M, Ellingsen Ø, Støylen A, Dalen H, et al. Baseline and exercise predictors of V˙O2peak in systolic heart failure patients: results from SMARTEX-HF. Med Sci Sports Exerc. 2020;52(4):810–9.

Publisher's Note

Appendix II

Paper II

Cognitive-behavioural therapy reduces psychological distress in younger patients with cardiac disease: a randomized trial. Holdgaard A, Eckhardt-Hansen C, Lassen CF, Kjesbu IE, Dall CH, Michaelsen KL, Sibilitz KL, Prescott E, Rasmusen HK. Eur Heart J. 2023 Jan 18:ehac792. doi: 10.1093/eurheartj/ehac792. Online ahead of print. PMID: 36649937

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Cognitive-behavioural therapy reduces psychological distress in younger patients with cardiac disease: a randomized trial

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See the editorial comment for this article 'Are we getting closer to treating heart and mind together and bridging the gap for individual patients attending cardiac rehabilitation?', by S. S. Pedersen *et al.*, https://doi.org/10.1093/eurheartj/ehac820.

Abstract

Aims To test whether usual outpatient cardiac rehabilitation (CR) supplemented by a cognitive-behavioural therapy (CBT) intervention may reduce anxiety and depression compared with usual CR.

Methods and results In this multicentre randomized controlled trial, 147 cardiac patients (67% men, mean age 54 years, 92% with coronary artery disease) with psychological distress defined as a hospital anxiety and depression scale (HADS) anxiety or depression score ≥8 were randomized to five sessions of group CBT plus usual CR (intervention, $n = 74$) or CR alone (control, $n = 73$). Patients with severe distress or a psychiatric diagnosis were excluded. The intervention was delivered by cardiac nurses with CBT training and supervised by a psychologist. A reference, non-randomized group (background, $n = 41$) of consecutive patients without psychological distress receiving usual CR was included to explore the effect of time on HADS score. The primary outcome, total HADS score after 3 months, improved more in the intervention than in the control group [the mean total HADS score improved by 8.0 (standard deviation 5.6) vs. 4.1 (standard deviation 7.8), $P < 0.001$]. Significant between-group differences were maintained after 6 months. Compared with the control group, the intervention group also had greater adherence to CR ($P = 0.003$), more improvement in the heart-related quality of life (HeartQoL) at 6 months ($P < 0.01$), and a significant reduction in cardiac readmissions at 12 months ($P < 0.01$). The background group had no significant change in HADS score over time.

Conclusion Brief CBT provided by cardiac nurses in relation to CR reduced anxiety and depression scores, improved HeartQoL and adherence to CR, and reduced cardiovascular readmissions. The programme is simple and may be implemented by CR nurses.

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Structured Graphical Abstract

Key Question

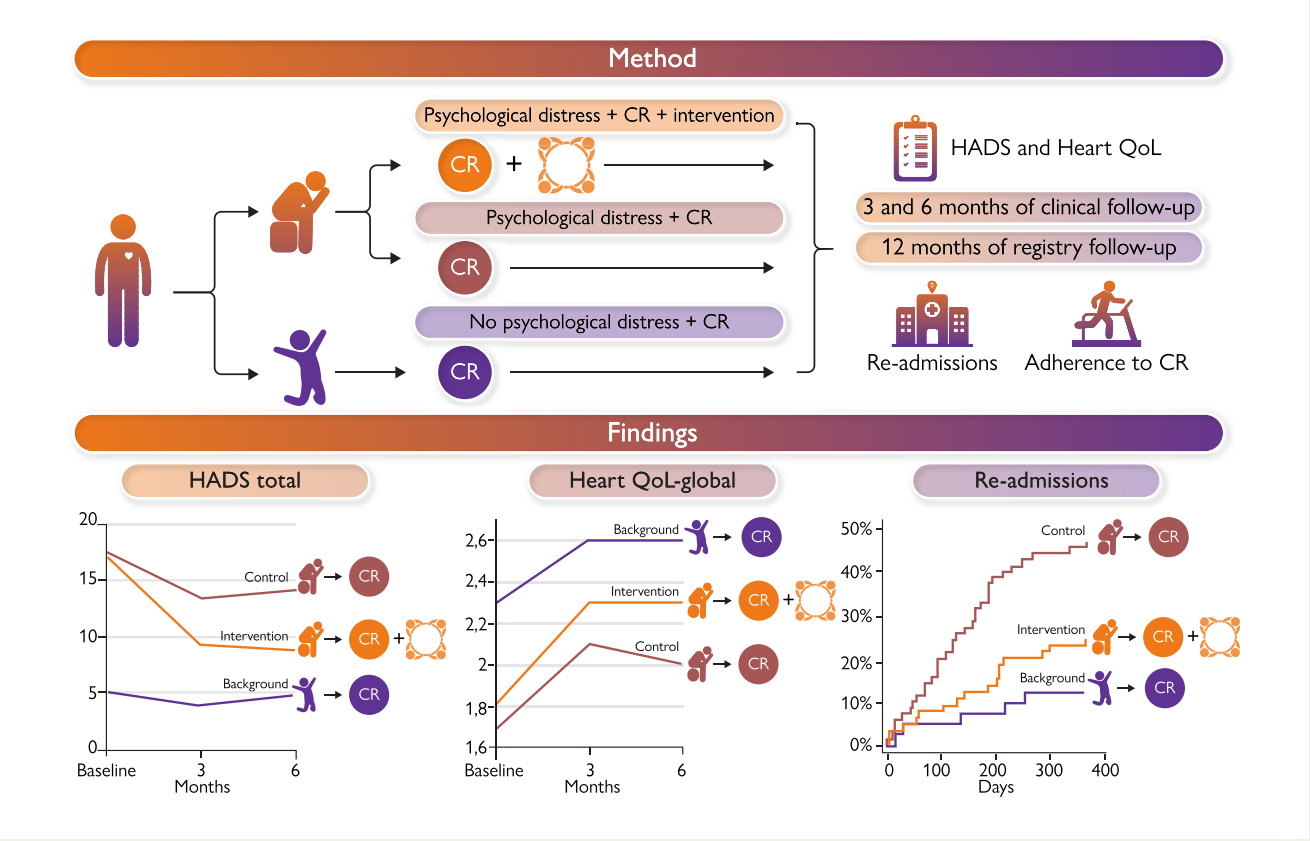
Can brief, group cognitive-behavioural therapy, provided as an adjunct to usual cardiac rehabilitation (CR), reduce psychological distress in patients with cardiovascular disease?

Key Finding

Five sessions of group cognitive-behavioural therapy reduced psychological distress measured as a significant reduction in hospital anxiety and depression scale (HADS) and increased heart quality of life (QoL). Additionally, adherence to CR increased, and the number of re-admissions decreased compared with CR alone.

Take Home Message

Brief group cognitive-behavioural therapy delivered by cardiac nurses may reduce psychological distress and morbidity in the short term, and may be integrated with existing CR programmes.



Graphical summary of the method and main findings of the present study. HADS, hospital anxiety and depression scale; HeartQoL, heart-related quality of life.

Keywords Coronary artery disease • Cardiac rehabilitation • Anxiety • Depression • Cognitive behavioural therapy • cardiac nursing

Introduction

The psychological impact of having coronary artery disease (CAD) is substantial. Anxiety and depression affect up to one-third of patients with CAD and are linked to impaired quality of life (QoL), increased morbidity, cardiac and all-cause mortality.[1–3] Among patients with psychological distress, younger patients and patients with high-risk-factor burdens and limited socioeconomic resources are overrepresented.[4,5] Untreated anxiety and depression also have an impact on the patient's work retention.[6–8] Concomitantly, hospitalization time has reduced substantially which is fortunate in the general population of cardiac patients but might not leave time to address the psychological burden of having a cardiac disease making an outpatient follow-up of even more eminent importance. Cardiac rehabilitation (CR) in patients with CAD has proved to reduce mortality and morbidity and has a Class IA recommendation[9] and, although less well documented, is also recommended in cardiac patients after valve surgery and other

conditions.[10,11] Traditionally CR interventions have focused on physical exercise and risk-factor management, whereas the management of psychological distress has received less attention. Consequently, management of psychological distress has not been systematically integrated into CR, although ESC guidelines emphasize recognition and intervention.[12,13]

A Cochrane review from 2017 reviewed 35 studies involving 10 703 patients with CAD randomized to multifactorial psychological interventions. The review concluded that beneficial effects of psychological interventions were found for cardiac mortality, anxiety, and depression, but due to substantial statistical heterogeneity for all psychological outcomes, future studies would benefit from testing specific psychological interventions.[14] A review by Reavell *et al.*[15] supported cognitive behavioural therapy (CBT) as an efficient treatment for anxiety and depression in patients with cardiac disease and concluded that to maximize effect, face-to-face sessions should be prioritized with a minimum of four sessions to ensure an effect. A newly published study by Wells *et al.*[16] tested the effect of six-group metacognitive, face-to-face sessions delivered in a single-blind, parallel controlled multicentre randomized controlled trial (RCT) added to CR in 332 cardiac patients with signs of anxiety or depression defined as a hospital anxiety and depression scale (HADS) score of 8 or above. The primary outcome of change in HADS score after 4 months improved significantly and the effect was maintained at 12 months. The study did not assess effect on repeat admissions, retention in the workforce, or other cardiac outcomes.

It is imperative that psychological interventions for anxiety and depression are developed and integrated into the CR setting so that they may be offered to all cardiac patients with psychological distress. This may not only improve patients' QoL and clinical outcomes but also has the potential to retain those with limited resources. It is well known that patients with psychological distress tend to be less adherent to CR,[17,18] but it remains unknown if psychological interventions in connection with CR may increase adherence.

Psychological distress may mimic cardiac symptoms such as palpitations and chest discomfort, and it may be difficult for health providers who are not trained in cardiology to manage cardiac patients with psychological distress. After receiving CBT training, cardiac nurses can fulfil this dual role[19] and probably also other CR professionals as showed in the study by Wells *et al.*[16] Furthermore, it is important that the intervention is well described and tested in a multicentre trial to ensure that it is widely implementable.

The main aim of this study was to evaluate the effect of brief, group CBT integrated in CR and delivered by nurses to reduce psychological distress in patients with a new CAD event and/or surgically treated valvular heart disease (VHD) with symptoms of anxiety, depression, or both. Main secondary outcomes were adherence to CR, retention in the work force and repeat hospitalization.

Methods

Study design

This was a multicentre, open-label, prospective, randomized trial with 3 and 6 months of clinical follow-up comparing group CBT plus usual CR with CR alone. The patients were recruited at three hospitals (Bispebjerg and Frederiksberg Hospital, Hvidovre and Amager Hospital, and North Zealand Hospital) in Denmark. The patients had a new CAD event and/or surgically treated VHD and psychological distress (*Figure 1*). Psychological distress was measured by the HADS. In the previously published protocol, the design was described in detail.[20]

Patients

Consecutive patients with CAD and/or surgically treated VHD referred to CR were screened for eligibility at their first visit with the following in- and exclusion criteria.

Inclusion criteria were:

- Referred to CR and accepting CR, patients with a new CAD event [ST or non-ST-elevation myocardial infarction (MI) and/or revascularized (percutaneous coronary intervention or coronary artery bypass graft)] within 3 months prior to first visit at CR and/or surgically treated VHD within 3 months prior to first visit
- HADS score ≥8 for HADS-A and/or HADS-D
- Age <65 years or, if >65 years to remain occupationally active
- Able to speak and understand Danish

Exclusion criteria were:

- Left ventricular ejection fraction <35%
- Other serious comorbidity expected to have a serious impact on life expectancy
- Known abuse of alcohol or euphoric drugs
- Known more serious psychopathology such as schizophrenia, bipolar disorder, severe personality disorder, and treatment with psychoactive drugs including selective serotonin reuptake inhibitors

The HADS score measures symptoms of anxiety (HADS-A, seven items) and depression (HADS-D, seven items). Greater scores indicate a higher degree of distress. On each subscale, scores below eight are regarded as normal.[21] A score of eight or greater is considered to be the cut-off for mild clinical symptoms and yields the optimal sensitivity and specificity for both HADS-A and HADS-D for identifying clinical caseness.[22] The psychiatrist evaluated patients with score of HADS-D ≥ 11 and Beck depression inventory (BDI) > 17, made a clinical evaluation and identified patients with severe depression or other serious psychiatric diagnoses, who were then excluded. Patients who declined this evaluation, or after evaluation by the psychiatrist were recommended another treatment were excluded from the study.

Eligible patients who accepted to participate in the study after receiving written and verbal information from a study nurse signed an informed consent form before randomization. Randomization was performed by a blinded independent researcher who was not involved in the trial and was unaware of the patients' characteristics. For randomization, we used STATA II, the Ralloc programme, with permuting random block sizes of 2, 4, and 6.

The patients were randomized to CR supplemented by five sessions of group CBT (intervention, I) or CR alone (control, C). Furthermore, a non-randomized group of consecutive patients fulfilling in- and exclusion criteria but without signs of psychological distress (i.e. HADS-A < 8 and HADS-D < 8) was recruited among the non-distressed over a shorter period of time and participated as a background group, receiving usual CR with re-evaluation after 3 and 6 months. The aim of this group was to follow the natural course, including any subsequent development of psychological distress during the follow-up period.

Usual cardiac rehabilitation

Patients in all three groups were offered the usual CR programme at their centre. CR programmes were group based and consisted of 8 weeks of exercise, twice weekly. All patients performed a cardiopulmonary exercise test (CPET) to determine the peak oxygen uptake (VO_2peak, mL/kg/min)[23] before beginning exercise training and most also at the end of the training programme. The exact number and time for the CPET are described in Supplementary material online, *Table S1*. Each session lasted 90 min and contained both moderate-intensity training (80% of VO_2peak) and resistance training. The other core components of CR were patient education on heart disease including lifestyle and medical risk-factor management,

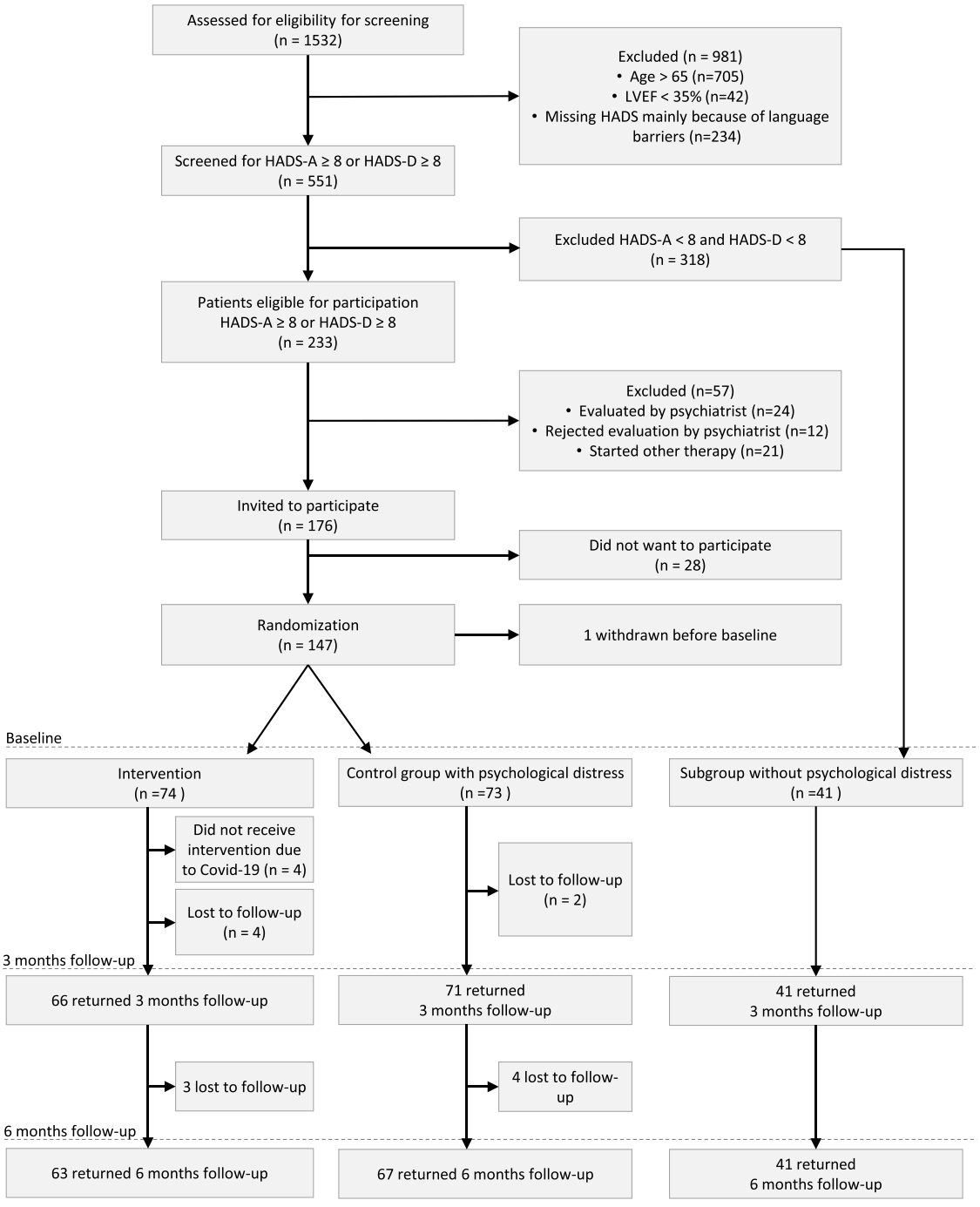


Figure 1 Patient flow chart. Patients in the intervention group followed cardiac rehabilitation and received five sessions of cognitive-behavioural therapy, whereas the control group followed standard cardiac rehabilitation. BDI, Beck depression inventory; CBT, cognitive-behavioural therapy; CR, cardiac rehabilitation; HADS, hospital anxiety and depression scale; HADS-A, the hospital anxiety and depression scale, anxiety subscale; HADS-D, the hospital anxiety and depression scale, depression subscale.

psychological issues, diet counselling once a week, and up-titration of medication according to guidelines. In addition, some patients also had individual sessions with a nurse, dietician, or cardiologist. The CR programmes were slightly different (either first visit lead by a nurse or a consultant cardiologist, and CPET also after exercise training at two sites otherwise indifferent) across the three hospitals but all offered the above core components (see Supplementary material online, *Table S2*).

Intervention

The intervention group received group CBT, which in this trial was a psycho-educational group course provided in addition to CR. The course consisted of five sessions facilitated by an experienced cardiac nurse as one scheduled 2 h session per week. Each group comprised three to four patients. The group CBT intervention is manualized, and each session had a set structure,

Table 1 Contents of the five sessions in the intervention

Session	Theme	Contents
1	Introduction to CBT and mapping of own values (individual values limited/ affected by cardiac disease)	• A matrix (22) was used to clarify which values were important to the patient • Clarify actions and barriers concerning alignment with values
2	Anxiety and anxiety reduction techniques	• Psychoeducation focusing on anxiety and its physiology, especially the role of the sympathetic nervous system • Anxiety circle is reviewed • Introduction to exposure and various types of strategies to cope with anxiety
3	Behavioural analysis (awareness of consequences of own behaviour)	• Deals with the analysis and consequences of current inappropriate behaviours both in the short and long term
4	Concerns and strategies for dealing with concerns	• Recognizing one's own thinking including worries and influence on behaviour • Explaining strategies including acceptance and diffusion to achieve change
5	How to cope with future psychological distress by using the CBT strategies	• Balancing demands and strengths with an emphasis on committing to nourishing and long-term strategies

homework was used, and sessions always ended with the opportunity to provide feedback. The same manual was used at all three hospitals.[24] Furthermore, nurses received feedback on sessions from the psychologist. The nurses had received education in CBT by a psychologist specialized in CBT and had subsequently received supervised training in delivering the intervention to a pilot group. The nurses received supervision by a psychologist as needed throughout the trial. In this trial, group CBT aimed at supporting patients thereby allowing them to cope with their heart disease.

Some of the overall components in the sessions are described in *Table 1*. A matrix[25] was used in the first session to help the patient clarify which values were important and which difficulties their heart disease had caused. The matrix was used throughout the course.

No restrictions were placed on concomitant care during the trial period. The programme was described in detail in the previously published protocol.[20]

Outcomes

The primary outcome was change in psychological distress measured by HADS total score[21] from baseline to the 3-month follow-up in the intervention group compared with the usual care group.

Secondary outcomes included HADS-A, HADS-D, adherence to CR (participation in >80% of planned training sessions, and education sessions) and return to work as well as the following outcomes measured at the 3- and 6-month follow-ups; adherence to lifestyle goals [glycated haemoglobin (HbA1c) < 48 mmol/L, blood pressure (BP) < 135/85 mmHg, body mass index (BMI) < 30 kg/m^2, and low-density lipoprotein (LDL) < 1.4 mmol/L], smoking status, physical activity (obtained in the interview with the nurse, and defined as days/week with >30 min of moderate physical activity) and heart-related quality of life (HeartQoL). The HeartQoL questionnaire measures heart-related QoL in patients with heart disease. It provides two subscales: The physical subscale consisting of 10 items and the emotional subscale consisting of 4 items, all of which are scored from 0–3. A higher score indicates a better QoL.[26,27] The HeartQoL questionnaire has proved to be a reliable instrument with a Cronbach's α between 0.80 and 0.91 for the global score and each subscale and to be responsive in patients with a wide spectrum of cardiac diagnoses.[28]

We assessed cardiac readmissions, all-cause mortality, fatal and non-fatal MI and coronary artery revascularization within 12 months from randomization. Cardiac readmissions covered all readmissions to emergency and cardiac departments for cardiac symptoms. Admissions to other departments of somatic disease were not included and admissions to psychiatric departments were assessed separately. Cardiac readmission was ascertained through electronic health records and adjudicated by an independent cardiologist blinded to treatment intervention.

Statistical analyses

We used descriptive statistics to compare baseline data across the groups with and without psychological distress and between the intervention and control groups. The normal distribution of all continuous variables was examined visually and by the Shapiro–Wilk test. Normally distributed variables were compared across groups using *t*-test or one-way analysis of variance and presented as mean ± standard deviation (SD). Data not following the normal distribution were compared using the Kruskal–Wallis test and presented as median (interquartile range). Categorical variables were compared across the groups using Pearson's χ^2 test.

To analyse the main outcome, i.e. change in total HADS from baseline to 3 months, we used linear regression mixed models, thus adjusting for the baseline HADS value. We also included centre (three sites) in the model, and analyses were tested for treatment–centre interaction. A priori, power estimates suggested that we would have 80% power to detect a 2.3 point difference in the total HADS score (delta HADS) between the intervention and control groups, due to the risk of dropout of patients included in this type of trial, the total number of patients included was increased by 15% to 148 patients as described in the previously published protocol.[20] The minimal clinically important difference of change in HADS is 1.7, and serves as an indicator of treatment success for interventions intended to improve the mental health of patients with cardiovascular disease.[29]

Secondary outcomes, including the HeartQol and other outcomes on a continuous scale, were compared across intervention and control groups with similar analysis, whereas dichotomized secondary outcomes [adherence to CR (>80%), return to work (yes/no), HbA1c < 48, BP < 135/85 mmHg, BMI < 30 kg/m^2, LDL <1.4 mmol/L, smoking status, and physical activity) were compared by logistic regression adjusting for treatment centre.

For clinical events (number of readmissions within 12 months of randomization), we compared outcomes across groups with Kaplan–Meier curves and time-to-event analyses (Cox regression) adjusting for centre.

The primary reported analyses were conducted as intention-to-treat and included all participants that attended follow-up at 3 and 6 months, respectively. In sensitivity analyses, we included information at all time points on patients' lost to follow-up by carrying forward the most recent available measurement. We planned for a per-protocol analyses defined by participation in ≥four of the five group sessions, but all patients fulfilled this criterion. There were no missing data on the primary outcome of HADS. For the questionnaire HeartQol, missing data in one or more of the questions were imputed as the mean value of the corresponding question across

the population if there were <20% missing data in the HeartQol questionnaire for the individual in question. Analyses were repeated after excluding patients with missing data.

We compared the primary outcome in intervention and control groups with the spontaneous variation in the non-distressed subgroup of 41 participants by separate mixed-models linear regression adjusting for baseline values.

A two-tailed *P*-value $P < 0.05$ was considered statistically significant. All statistical analyses were performed using Stata SE 17 v17.0.116 (StataCorp LP).

Ethics

The trial was performed in accordance with the Declaration of Helsinki, and all patients gave informed consent after written and oral information. The trial was initiated following approval by the Danish Data Protection Agency and the regional ethics committee (H-16042832). The trial is registered with www.ClinicalTrials.gov (NCT04254315).

Results

Patient characteristics

From February 2017 to March 2021, 1532 patients with a new CAD event and/or surgically treated VHD were screened; 176 were invited to participate; and 147 patients were enrolled in the study (*Figure 1*). Among the patients with a high depression score and evaluated by the psychiatrist, eight (25%) were subsequently included in the study. The remaining 57 patient with HADS-D ≥ 11 and BDI > 17 were excluded either because they did not want to be evaluated by a psychiatrist, were already started other therapy, or were recommended another treatment by the psychiatrist (*Figure 1*). Furthermore, among the 318 screened but non-distressed patients, a background group of 41 consecutive patients were recruited during a shorter period of time serving as a reference group (*Figure 1*).

After randomization, eight (12%) were excluded in the intervention group due to the COVID-19 lockdown (four patients) or were lost to follow-up as they did not wish to continue in the trial or participate in follow-ups (four patients). A total of 66 (89%) patients received the full intervention, defined as four or more of the five sessions. At 3-month follow-up, two patients in the control group were lost to follow-up. At the 6-month follow-up, three (5%), four (6%), and none were lost to follow-up in the intervention, control, and background groups, respectively. The last follow-up was conducted in September 2021.

The two groups with psychological distress, i.e. the intervention and the control groups, were similar with respect to clinical and demographic characteristics, with the exception of significantly more patients having a coronary artery bypass graft operation in the control group (*Table 2*). The mean age was 54 ± 8 years, 67% were males and 92% had CAD as their index event. Approximately 89% of patients scored ≥8 on HADS-A and 50% ≥8 on HADS-D with no difference between the intervention and control groups (see Supplementary material online, *Table S3*). The background group without psychological distress was similar to the groups with psychological distress with the exception of a male preponderance (85% vs. 67%, $P = 0.03$), higher age (57 ± 6 vs. 54 ± 6 years) and a higher proportion of patients working before the event (98% vs. 78%).

Outcomes

At 3 months, the mean total HADS score improved by 8.0 (SD 5.6) in the intervention group vs. 4.1 (SD 7.8) in the control group (*P* for difference <0.001). Both subscales, i.e. anxiety and depression, also

Table 2 Demographic and clinical characteristics for the three groups at baseline

	With psychological distress		Without psychological distress
	Intervention (*n* = 74)	Control (*n* = 73)	Background (*n* = 41)
Male sex	45 (61%)	54 (74%)	35 (85%)
Age (years), mean (SD)	54 (8)	55 (7)	57 (6)*
BMI (kg/m^2), mean (SD)	28,2 (5,2)	27.1 (5.0)	27.2 (4.8)
Living alone	24 (34%)	31 (43%)	9 (23%)
Education			
No education	6 (9%)	13 (18%)	7 (17%)
Short-term education	25 (37%)	22 (31%)	13 (32%)
Medium-term education	20 (29%)	19 (27%)	11 (27%)
Higher education	17 (25%)	17 (24%)	10 (24%)
Working status at event			
Working	60 (86%)	51 (71%)	40 (98%)*
Unemployed	8 (11%)	14 (19%)	1 (2%)
Sick leave	2 (3%)	7 (10%)	0 (0%)
LVEF (%), median (IQR)	55 (50–60)	50 (50–60)	60 (50–60)
LVEF ≤ 40%	8 (11%)	7 (9%)	4 (10%)
Index event			
STEMI	25 (34%)	31 (42%)	13 (32%)
NSTEMI	29 (39%)	16 (22%)	9 (22%)
UAP	9 (12%)	8 (11%)	6 (15%)
Stable AP	4 (5%)	13 (18%)	12 (29%)
Heart valve disease	6 (8%)	6 (8%)	1 (2%)
Aorta aneurysm	1 (1%)	0 (0%)	0 (0%)
PCI	52 (74%)	46 (63%)	30 (73%)
CABG	5 (7%)	14 (19%)	7 (17%)
Heart valve replacement			
Aorta	3 (4%)	3 (4%)	3 (7%)
Mitral	4 (5%)	3 (4%)	0 (0%)
NYHA class			
≥ NYHA Class II	16 (23%)	8 (11%)	6 (15%)
CCS class			
CCS class <1	64 (93%)	66 (92%)	41 (100%)
Cardiac history prior to index event	6 (9%)	7 (10%)	3 (7%)
COPD	3 (4%)	0 (0%)	3 (7%)

Continued

Table 2 ***Continued***

	With psychological distress		Without psychological distress
	Intervention ($n = 74$)	Control ($n = 73$)	Background ($n = 41$)
Kidney disease	2 (3%)	4 (6%)	4 (10%)
Hypertension	31 (44%)	33 (46%)	22 (54%)
Dyslipidaemia	42 (59%)	43 (60%)	30 (73%)
Diabetes mellitus	10 (14%)	9 (13%)	6 (15%)
Family history	34 (50%)	32 (47%)	18 (45%)
Current smoker	12 (17%)	13 (18%)	5 (13%)
Medication			
Other antiplatelet medication	52 (75%)	51 (71%)	31 (76%)
Statin	61 (87%)	65 (90%)	38 (93%)
Beta-blocker	35 (50%)	34 (49%)	15 (37%)
ACE inhibitor	28 (40%)	31 (44%)	12 (30%)
Diabetes medication	9 (12%)	8 (11%)	5 (12%)
VO_2peak (mL/kg/min), mean (SD)	23.0 (6.4)	23.9 (6.4)	25.9 (6.3)*
Physical activity (>30 min/day)	2 (0–5)	2 (0–5)	3 (0–5)
HADS total, median (IQR)	17 (14–21)	17 (13–21)	5 (3–7)*
HADS anxiety, median (IQR)	10 (8–12)	10 (8–13)	3 (2–5)*
HADS depression, median (IQR)	7 (5–10)	8 (5–10)	1 (1–3)*

The group of distressed patients compared with the group of patients with no distress. ACE, angiotensin-converting enzyme; BMI, body mass index; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society Angina Classification; COPD, chronic obstructive pulmonary disease; HADS, hospital anxiety and depression scale; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; SD, standard deviation; UAP, unstable angina pectoris; VO_2peak, peak oxygen uptake.
*$P < 0.05$.

improved significantly more in the intervention group (*Figure 2* and Supplementary material online, *Tables S3* and *S4*). These differences were maintained at the 6-month follow-up. No difference was observed in treatment effect across the three sites (no treatment–centre interaction), between genders or between CAD and VHD; however, the statistical power to detect interaction was limited. The background group without psychological distress had no significant change in total HADS score at the 3- and 6-month follow-ups. Results were similar when carrying forward the most recent available measurement for patients' lost to follow-up.

HeartQol improved significantly in all three groups with no significant difference at the 3-month follow-up between the intervention and control groups in global score or physical/emotional subscores (*Figure 3* and Supplementary material online, *Table S5*). At the 6-month follow-up, significant differences were detected in favour of the intervention group for the total and emotional score but not for the physical score ($P = 0.05$). The background group had a significantly ($P < 0.001$) higher HeartQoL at baseline and remained higher than the groups with psychological distress at the 3- and 6-month follow-up. There was no difference in effect between genders (no treatment–sex interaction) and results were similar after excluding participants with missing data (not imputed) and carrying forward the most recent available measurement for patients' lost to follow-up.

No significant differences were observed between the intervention and control groups with respect to risk-factor control (HbA1c, BP, LDL, and physical activity) at the 3- and 6-month follow-up (*Table 3*). We did, however, detect a significant difference in adherence to the physical training sessions and education sessions in favour of the intervention group ($P = 0.02$). Among the distressed patients, 78% had returned to work at 6 months in the intervention group vs. 67% in the control group ($P = 0.11$).

After 12 months, one patient in the intervention group died due to cancer. Sixteen (25%) patients in the intervention group had one or more cardiovascular readmissions vs. 33 (49%) in the control group (*Figure 4* and Supplementary material online, *Table S6*). The hazard ratio for hospital admission for the intervention group vs. control group adjusted for centre was 0.43 (95% confidence interval 0.24–0.80) and the between-group difference was mainly due to higher rate of emergency room contact, hospital admission due to angina and angiography in the control group, whereas no differences were seen for MI or revascularization. There was no treatment– gender interaction. Only five patients in the background group had one or more cardiovascular readmissions. No fatal and two non-fatal MIs were recorded (one in the control and one in the background group). Twenty-two subacute coronary angiographies were performed among all participants after their primary event. The number of revascularisations was equally distributed among the participants: two in the intervention group, two in the control group, and one in the background group.

Discussion

In this trial, five sessions of group CBT added to CR significantly reduced anxiety and depression compared with CR alone among patients with psychological distress. Improvements in the primary outcome of total HADS score at 3 months as well as subscales on anxiety and depression were maintained at the 6-month follow-up. Corresponding improvements were seen for HeartQoL at 6 months and adherence to the physical training sessions during CR, whereas no differences were recorded in other risk-factor-related secondary outcomes. Furthermore, we found a significant reduction in cardiac readmissions after 12 months in the intervention group compared with the control group (*Structured Graphical Abstract*).

Anxiety, depression and quality of life

The latest Cochrane review on the effectiveness of psychological interventions[14] included 35 RCT trials with a broad range of psychological interventions and concluded that these resulted in small to moderate improvements in depressive symptoms, anxiety and stress; however, considerable uncertainty surrounded these effects due to methodological and statistical heterogeneity. For interventions by CBT a recent meta-analysis of 22 RCTs of nearly 5000 patients with CAD found that CBT significantly improved anxiety, depression and health-related

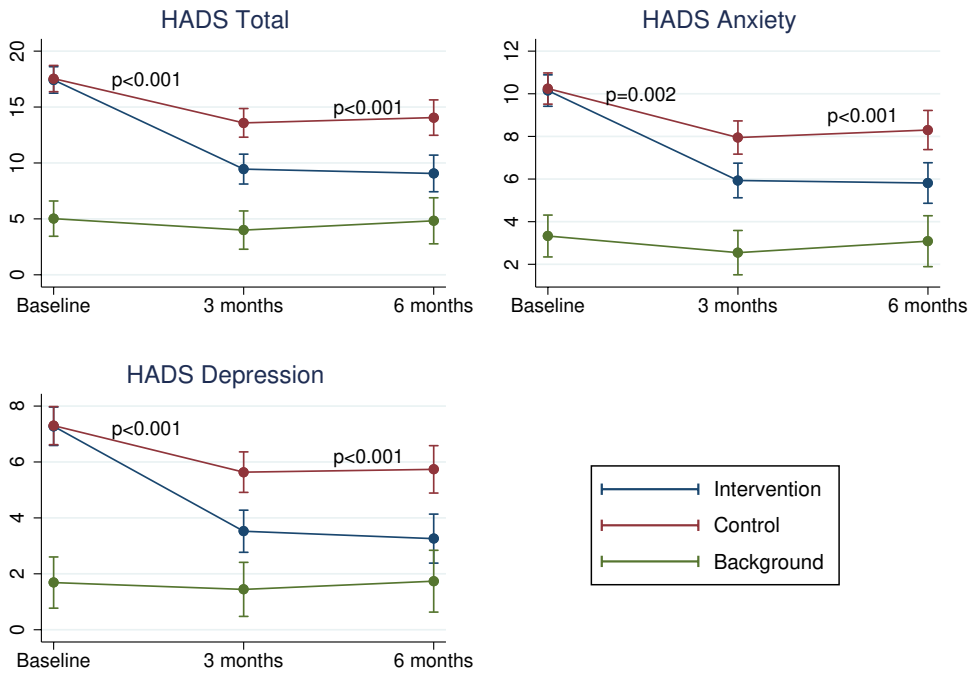


Figure 2 Change in hospital anxiety and depression scale score in the intervention, control, and background groups. Estimated total hospital anxiety and depression scale score, subscore on depression, and subscore on anxiety at baseline, and after 3 and 6 months for the three groups from mixed models adjusting for centre. *P*-values denote comparison of Δ hospital anxiety and depression scale between the intervention and control groups.

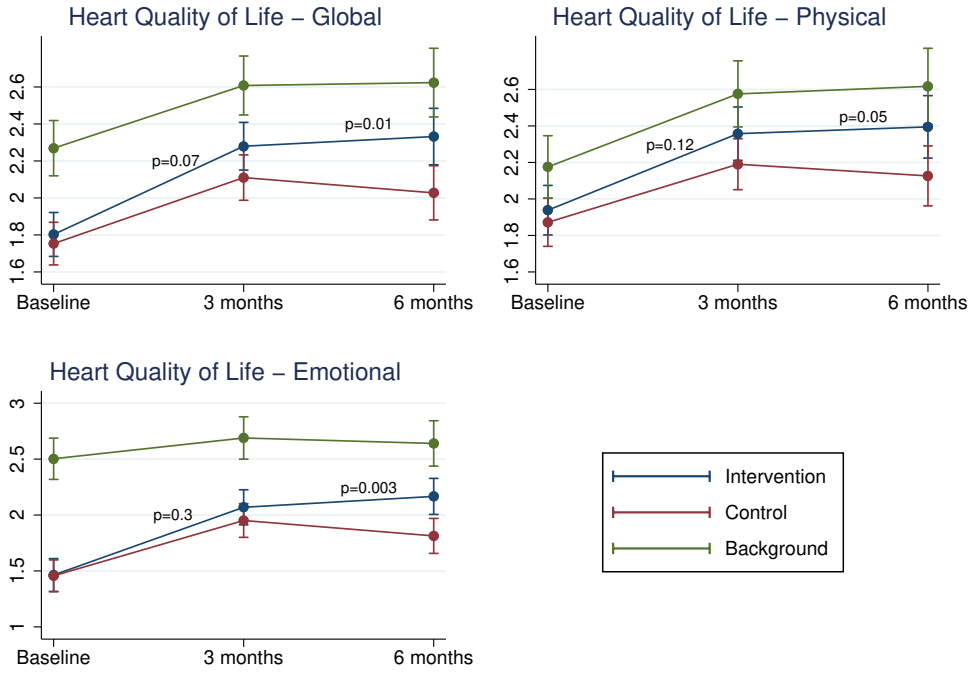


Figure 3 Change in HeartQoL score in the intervention, control and background group. HeartQoL-global score, subscore on HeartQol-physical and subscore on HeartQol-emotional at baseline, and after 3 and 6 months for the three groups. *P*-values denote comparison of ΔHeartQoL between the intervention and control groups from mixed models adjusted for centre effect.

Table 3 Change in risk factors in the intervention and the control group

	Baseline			3-Month follow-up			6-Month follow-up		
	Intervention $n = 74$	Control $n = 73$	*P*-value	Intervention $n = 66$	Control $n = 71$	*P*-value	Intervention $n = 63$	Control $n = 67$	*P*-value
HbA1c < 48 mmol/mol	52 (76%)	65 (93%)	0.007	54 (86%)	65 (92%)	0.28	56 (88%)	57 (90%)	0.59
BP < 135/85 mmHg	42 (61%)	44 (61%)	0.98	42 (65%)	47 (67%)	0.76	33 (52%)	40 (62%)	0.30
LDL < 1.4 mmol/L	21 (30%)	25 (35%)	0.59	27 (42%)	30 (43%)	0.82	26 (41%)	30 (46%)	0.53
BMI <30 kg/m^2	56 (76%)	50 (68%)	0.27	48 (72%)	49 (69%)	0.75	43 (68%)	47 (70%)	0.92
Current smoker	12 (17%)	13 (18%)	0.92	10 (15%)	8 (11%)	0.52	7 (11%)	8 (12%)	0.83
Physical activity 30 min > 4 days/week	23 (31%)	25 (34%)	0.68	34 (46%)	42 (58%)	0.16	42 (57%)	43 (59%)	0.79
Rehabilitation completed (training sessions > 80%)				51 (77%)	40 (56%)	0.010			

WHO risk > 29.9. *P*-value denotes Δ in risk factors between the intervention and control groups.
BMI, body mass index; BP, blood pressure; HbA1c, glycated haemoglobin; LDL, low-density lipoprotein.

QoL.[30] The included trials were highly variable in their mode of delivery; however, most were individual, had a treatment course > 12 weeks, comprised more than ten sessions; and in the majority of the trials, a therapist or psychologist delivered the intervention. Consequently, most of these interventions are not accessible or standardized for implementation to a CR setting. The current trial addresses these barriers to implementation by testing the effect of brief, group CBT delivered by CR nurses and integrated into usual CR. The results support the evidence that CBT is an effective treatment for depression and anxiety in cardiac patients. The most comparable study is a recent multicentre RCT with the participation of 332 cardiac patients in UK.[16] This study found similar effects of brief, group-based intervention delivered by CR staff including cardiac nurses and the intervention consisted of six sessions. The intervention was metacognitive therapy, which focuses on the purpose of one's thinking rather than the content of a given thought. In the present study the CBT method comprised both content and the purpose of a given thought to give patients more options for dealing with distressing thoughts and emotions.[20] The two studies have very similar results on the primary outcome of HADS after 3–4 months, with a difference in HADS score of >3 between groups. This is a considerably greater effect than reported in previous studies using individual or group CBT, as reported in the meta-analyses.[30]

The aim of this trial was to test a simplified delivery of CBT. A widely accessible and more inexpensive form of CBT is internet-based CBT (iCBT). This approach was tested in the U-CARE study ($n = 239$) with 14 weeks of iCBT vs. usual care, but no significant reduction in anxiety and depression was found.[31] Also the above-mentioned meta-analysis included four trials using iCBT, showing mixed results and a higher dropout rate.[30] In this trial we had only five sessions, in the study by Wells *et al.* only six, yet had significant effect of the intervention. Interestingly, in a recent Danish RCT of patients with a newly implanted cardioverter defibrillator, CBT delivered by cardiac nurses with number of sessions individualized to a target HADS score found that the therapy was effective with a median of six sessions (range 2–15).[32] In the meta-analyses, duration of treatment course was not predictive of effect.[30] Thus, there is consistent data to support that CBT is effective also when delivered as in relatively few group sessions.

We saw a reduction in HADS also in the control group. As also shown by others,[33] this indicates that the natural course of psychological distress after a cardiac event is stress alleviation, perhaps reinforced by CR, but that the distressed patients do not spontaneously normalize their level of distress. In contrast, the background group without distress at baseline did not change their level of distress within the first 6 months indicating also that screening for psychological distress at the initiation of CR is necessary and the right time to find those with distress.

Adherence to CR and risk-factor management

Anxiety and depression have been shown to adversely affect risk-factor management and adherence to CR.[34,35] We found that the patients in the intervention group were significantly more adherent to the training sessions, but we found no difference between the groups in terms of improvement of cardiovascular risk factors. However, risk-factor control was very good in both groups and left little room for improvement. At 6-month follow-up, most patients had returned to work with no significant difference between the intervention and control groups (78% vs. 67%, $P = 0.11$). In the non-distressed background group 98% had returned to work. The proportion that returns to work is similar to the EUROASPIRE IV study,[36] in which 76% of patients had returned to work within 6 months to 3 years. We have only followed the patient's working status for 6 months.

Readmission

Previous studies have found a strong association between psychological distress and readmissions due to cardiac events.[37] Our study was in size and follow-up period not designed for morbidity and mortality as primary outcomes. However, we did find significantly higher rates of readmission among patients with psychological distress compared with the reference group; and we also found that the intervention group experienced a 57% lower risk of readmissions within the first 12 months after randomization. Interestingly, no differences were observed in rates of MI or revascularization. This may indicate that by targeting

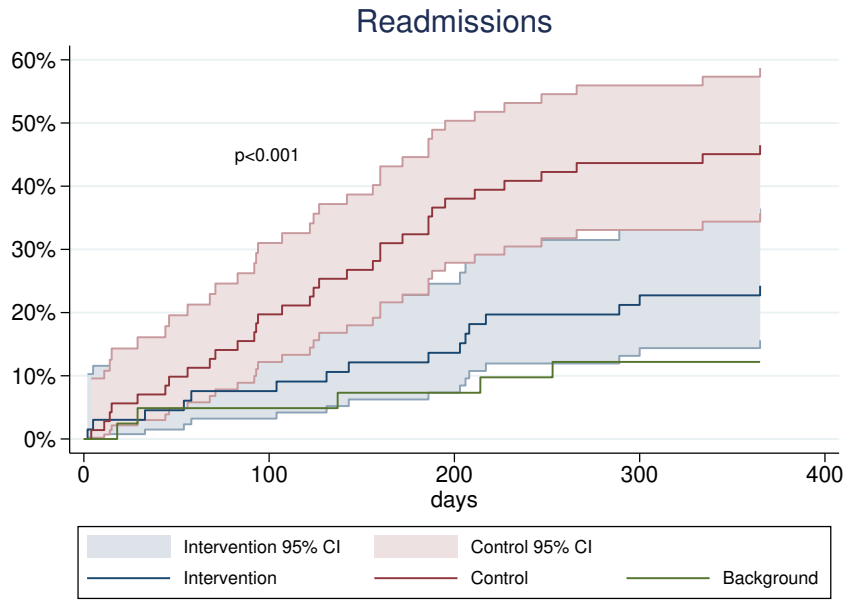


Figure 4 Time-to-event curves for cardiac readmission in the intervention group compared with the control group at the 12-month follow-up change in hospital anxiety and depression scale score points. CI, confidence interval.

and alleviating psychological distress early after an event, many unnecessary readmissions may be avoided. Our findings are consistent with findings from another study reporting that patients with psychological distress are more likely to experience and report chest pain and might have a lower threshold for emergency visits and readmissions.[38] A high number of patients with panic attacks were found in another study through routine psychological screening with HADS in the emergency room. And also an association between a certain type of personality (Type D personality) and readmissions which we did not test for.[39]

In perspective, CBT seems an effective treatment for anxiety and depression in patients with CAD and VHD. The brief, CBT was provided by experienced cardiac nurses at three different centres and with an equal effect at all three centres. The programme is simple, feasible, and may be integrated within existing CR programmes. Whether a similar effect can be achieved in other cardiac patients with psychological distress and whether the effects are maintained are yet to be discovered.

Strengths and limitations

Although the results of the present trial are encouraging, some limitations should be acknowledged. Our study targeted patients with signs of psychological distress at entry but without psychiatric diagnosis or treatment. With this approach the intervention group were more homogenous and expected to benefit from the group session and at the same time ensuring that the cardiac experienced nurses but unexperienced in relation to psychiatric disease could deliver a manageable CBT-based intervention. However, this also means that the results may not apply to patients with more severe psychological distress. Patients were further selected as only patients who were referred to and accepted to participate in CR were included. Patients who do not participate in CR are known to have greater comorbidity and more psychological distress.[40] According to a mandatory national clinical registry (Danish Heart Rehabilitation Database[41]), 32% of eligible CAD patients in 2017 and 46% in 2021 were referred to CR in our capital region covering the participating hospitals of this study. Thus, it is likely that many cardiac patients with psychological distress were not identified, and our results do not apply to these. We did, however, systematically screen all patients referred to CR and among those found eligible, only 16% declined. Thus, we believe that the results would apply to cardiac patients with psychological distress referred to CR. However, patients with VHD constitute a minor part of the study population and although we found no signs of effect modification, results may mainly apply to patients with CAD. The interpretation should also take into account that this study has a limited diversity of race due to a single country trial.

Due to the nature of the intervention, it was not possible to blind patients and CR staff to group allocation. Randomization and statistical outcome analyses were, however, all blinded to reduce the risk of selection, detection, and interpretation bias. We did not measure the negative impact of the focus on psychological distress in the intervention nor did we determine the effectiveness of CBT treatment in relation to a sham intervention. The patients in the intervention group received both CBT and CR, which gives greater number of patient contact hours and this may have contributed to the effect and believer bias from both patients and from the healthcare system. It is well known from psychotherapy that the character of the therapeutic relationship has influence on the treatment effect. Common factors such as empathy, patient expectations, and agreement about goals among other factors influence the outcome.[42]

The intervention was conducted in accordance with a structured manual for each session, but we did not measure adherence to the manual. To ensure the quality of the intervention, supervision was conducted by a psychologist specializing in the CBT methodology. Finally,

the methods of measuring anxiety, depression, and QoL are validated and widely used.[26,27,43]

In the control group, revascularization by coronary artery bypass grafting was more frequent than in the intervention group. This could have caused more frequent hospitalizations but the causes we found were not related to postoperative complications and therefore we do not expect it to impact results.

The background group of non-distressed patients were consecutively recruited over a shorter period of time compared with the distressed group, and consisted of less females, were older and to a higher degree at work before the event and therefore not completely matched with the distressed group. As women experience CAD almost 10 years later than men[44] and psychological distress is less frequent in men[45,46] our gender distribution in a consecutive group of younger CAD patients is as expected. Furthermore, lower socioeconomic status including non-employment is associated with a higher degree of distress.[5] The background group should therefore not be viewed as a control group but mirrors non-distressed younger CAD patients in every-day clinic.

Conclusion

Brief CBT delivered by cardiac nurses in relation to CR to cardiac patients with psychological distress had a clinically relevant effect on anxiety and depression, improved HeartQoL at 6 months, and adherence to CR and reduced cardiovascular readmissions. The CBT programme is simple, brief and feasible with existing CR programmes.

Supplementary data

Supplementary data are available at *European Heart Journal* online.

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Conflict of interest: All authors declare no conflict of interest for this contribution.

Data availability

Danish legislation does not allow us to share data even if anonymized. Therefore, the data will be made available in aggregated form by the authors upon request.

References

1. Norlund F, Lissåker C, Wallert J, Held C, Olsson EM. Factors associated with emotional distress in patients with myocardial infarction: results from the SWEDEHEART registry. *Eur J Prev Cardiol* 2018;**25**:910–920. https://doi.org/10.1177/2047487318770510
2. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, *et al.* Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American heart association. *Circulation* 2014;**129**:1350–1369. https://doi.org/10.1161/CIR.0000000000000019
3. Palacios J, Khondoker M, Mann A, Tylee A, Hotopf M. Depression and anxiety symptom trajectories in coronary heart disease: associations with measures of disability and impact on 3-year health care costs. *J Psychosom Res* 2018;**104**:1–8. https://doi.org/10.1016/j.jpsychores.2017.10.015
4. Murphy B, Le Grande M, Alvarenga M, Worcester M, Jackson A. Anxiety and depression after a cardiac event: prevalence and predictors. *Front Psychol* 2020;**10**:3010. https://doi.org/10.3389/fpsyg.2019.03010
5. Lazzarino AI, Hamer M, Stamatakis E, Steptoe A. Low socioeconomic status and psychological distress as synergistic predictors of mortality from stroke and coronary heart disease. *Psychosom Med* 2013;**75**:311–316. https://doi.org/10.1097/PSY.0b013e3182898e6d
6. Smedegaard L, Numé A, Charlot M, Kragholm K, Gislason G, Hansen PR. Return to work and risk of subsequent detachment from employment after myocardial infarction: insights from Danish nationwide registries. *J Am Heart Assoc* 2017;**6**:e006486. https://doi.org/10.1161/JAHA.117.006486
7. Stendardo M, Bonci M, Casillo V, Miglio R, Giovannini G, Nardini M, *et al.* Predicting return to work after acute myocardial infarction: socio-occupational factors overcome clinical conditions. *PLoS One* 2018;**13**:e0208842. https://doi.org/10.1371/journal.pone.0208842
8. de Jonge P, Zuidersma M, Bültmann U. The presence of a depressive episode predicts lower return to work rate after myocardial infarction. *Gen Hosp Psychiatry* 2014;**36**:363–367. https://doi.org/10.1016/j.genhosppsych.2014.03.006
9. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, *et al.* 2016 European Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2016;**37**:2315–2381. https://doi.org/10.1093/eurheartj/ehw106
10. Taylor RS, Dalal HM, McDonagh STJ. The role of cardiac rehabilitation in improving cardiovascular outcomes. *Nat Rev Cardiol* 2022;**19**:180–194. https://doi.org/10.1038/s41569-021-00611-7
11. Borregaard B, Ekholm O, Riber L, Sørensen J, Møller JE, Thrysoe L, *et al.* Patient-reported outcomes after aortic and mitral valve surgery – results from the DenHeart study. *Eur J Cardiovasc Nurs* 2018;**17**:246–254. https://doi.org/10.1177/1474515117731391
12. Vaccarino V, Badimon L, Bremner JD, Cenko E, Cubedo J, Dorobantu M, *et al.* Depression and coronary heart disease: 2018 position paper of the ESC working group on coronary pathophysiology and microcirculation. *Eur Heart J* 2020;**41**:1687–1696. https://doi.org/10.1093/eurheartj/ehy913
13. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, *et al.* 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. *Eur J Prev Cardiol* 2022;**29**:5–115. https://doi.org/10.1093/eurjpc/zwab154
14. Richards SH, Anderson L, Jenkinson CE, Whalley B, Rees K, Davies P, *et al.* Psychological interventions for coronary heart disease. *Cochrane Database Syst Rev* 2017;**4**:CD002902. https://doi.org/10.1002/14651858.CD002902.pub4
15. Reavell J, Hopkinson M, Clarkesmith D, Lane DA. Effectiveness of cognitive behavioral therapy for depression and anxiety in patients with cardiovascular disease: a systematic review and meta-analysis. *Psychosom Med* 2018;**80**:742–753. https://doi.org/10.1097/PSY.0000000000000626
16. Wells A, Reeves D, Capobianco L, Heal C, Davies L, Heagerty A, *et al.* Improving the effectiveness of psychological interventions for depression and anxiety in cardiac rehabilitation: PATHWAY—a single-blind, parallel, randomized, controlled trial of group metacognitive therapy. *Circulation* 2021;**144**:23–33. https://doi.org/10.1161/CIRCULATIONAHA.120.052428
17. McGrady A, McGinnis R, Badenhop D, Bentle M, Rajput M. Effects of depression and anxiety on adherence to cardiac rehabilitation. *J Cardiopulm Rehabil Prev* 2009;**29**:358–364. https://doi.org/10.1097/HCR.0b013e3181be7a8f
18. Edwards BL, Sydeman SJ. Depression is associated with reduced outpatient cardiac rehabilitation completion rates: a Systematic Literature Review and Meta-analysis. *J Cardiopulm Rehabil Prev* 2019;**39**:365–372. https://doi.org/10.1097/HCR.0000000000000419
19. Tyrer H, Tyrer P, Lisseman-Stones Y, McAllister S, Cooper S, Salkovskis P, *et al.* Therapist differences in a randomised trial of the outcome of cognitive behaviour therapy for health anxiety in medical patients. *Int J Nurs Stud* 2015;**52**:686–694. https://doi.org/10.1016/j.ijnurstu.2014.11.013
20. Holdgaard A, Eckhardt-Hansen C, Lund T, Lassen CF, Sibiliz KL, Høfsten DE, *et al.* Intensive group-based cognitive therapy in patients with cardiac disease and psychological distress—a randomized controlled trial protocol. *Trials* 2021;**22**:455. https://doi.org/10.1186/s13063-021-05405-3
21. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**:361–370. https://doi.org/10.1111/j.1600-0447.1983.tb09716.x
22. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the hospital anxiety and depression scale an updated literature review. *J Psychosom Res* 2002;**52**:69–77. https://doi.org/10.1016/S0022-3999(01)00296-3
23. Guazzi M, Adams V, Conraads V, Halle M, Mezzani A, Vanhees L, *et al.* Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. *Eur Heart J* 2012;**33**:2917–2927. https://doi.org/10.1093/eurheartj/ehs221
24. Beck JS, Beck JS. *Cognitive Behavior Therapy: Basics and Beyond*. 2nd ed. New York: Guilford Press; 2011.
25. Polk KL, Schoendorff B, eds. *The ACT Matrix: A New Approach to Building Psychological Flexibility Across Settings & Populations*. Oakland, CA: Context Press, an imprint of New Harbinger Publications, Inc; 2014.

26. Oldridge N, Höfer S, McGee H, Conroy R, Doyle F, Saner H. The HeartQoL: part I. Development of a new core health-related quality of life questionnaire for patients with ischemic heart disease. *Eur J Prev Cardiol* 2014;**21**:90–97. https://doi.org/10.1177/2047487312450544
27. Oldridge N, Höfer S, McGee H, Conroy R, Doyle F, Saner H. The HeartQoL: part II. Validation of a new core health-related quality of life questionnaire for patients with ischemic heart disease. *Eur J Prev Cardiol* 2014;**21**:98–106. https://doi.org/10.1177/2047487312450545
28. Oldridge N, Saner H, McGee HM. The euro cardio-QoL project. An international study to develop a core heart disease health-related quality of life questionnaire, the HeartQoL. *Eur J Cardiovasc Prev Rehabil* 2005;**12**:87–94. https://doi.org/10.1097/01.hjr.0000159408.05180.0e
29. Lemay KR, Tulloch HE, Pipe AL, Reed JL. Establishing the minimal clinically important difference for the hospital anxiety and depression scale in patients with cardiovascular disease. *J Cardiopulm Rehabil Prev* 2019;**39**:E6–E11. https://doi.org/10.1097/HCR.0000000000000379
30. Li Y-N, Buys N, Ferguson S, Li Z-J, Sun J. Effectiveness of cognitive behavioral therapy-based interventions on health outcomes in patients with coronary heart disease: a meta-analysis. *World J Psychiatry* 2021;**11**:1147–1166. https://doi.org/10.5498/wjp.v11.i11.1147
31. Humphries SM, Wallert J, Norlund F, Wallin E, Burell G, von Essen L, *et al.* Internet-based cognitive behavioral therapy for patients reporting symptoms of anxiety and depression after myocardial infarction: U-CARE heart randomized controlled trial twelve-month follow-up. *J Med Internet Res* 2021;**23**:e25465. https://doi.org/10.2196/25465
32. Berg SK, Rasmussen TB, Herning M, Svendsen JH, Christensen AV, Thygesen LC. Cognitive behavioural therapy significantly reduces anxiety in patients with implanted cardioverter defibrillator compared with usual care: findings from the screen-ICD randomised controlled trial. *Eur J Prev Cardiol* 2020;**27**:258–268. https://doi.org/10.1177/2047487319874147
33. Zheng X, Zheng Y, Ma J, Zhang M, Zhang Y, Liu X, *et al.* Effect of exercise-based cardiac rehabilitation on anxiety and depression in patients with myocardial infarction: a systematic review and meta-analysis. *Heart Lung* 2019;**48**:1–7. https://doi.org/10.1016/j.hrtlng.2018.09.011
34. Pogosova N, Saner H, Pedersen SS, Cupples ME, McGee H, Höfer S, *et al.* Psychosocial aspects in cardiac rehabilitation: from theory to practice. A position paper from the cardiac rehabilitation section of the European Association of Cardiovascular Prevention and Rehabilitation of the European Society of Cardiology. *Eur J Prev Cardiol* 2015;**22**:1290–1306. https://doi.org/10.1177/2047487314543075
35. Pedersen SS, von Känel R, Tully PJ, Denollet J. Psychosocial perspectives in cardiovascular disease. *Eur J Prev Cardiol* 2017;**24**:108–115. https://doi.org/10.1177/2047487317703827
36. de Cauter JV, Bacquer DD, Clays E, Smedt DD, Kotseva K, Braeckman L. Return to work and associations with psychosocial well-being and health-related quality of life in coronary heart disease patients: results from EUROASPIRE IV. *Eur J Prev Cardiol* 2019;**26**:1386–1395. https://doi.org/10.1177/2047487319843079
37. Lauzon C, Beck CA, Huynh T, Dion D, Racine N, Carignan S, *et al.* Depression and prognosis following hospital admission because of acute myocardial infarction. *CMAJ Can Med Assoc J* 2003;**168**:547–552
38. Mayou RA, Gill D, Thompson DR, Day A, Hicks N, Volmink J, *et al.* Depression and anxiety as predictors of outcome after myocardial infarction. *Psychosom Med* 2000;**62**:212–219. https://doi.org/10.1097/00006842-200003000-00011
39. Kuijpers PM, Denollet J, Wellens HJ, Crijns HM, Honig A. Noncardiac chest pain in the emergency department: the role of cardiac history, anxiety or depression and type D personality. *Eur J Cardiovasc Prev Rehabil* 2007;**14**:273–279. https://doi.org/10.1097/HJR.0b013e32801da0fc
40. Resurrección DM, Moreno-Peral P, Gómez-Herranz M, Rubio-Valera M, Pastor L, de Almeida JMC, *et al.* Factors associated with non-participation in and dropout from cardiac rehabilitation programmes: a systematic review of prospective cohort studies. *Eur J Cardiovasc Nurs* 2019;**18**:38–47. https://doi.org/10.1177/1474515118783157
41. Zwisler AD, Rossau HK, Nakano A, Foghmar S, Eichhorst R, Prescott E, *et al.* The Danish cardiac rehabilitation database. *Clin Epidemiol* 2016;**8**:451–456. https://doi.org/10.2147/CLEP.S99502
42. Finsrud I, Nissen-Lie HA, Vrabel K, Høstmælingen A, Wampold BE, Ulvenes PG. It's the therapist and the treatment: the structure of common therapeutic relationship factors. *Psychother Res J Soc Psychother Res* 2022;**32**:139–150. https://doi.org/10.1080/10503307.2021.1916640
43. Christensen AV, Dixon JK, Juel K, Ekholm O, Rasmussen TB, Borregaard B, *et al.* Psychometric properties of the Danish Hospital Anxiety and Depression Scale in patients with cardiac disease: results from the DenHeart survey. *Health Qual Life Outcomes* 2020;**18**:9. https://doi.org/10.1186/s12955-019-1264-0
44. Anand SS, Islam S, Rosengren A, Franzosi MG, Steyn K, Yusufali AH, *et al.* Risk factors for myocardial infarction in women and men: insights from the INTERHEART study. *Eur Heart J* 2008;**29**:932–940. https://doi.org/10.1093/eurheartj/ehn018
45. Pogosova N, Kotseva K, De Bacquer D, von Känel R, De Smedt D, Bruthans J, *et al.* Psychosocial risk factors in relation to other cardiovascular risk factors in coronary heart disease: results from the EUROASPIRE IV survey. A registry from the European Society of Cardiology. *Eur J Prev Cardiol* 2017;**24**:1371–1380. https://doi.org/10.1177/2047487317711334
46. Olsen SJS, Schirmer H, Wilsgaard T, Bønaa KH, Hanssen TA. Cardiac rehabilitation and symptoms of anxiety and depression after percutaneous coronary intervention. *Eur J Prev Cardiol* 2018;**25**:1017–1025. https://doi.org/10.1177/2047487318778088

Appendix III

Paper III

The experience of group cognitive behavioural therapy among patients with heart disease and psychological distress. Annette Holdgaard, Frey Toiberg, Eva Prescott, Hanne Kruuse Rasmusen, Bente Martinsen

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The experience of group cognitive behavioural therapy among patients with heart disease and psychological distress

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Abstract

Aim

The psychological impact of coronary artery disease (CAD) is substantial. Up to one-third of patients with CAD suffer from anxiety and depression. Untreated anxiety and depression are linked to impaired quality of life and increased morbidity and mortality. However, psychological interventions for treating psychological distress are sparse. Thus, this study aimed to build insights into patients' experiences with participation in group cognitive behavioural therapy as a supplement to cardiac rehabilitation.

Methods and results

In this qualitative study, 11 interviews with patients with cardiac disease and psychological distress were conducted (the interview was conducted within a month after group cognitive behavioral therapy was ended), transcribed and analysed using qualitative content analysis. The patients participated in a large randomised controlled trial (RCT), which compared usual out-patient cardiac rehabilitation (CR) with CR supplemented by brief nurse-led, group cognitive-behavioural therapy. Three main themes emerged from the analysis: The a) significance of time, b) mirroring as a way of normalising and 3) body and mind as a unity.

Conclusion

The findings of this study emphasise that patients with heart disease and resulting psychological distress who receive cognitive behavioural therapy experienced that the therapy diminished their symptoms of anxiety and depression and facilitated their rehabilitation process. Based on the findings, our suggestion is to integrate cognitive behavioural therapy into usual cardiac rehabilitation to ensure that heart and mind are treated together.

Keywords: Interview study, Coronary artery disease, Cardiac rehabilitation, Psychological intervention, Nursing

Key messages

What is already known about this subject?

- Anxiety and depression are significantly more prevalent among individuals with coronary artery disease (CAD), with rates up to three times higher than the general population. These psychological conditions are associated with adverse outcomes, such as reduced treatment adherence, diminished quality of life, delayed or prolonged return to work, increased healthcare utilization, heightened risk of future cardiac events, and elevated mortality risk in CAD patients.
- Cardiac rehabilitation (CR) is a well-established, evidence-based, multidisciplinary approach that has consistently demonstrated its ability to lower mortality and morbidity rates in CAD patients. Historically, CR has primarily emphasized physical training and risk-factor management, while psychological distress management has received less attention.
- Several studies indicate that cognitive-behavioral therapy is an effective treatment for psychological distress in CAD patients. However, it is often perceived as costly and time-consuming, making its integration into standard CR programs challenging. There is a pressing need for more efficient and patient-accepted psychological interventions that can be seamlessly incorporated into CR to address this crucial aspect of CAD patient care.

What does this study add?

- Examining the subjective value of brief group cognitive-behavioral therapy in patients grappling with cardiac disease and psychological distress, this study found that the majority of participants held a positive perception of the group-based approach and the delivery of the intervention by cardiac nurses. Moreover, many patients demonstrated a clear grasp of the cognitive tools designed to help them manage symptoms related to anxiety and depression.
- An essential aspect of the intervention was fostering an understanding of the profound interplay between the body and mind. This newfound insight enabled patients to differentiate between symptoms arising from anxiety and those stemming from cardiac issues, emphasizing the significance of this awareness in the context of their treatment.

How might this impact on clinical practice?

- In the context of increasing calls for the integration of physical and mental health services this study indicates that group cognitive behavioural therapy provided by cardiac nurses is suitable for patients with cardiac disease and psychological distress. The patients experienced that cognitive behavioural therapy diminished their symptoms of anxiety and depression and facilitated their rehabilitation process. The programme is simple and integrating CBT as an essential part of usual CR ensures that heart and mind are treated in unison, easing patients' suffering.

Introduction

Coronary artery disease (CAD) is a chronic condition, which often has an acute onset with acute myocardial infarction (AMI). Despite significant advances in treatment, CAD remains the leading cause of death worldwide. In Europe, the number of patients living with CAD has increased due to the ageing of the population and more patients surviving owing to better treatment (1,2). CAD is also increasingly common in the working-aged population (3). According to Danish Heart Statistics, more than 56,000 individual are diagnosed with cardiovascular disease (CVD) annually, and approximately 36% of these are between 35 and 65 years old (4). AMI constitutes a threat to the patient's life. The sudden confrontation with a life-threatening illness may trigger various psychological responses such as anxiety, stress and depression. It is estimated that up to 33% of patients report psychological distress 12 months after myocardial infarction (5,6). The importance of recognising patients with anxiety and depression is underlined by studies showing that psychological distress impairs QoL and is associated with increased rates of cardiac and all-cause mortality (7,8). 2021, The American Heart Association has stressed the importance of seeing the mind, heart and body as interconnected and interdependent and the need to address this holistic view in the treatment of CAD (9). Identifying patients with anxiety and depression is crucial to improve health outcomes but treatment options for patients who screen positive for anxiety and depression remains limited. A recent metanalysis of 22 RCTs found that cognitive behavioural therapy (CBT) improved anxiety, depression and health-related QoL being most effective when the therapy was individual and when psycho-education, behavioural and cognitive strategies are emphasised as the core intervention strategies (10). Only few studies have examined patients' experiences of group CBT, and no studies have included participants living with CAD but rather other patients suffering from anxiety and depression. In contrast to the metanalysis, these studies (11,12) showed advantages of forming part of a group. This is supported by Tuner et al. (13) who also found that patients with CAD prefer attending rehabilitation programmes in groups, believing that it may be beneficial to interact with other cardiac patients (13). However, living with anxiety and/or depression due to CAD seems to make people reluctant to share their concerns with other patients in the context of CR (14). Another approach coined 'metacognitive therapy' (MCT), i.e. learning how to control repetitive negative thinking (e.g., worrying), was found to generate experiences of changes and improvement in the thinking and emotions of some CR patients, whereas others experienced difficulties in interpreting some of the techniques, not feeling that their needs were met (15).

Thus, the complexity of treating psychological distress among people with CAD is high and our knowledge of this field is fragmented. Even so, it is evident that the treatment must include body and mind alike. However, although CBT seems effective, it is still not widely implemented in CR. A main barrier is the

perceived need for a comprehensive, time-consuming intervention, which is not possible in the context of a standard CR programme. Aiming to meet the need to treat both the physical and psychological consequences of heart disease in Denmark, this study examines an intervention in which people with a new CAD event were provided brief group CBT integrated in CR (16). Thus, the aim of the present study was to describe patient's experiences with brief group CBT as a part of their CR.

Methods

This qualitative study was conducted as part of a larger RCT that compared usual care with usual out-patient CR supplemented by a brief nurse-led group CBT (17,18).

The methodological approach was content analysis as described by Graneheim and Lundman (19) and Graneheim et al. (20). This method is used to identify patterns and variations in patients' experiences with brief group CBT and to systematise differences and similarities in these experiences (19).

The intervention

The intervention was based on CBT principles and included aspects from acceptance and commitment therapy (ACT) (16,21). CBT is an established and recognised evidence-based psychotherapeutic method based on clinical experience, theory and research. Three categories of CBT have been defined. The first originates from behavioural therapy; the second rests on theories about thoughts and their influence on the body, emotions and actions (cognitive therapy); whereas the third CBT category (in line with ACT, MCT and mindfulness-based therapy) is based on acceptance of one's thoughts and feelings. In cognitive therapy, focus is on which of the patient's thoughts and behavioural patterns may create and maintain current problems and influence functional levels. By changing thoughts and patterns of behaviour, the level of functioning and/or QoL may also be changed (16,22). In ACT, the focus is rather on accepting the current situation combined with a commitment to changing inappropriate behaviour. In this context, focus is devoted to the purpose of one's thinking rather than to the contents of a given thought (17,21).

The intervention consists of weekly therapy sessions for five weeks. Each treatment session has a theme and a firm structure that includes homework and always concludes with an opportunity to provide feedback (28). The homework is used to train strategies to cope with the limitations of the heart disease (for instance exposure to cope with anxiety). Each group session lasted two hours with 3-4 patients in each group. The CBT intervention was facilitated by an experienced cardiac nurse with special training and education in CBT, and was supervised by a psychologist.

After the patients had been discharged and had their first visit in the Cardiac Rehabilitation Unit, they had to wait for a minimum of 2-3 weeks due to limited resources, before being included in the CBT intervention.

Clinical setting

Data were collected among patients who had participated in CR supplemented with group CBT in three Danish university hospitals.

Participants

A purposive sample of 20 patients who had participated in the therapy were invited to participate. The nurses who facilitated the group therapy helped the researcher identify patients. Variation was sought in terms of gender, age, education, marital status, geography and heart diagnosis (Table 1). The patients were invited to participate at the end of the intervention, and the interview was conducted within a month after their group CBT had concluded. After 11 interviews, the first and the last author agreed on sufficient variation and an appropriate amount of data to be able to answer the research question (23).

Table 1: Patient characteristics

Patient no.	Gender	Age	Married/ Cohabiting	Diagnosis
1	Male	59	-	STEMI + PCI
2	Female	58	+	NSTEMI + PCI
3	Male	61	-	NSTEMI + PCI
4	Female	52	+	STEMI + PCI
5	Female	39	-	NSTEMI + PCI
6	Male	56	+	NSTEMI + PCI
7	Male	56	-	STEMI + PCI
8	Male	55	-	NSTEMI + PCI
9	Male	40	+	NSTEMI + PCI
10	Male	64	-	STEMI + PCI
11	Male	41	+	Heart valve disease

NSTEMI, non-ST-segment-elevation myocardial infarction, PCI, percutaneous coronary intervention; STEMI, ST-segment-elevation myocardial infarction.

Data collection

Semi-structured interviews were conducted to give the participants an opportunity to express their experience of participating in group CBT. To assure consistency and openness, an interview guide (23) was developed and used (Table 2). Due to Covid-19, the interviews were conducted using Facetime and Skype, which made it possible to see each other despite physical distance. The interviews lasted between 35 and 50 minutes and were conducted from April 2020 to January 2021.

Table 2 Example of questions from the interview guide

• What were your expectations for the group cognitive behavioral therapy? • What did you experience in terms of mental reactions after you were diagnosed with heart disease? • What role has the course played in your way of dealing with your situation? • How has it changed your mental well-being?

Patient involvement statement

No patients were involved in the design of our study.

Analysis

Content analysis is suitable for identifying patterns and themes in a given qualitative material and is appropriate to answer questions about what, why and how (19,20). Content analysis deals with both manifest and latent content. Manifest content analysis focuses on the visible and obvious components in a text, only to describe what is observed. This is suitable when the aim is evaluation to determine the value of a certain course(24). Why this approach was chosen for this study.

Initially, the eleven interviews were read several times to become acquainted with the data and to establish an overall picture of patients' experiences of participating in intensive group CBT. Each of the transcriptions were subsequently divided into meaning units. The meaning units were condensed while still preserving the core content. Subsequently, the condensed meaning units were labelled with a code at a level of higher abstraction to establish ´What the text says´.

Codes were compared in terms of similarities and differences concerning patients' experiences. The codes enabled the researchers to structure the text into categories and sub-categories that shared commonalities of content (Table 3). This was followed by an expression of the latent and interpretive content of the text. At this stage of the analysis, the question ´What the text talks about´ was directed towards identifying themes that covered the categories. Finally, the researchers interpreted the identified meanings and described a new whole. During the entire process, the three authors (AH,FT,BM) discussed the emerging patterns aiming to establish themes that covered patients' experiences of participating in the intervention. Quotes from the transcribed material were used to elaborate on the findings.

Table 3: Domains, categories and theme

Category – manifest level	Theme – latent level
Life has stopped while waiting for the first visit. The heart disease reminds one that time is precious. Pressure to recover within the five-week course. Fear of being alone when the course ends. Time is limited when taking care of heart disease while managing family life and resuming working life all at once.	The significance of time

Ethical considerations

Written and verbal information about the study was given to all participants and informed consent was obtained. Participants were informed that their names and other personal information would be anonymised to maintain confidentiality. They were also informed that they could withdraw from the study at any time without any consequences for their further treatment.

Results

The established categories highlight key aspects of patients' experiences of participating in brief group CBT. Overall, they were positive about participating in the group course. Their heart disease had affected them both physically and mentally, and they had continuously experienced a wide range of concerns and were constantly alert to symptoms from their heart.

The significance of time

Revising the interviews and the categories, it became evident that the heart disease had been a great shock and that life had suddenly become frail. The patients' experiences were marked by ambivalence. On one hand, most of the patients felt gratitude that the treatment was so rapid and that they were quickly discharged from hospital. On the other hand, they felt insecure and isolated in their new situation. The period between discharge from the hospital and the first visit to the CR unit was experienced as extremely long. During their admission, they looked forward to returning to their homes; but once at home, they experienced great uncertainty as they were alone with the responsibility for monitoring their symptoms and general condition.

"Well… I tried a bunch of things while waiting, but doctors and hospitals cannot keep in touch constantly. I couldn't call 112 and let them know that I wanted to be admitted."

(Participant 6)

The patients described increased awareness of their body in the period after being discharged; a period characterised by various worries and anxiety, which made them feel vulnerable why they avoided certain activities. Some patients experienced symptoms of dizziness and breathlessness, which kept them from going out. They considered their body unreliable, and some patients felt that time was slipping by, that their normal life had stopped and that they were forced to adpting a more passive role. Starting group therapy was experienced as a way of moving forward and returning to a kind of normality. Also, participating in group therapy was described as a valuable help to starting personal development and moving forward safely.

"…But, in fact, what I missed the most was getting on with my life again rather than simply observing while time passed and I had no idea about how to move forward."

(Participant 1)

The length of the group therapy was also challenging in some cases as some patients felt pressure to recover within the five-week course. Especially patients who experienced a high degree of anxiety and lived alone found that group therapy was very supportive and they expressed a need for more sessions to work with the tools to reduce the anxiety and be supported by their fellow patients. During the course, the patients became aware that their heart disease was life-changing and that returning to life as it had been before was no longer an option. The cognitive tools needed to be integrated into their lives and they also expressed a wish to follow their fellow patients for an unlimited period of time.

"*And that it may well run for a longer period of time. Because this is taking so long. If you were well after 14 days, it would be fine with a short course, but because I must live with this for the rest of my life, I need support for a longer period of time".*

(Participant 3)

The information given to the patients before discharge concerning full recovery was not in accordance with what the patients in the study experienced. They were told that they would recover fully within 14 days, but the material in this study showed that this was not the case. This discrepancy in time perspective gave rise to many concerns. More specifically, patients worried that something was wrong with them because they were unable to return to work within 14 days.

Some of the patients experienced the time spent in rehabilitation as very stressful. They felt that time was limited and that it was difficult to attend to their heart disease while managing their family life and resuming their working life.

"…and you beed to improve your life style and be physically active, and you feel that you're not progressing fast enough, or that this cannot get done fast enough. And there is not sufficient time. At the same time, you have a normal life to live at the same time in which you need to do your work and care for your children. It's actually quite stressful, having so many things that need changing and thinking about".

(Participant 9)

For those who felt exhausted from the combination of rehabilitation, work and family obligations, the intervention was helpful because it helped them to find strategies allowing them to make decisions to reduce their workload and to talk more openly about the pressure they felt. They became aware of the need to set limits to their own expectations and those of others.

Mirroring as a way of normalising

Finally, being part of a group was experienced as a great relief. During the lonely period at home, a great need for meeting other people in the same situation arose and the group therapy provided this opportunity. In the group, it was possible to voice to one's worries without considerations for relatives and also to compare symptoms and trajectories. The patients described the group as a special place where it was easy to achieve genuine understanding from both healthcare professionals and fellow patients. In this setting, it was acceptable to share frustrations and difficult feelings. Loneliness was a common experience that could be shared:

"*It is a very lonely process to fall so ill. Even if you have family close by, you need to be understood by them. And you do this automatically when you sit in a room with others who have also had a traumatic experience".*

(Participant 11)

The material showed that meeting people in the same situation was important to achieving insights into one's new situation. Fellow patients' who struggled with anxiety and dark thoughts made patients recognise that their own reactions were expected and therefore normal. They also expressed the importance of meeting in a small group as a foundation for sharing and interacting with each other. The patients described how the intervention had helped them adapt better to their situation, and some felt

that it had accelerated their rehabilitation process.

"*It has been such incredibly important pieces in moving forward. Everyone has these stupid thoughts and it's actually the same things we experience".*

(Participant 1)

Some patients felt very ashamed of being emotionally unstable, especially in relation to their children and other relatives, whom they did not want to burden. In the group, it was acceptable to talk about all kinds of reactions, and the healthcare professionals listened and supplemented with professional knowledge. In the group, the tone was candid and nobody needed to contain oneself. Therefore, the patients experienced that they could freely voice their concerns:

"*I actually think that it is extremely important to form part of a group. We were able to support each other in taking some measures and, actually, we saw progress from one session to the next. The nurse hadn't tried having a blood clot in the heart, so we were not all in the same boat, so to speak, but I was, indeed, with the other group participants."*

(Participant 1)

The patients described a need to share existential thoughts about life and death and about what mattered to them. The matrix introduced in the first group session was experienced as a helpful tool to reconsider which values they wanted to prioritise in the future. The patients inspired each other in the process of accepting their new life situation. During therapy, they also trained their use of cognitive tools to manage worries. Experiencing that the worries and reactions were addressed by the healthcare professionals was important in their process towards accepting their new life situation. However, one issue was not eased by group therapy even though it was shared by the patients: feeling a pressure to return to work quickly generated uneasiness and thoughts about how a stressful work life would affect their heart disease. This pressure was experienced as a considerable threat that was not diminish by sharing it with fellow patients in the group.

Body and mind as a unity

Through all the interviews, it was evident that the heart condition had generated a new awareness of the body. For some of the patients, any symptoms from the chest region caused anxiety and led to worries about a new heart attack. Participating in group therapy made them patients understand the connection between their body and mind, and some became aware that they suffered from anxiety. Patients suffering

from anxiety learned how to handle their anxiety and gained awareness that anxiety attacks are of limited duration.

Psychoeducation was particularly effective in facilitating this recognition. For patients, it was a relief to experience that breathing exercises allowed them to calm their agitated nervous system.

"*You need to endure the 20 or 30 minutes it takes, and then you are more or less back to your old self again. Yesterday, I learned that it passes. Anxiety is an emotion and anxiety passes. I would have liked to know that when I was discharged".*

(Participant 5)

Experiencing the body as unreliable was a pervasive challenge for some of the patients. The increased awareness of all symptoms from the heart meant that a simple extra heartbeat was interpreted as potentially dangerous, which, in turn, led to even more symptoms from the heart. The practical part (physical exercises) of the CR addressed this aspect, and the patients talked about the importance of testing the heart within a secure environment. Some mentioned that when the heart rate rose, they felt insecure and therefore reduced their training intensity, but participating in the group made them use their new knowledge to train with more confidence, knowing how the nervous system worked and being aware of its interactions with the mind.

"It would be interesting to see this mental training integrated into the physical training and really integrate the body and mind more with the rehabilitation. I think there may be some exciting synergies in it, and the physical training also has a big impact on mental well-being".

(Participant 1)

For some patients, it was of considerable importance that it was nurses with specific experience in CR who delivered the CBT in the context of CR. Some of the patients stressed that it was crucial to them that the nurse had comprehensive knowledge about their specific heart disease as they have tried therapy where this was not the case.

Discussion

The theme 'Mirroring as a way of normalising" indicated that the patients had a strong desire to talk about their thoughts and concerns and did not feel that these needs had been recognised or addressed by the healthcare professionals during their ordinary rehabilitation. They felt vulnerable as they were trying to

cope with existential changes and adapt to their new life conditions. The group conversations with other patients about their thoughts and concerns made the situation more bearable. The mind, heart and body are interconnected and interdependent; but even so, less attention has been given to psychological health than to physical health (9). The theme “Body and mind as a unity” showed that this connection was recognized and made sense for patients when they learned about the interaction between thoughts, feelings, bodily symptoms and behaviour. This knowledge was experienced as important in the process of diminishing the symptoms of anxiety and depression.

The patients in the present study were struggling with loneliness adrift from professional help following hospital discharge. The information given at the hospital was considered insufficient for them to be able to cope with the responsibility for monitoring their own heart. A wide range of questions and concerns appeared while the patients were waiting for the first group gathering. These findings are in line with those reported in previous research, which also showed that patients felt left alone in the time before attending other rehabilitation programmes, suggesting that psychological support must commence earlier than is currently the case (13). For most patients, the transition period made it difficult to handle emotional distress; for some patients, passive waiting aggravated emotional stress. The patients experienced this period as being in a vacuum where they were constantly attentive to potential symptoms from their heart and did not dare become involved in any type of physical effort.

Chronological time is measured by calendar and clock time and is the most dominant temporal structure underpinning health service delivery in Western societies(25). However, a sudden serious heart disease had affected patients’ experience of time and bearing on time, as described in a narrative review by Jowsey (25). Illness induces new relationships of flow of life as the flow is disrupted when a human becomes ill. Disruption made patients attentive to what Jowsey (25) coined ‘biographical time’, referring to the summative period of time allotted to an individual (25). The patients were reminded of their mortality and the importance of time and how it is used as their future all of a sudden became uncertain. For the youngest patients, heart disease was seen as particularly disruptive because of their cultural assumptions that this type of condition should not be experienced until later in life. The time perspective was further emphasised when patients were responsible for younger children.

McPhillips et al. (14) reported that patients with psychological distress experienced a lack of approaches meeting their needs in the context of traditional CR, where focus was mainly on physical training. Patients harbour a wide range of worries but do not want to discuss them, so they hope to feel better as time passes, and and they become reassured that the distress and worries they experience are normal. This is in opposition to the theme “Mirroring as a way of normalising” describing the patients´ need for sharing

thoughts and worries as an important way to get insight into one's new situation and improving their physical and mental wellbeing. A recent metanalysis (10) showed that CBT improved anxiety, depression and QoL and was more effective when the therapy provided was tailored to the individual's needs. Our study underpins these findings and further illustrates the advantage of group CBT. The group provided patients with a sense of fellowship because others shared their conditions. The possibility of learning and exchanging information between patients was also experienced as a strength. They gained greater courage to confront their anxiety through the development of different individual strategies. Sharing experiences and forming part of a community where all individuals shared the same conditions may have normalised their feelings as suggested by Abrahamsson et al. (11).

Further, our findings showed that nurses' specific knowledge of cardiology was much appreciated as patients lacked knowledge about their body which calls for a thorough understanding of how mental and somatic symptoms overlap and interact. In line herewith, McPhillips et al. (15) noted that CR staff's delivery of treatment and their knowledge of cardiology were highlighted by patients to be of central importance.

Methodological considerations

Often, vulnerable patients refuse to participate in research (26); however, in this study, all patients accepted. Gratitude for being taken care of and getting the opportunity to participate in a specialised programme on psychological distress may also have played a role. The patients were recruited as part of a randomised trial (18), which may have compromised the variation valued in qualitative research (27). However within the group of potential participants, we strove for maximum variation in terms of the following parametres: gender, age and geography, job and life circumstances. Some of the patients had small children to take care and held demanding jobs, while others were on the edge of the labour market. As patients who do not participate in CR are known to have greater comorbidity and more psychological distress (28), a risk exists that the findings in this study may be too positive. Therefore, generalisation of the findings to the most vulnerable patients may be limited. However, in the right context, comparisons with other CAD diagnoses and settings seems reasonable. Nearly one-third of outpatients with heartfailure suffer from symptoms of anxiety and depression, and patients of a younger age are over-represented in this group (29). Thus, it might be possible to use the findings in this study in the rehabilitation of patients with heart failure both in the out patient clinic at the hospital and in the outpatient municipality setting where more patients will undergo rehabilitation in the future.

Conclusion

Our findings highlighted that patients with heart disease and resulting psychological distress who receive CBT experienced that therapy diminished their symptoms of anxiety and depression and facilitated their rehabilitation process. On the contrary the waiting time following discharge from the hospital to the first group meeting was identified as particularly burdensome. Patients felt isolated with their symptoms and concerns for their heart, and were unabale to handle the psychological distress. Attending the intervention group was experienced as a relief because sharing and reflecting with fellow patients helped them normalise their feelings and accept their current situation. Getting to know the deep connection between body and mind as part of the intervention was essential as this insight allowed patients to distinguish between symptoms of anxiety and symptoms originating from the heart.

Based on the findings, our conclusion is that integrating CBT as an essential part of usual CR is a means of ensurig that heart and mind are treated in unison which will ease patients' suffering. In addition, the time from discharge to the first visit in the group must be as short as possible to prevent progression of anxiety and depression.

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accordance with the ethical guidelines of the Nordic Nurses Federation and the Helsinki Declaration.

Patient consent for publication Not required.

Data availability

The data underlying this article cannot be shared publicly under Danish Law. Also, permission to store data (the interviews and the transcripts) expired with the publication of this article.

References

1. Townsend N, Kazakiewicz D, Lucy Wright F, Timmis A, Huculeci R, Torbica A, m.fl. Epidemiology of cardiovascular disease in Europe. Nat Rev Cardiol. februar 2022;19(2):133–43.

2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, m.fl. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. J Am Coll Cardiol. 22. december 2020;76(25):2982–3021.

3. Andersson C, Vasan RS. Epidemiology of cardiovascular disease in young individuals. Nat Rev Cardiol. april 2018;15(4):230–40.

4. The Danish Heart Foundation, National Institute of Public Health (University of Southern Denmark). Danish Heart Statistics. Available from: www. hjertetal.dk.

5. Norlund F, Lissåker C, Wallert J, Held C, Olsson EM. Factors associated with emotional distress in patients with myocardial infarction: Results from the SWEDEHEART registry. Eur J Prev Cardiol. juni 2018;25(9):910–20.

6. Lichtman Judith H., Bigger J. Thomas, Blumenthal James A., Frasure-Smith Nancy, Kaufmann Peter G., Lespérance François, m.fl. Depression and Coronary Heart Disease. Circulation. 21. oktober 2008;118(17):1768–75.

7. Murphy B, Le Grande M, Alvarenga M, Worcester M, Jackson A. Anxiety and Depression After a Cardiac Event: Prevalence and Predictors. Front Psychol [Internet]. 2020 [henvist 23. marts 2020];10. Tilgængelig hos: https://www.frontiersin.org/articles/10.3389/fpsyg.2019.03010/full

8. van Dijk MR, Utens EM, Dulfer K, Al-Qezweny MN, van Geuns RJ, Daemen J, m.fl. Depression and anxiety symptoms as predictors of mortality in PCI patients at 10 years of follow-up. Eur J Prev Cardiol. 1. marts 2016;23(5):552–8.

9. Levine GN, Cohen BE, Commodore-Mensah Y, Fleury J, Huffman JC, Khalid U, m.fl. Psychological Health, Well-Being, and the Mind-Heart-Body Connection: A Scientific Statement From the American Heart Association. Circulation. 9. marts 2021;143(10):e763–83.

10. Li YN, Buys N, Ferguson S, Li ZJ, Sun J. Effectiveness of cognitive behavioral therapy-based interventions on health outcomes in patients with coronary heart disease: A meta-analysis. World J Psychiatry. 19. november 2021;11(11):1147–66.

11. Abrahamsson C, Nordling B, Michelsen CS, Norlander T. Patients' Experiences after Cognitive Behavior Group Therapy: From Anxiety to Feelings of Perceived Security. Psychology. 8. maj 2018;9(5):1176–93.

12. Nielsen M. CBT group treatment for depression. Cogn Behav Ther. ed 2015;8:e8.

13. Turner KM, Winder R, Campbell JL, Richards DA, Gandhi M, Dickens CM, m.fl. Patients' and nurses' views on providing psychological support within cardiac rehabilitation programmes: a qualitative study. BMJ Open. 1. september 2017;7(9):e017510.

14. McPhillips R, Salmon P, Wells A, Fisher P. Cardiac Rehabilitation Patients' Accounts of Their Emotional Distress and Psychological Needs: A Qualitative Study. J Am Heart Assoc Cardiovasc Cerebrovasc Dis. 1. juni 2019;8(11):e011117.

15. McPhillips R, Capobianco L, Cooper BG, Husain Z, Wells A. Cardiac rehabilitation patients experiences and understanding of group metacognitive therapy: a qualitative study. Open Heart. 1. juli 2021;8(2):e001708.

16. Beck JS, Beck JS. Cognitive behavior therapy: basics and beyond. 2nd ed. New York: Guilford Press; 2011. 391 s.

17. Holdgaard A, Eckhardt-Hansen C, Lund T, Lassen CF, Sibiliz KL, Høfsten DE, m.fl. Intensive group-based cognitive therapy in patients with cardiac disease and psychological distress—a randomized controlled trial protocol. Trials. 16. juli 2021;22(1):455.

18. Holdgaard A, Eckhardt-Hansen C, Lassen CF, Kjesbu IE, Dall CH, Michaelsen KL, m.fl. Cognitive-behavioural therapy reduces psychological distress in younger patients with cardiac disease: a randomized trial. Eur Heart J. 18. januar 2023;ehac792.

19. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today. februar 2004;24(2):105–12.

20. Graneheim UH, Lindgren BM, Lundman B. Methodological challenges in qualitative content analysis: A discussion paper. Nurse Educ Today. september 2017;56:29–34.

21. Hallis L, Cameli L, Bekkouche NS, Knäuper B. Combining Cognitive Therapy With Acceptance and Commitment Therapy for Depression: A Group Therapy Feasibility Study. J Cogn Psychother. 2017;31(3):171–90.

22. Arendt M. Kognitiv terapi: nyeste udvikling. 2012.

23. Kvale S, Brinkmann S. Interviews : learning the craft of qualitative research interviewing. 3. edition. Thousand Oaks, Calif.: Sage Publications; 2014. xviii, 405 sider s.

24. Kleinheksel AJ, Rockich-Winston N, Tawfik H, Wyatt TR. Demystifying Content Analysis. Am J Pharm Educ. januar 2020;84(1):7113.

25. Jowsey T. Time and chronic illness: a narrative review. Qual Life Res. 1. maj 2016;25(5):1093–102.

26. Badu E, O'Brien AP, Mitchell R. An integrative review on methodological considerations in mental health research – design, sampling, data collection procedure and quality assurance. Arch Public Health. 10. oktober 2019;77:37.

27. Malterud K. Qualitative research: standards, challenges, and guidelines. The Lancet. 11. august 2001;358(9280):483–8.

28. Resurrección DM, Moreno-Peral P, Gómez-Herranz M, Rubio-Valera M, Pastor L, Caldas de Almeida JM, m.fl. Factors associated with non-participation in and dropout from cardiac rehabilitation programmes: a systematic review of prospective cohort studies. Eur J Cardiovasc Nurs. januar 2019;18(1):38–47.

29. Dekker RL, Lennie TA, Doering LV, Chung ML, Wu JR, Moser DK. Coexisting anxiety and depressive symptoms in patients with heart failure. Eur J Cardiovasc Nurs. 1. april 2014;13(2):168–76.