SheppHeart$_{CABG}$

Shaping outcomes by exercise training and psycho-education in phase 1 for coronary artery bypass grafting patients

A 2 x 2 factorial randomised clinical pilot trial

Phase 1 comprehensive cardiac rehabilitation

Protocol registration:

Regional Ethics Committee: H-3-2013-112

Danish Data Protection Agency: 2007-58-0015

ClinicalTrials.gov: XX

Abstract

Background: Patients undergoing coronary artery bypass graft surgery often experience a range of problems and symptoms related to the procedure and the underlying heart disease. These problems include anxiety and depressive symptoms, immobility issues, complications such as wound seeping, neck and shoulder pains, interrupted and insufficient sleep. Over the last 2 decades, cardiac rehabilitation has become recognized as a significant component in the continuum of care for persons with cardiovascular disease. Furthermore, cardiac rehabilitation has undergone a significant evolution moving from a focused exercise intervention to a comprehensive disease management program. In Guidelines for Coronary Artery Bypass Graft Surgery cardiac rehabilitation is described to include early ambulation during hospitalisation, and outpatient prescriptive exercise training beginning 6-8 weeks following surgery. Our hypothesis is that physical exercise with moderate intensity and a psycho-educative component as a part of cardiac rehabilitation can begin in early postoperatively during hospitalising. Results from studies on phase 1 rehabilitation in coronary artery bypass graft surgery patients are promising. However, no randomised trials have been conducted, and evidence is therefore lacking.

Objective: The objective of this pilot trial is to investigate the effect of a phase 1 comprehensive cardiac rehabilitation programme consisting of a psycho-educative component, an exercise-training component including pulmonary training, cycling, neck and shoulder exercises, these in combination plus treatment as usual and treatment as usual in patients who undergo coronary artery bypass grafting.

Design: SheppHeart$_{CABG}$ is an investigator-initiated 2 x 2 factorial randomised clinical pilot trial with blinded outcome assessment. Recruitment from one site with 1:1:1:1 central randomisation to phase 1 rehabilitation; 1) exercise-training plus usual care, 2) psycho-educative plus usual care 3) exercise-training and psycho-educative plus usual, 4) usual care alone.

Population: Patients above 18 years with ishaemic heart disease, who have to undergo elective coronary artery bypass grafting, speak and understand Danish and provide a written informed consent will be included. The following patients will be excluded from the trial: patients at intermediate or high risk to their cardiovascular status according to guidelines, patients with neurological or orthopaedic deficits which prevent training and patients who do not wish to participate.

Number of participants: 60 participants will be included.

Interventions: All patients receive usual care. Patients allocated to the experimental groups are either, 1) following a physical exercise rehabilitation programme, 2) a psycho-educative rehabilitation programme, or 3) the physical exercise and psycho-educative rehabilitation programmes combined. The control group will receive usual care alone. The physical exercises consist of; deep breathing exercises and breathing exercises using incentive spirometry with expiratory positive pressure airway, cycling exercises during hospitalisation and an individualised exercise programme running from discharge to 4 weeks following surgery. The psycho-educative rehabilitation programme consists of four psycho-educative consultations with a specially trained nurse. The last consultation will take place 4 weeks following surgery.

Outcomes: The explorative outcome measures consist of two parts: physical capacity and mental and physical health. Physical capacity is measured by peak VO_2 max and 6 minutes' walk test at discharge and 4 weeks following surgery. Perceived mental and physical health is measured by the Medical Outcome Study Short Form 36 (SF-36) at admission, discharge and 4 weeks following surgery. Furthermore questionnaires measuring anxiety and depression (Hospital Anxiety and Depression Scale), health-related quality of life (HeartQoL), fatigue (MFI-20) cognitive and emotional representation of illness (B-IPQ), physical activity (IPAQ), self-rated health (EQ-5D), sleep (PSQI) and pain (ÖMPSQ).

Safety: There are no previous reports of risks associated with psycho-educational consultations. Physical exercise is tested extensively in patients with heart disease and is considered safe and will meet the applicable requirements for safety during training of cardiac patients. The interventions are considered safe for patients at low risk according to their cardiovascular status.

Ethical considerations: The trial is performed in accordance with the Declaration of Helsinki in its latest form. All patients must give informed consent prior to participation and the trial is initiated after approval by the Danish Data Protection Agency and the regional ethics committee. The trial will be registered at www.clinicaltrials.gov before randomisation of the first participant.

Funding and organisation: $SheppHeart_{CABG}$ is conducted as part of the Heart Center, Rigshospitalet. The pilot trial will be financed by grants for health research.

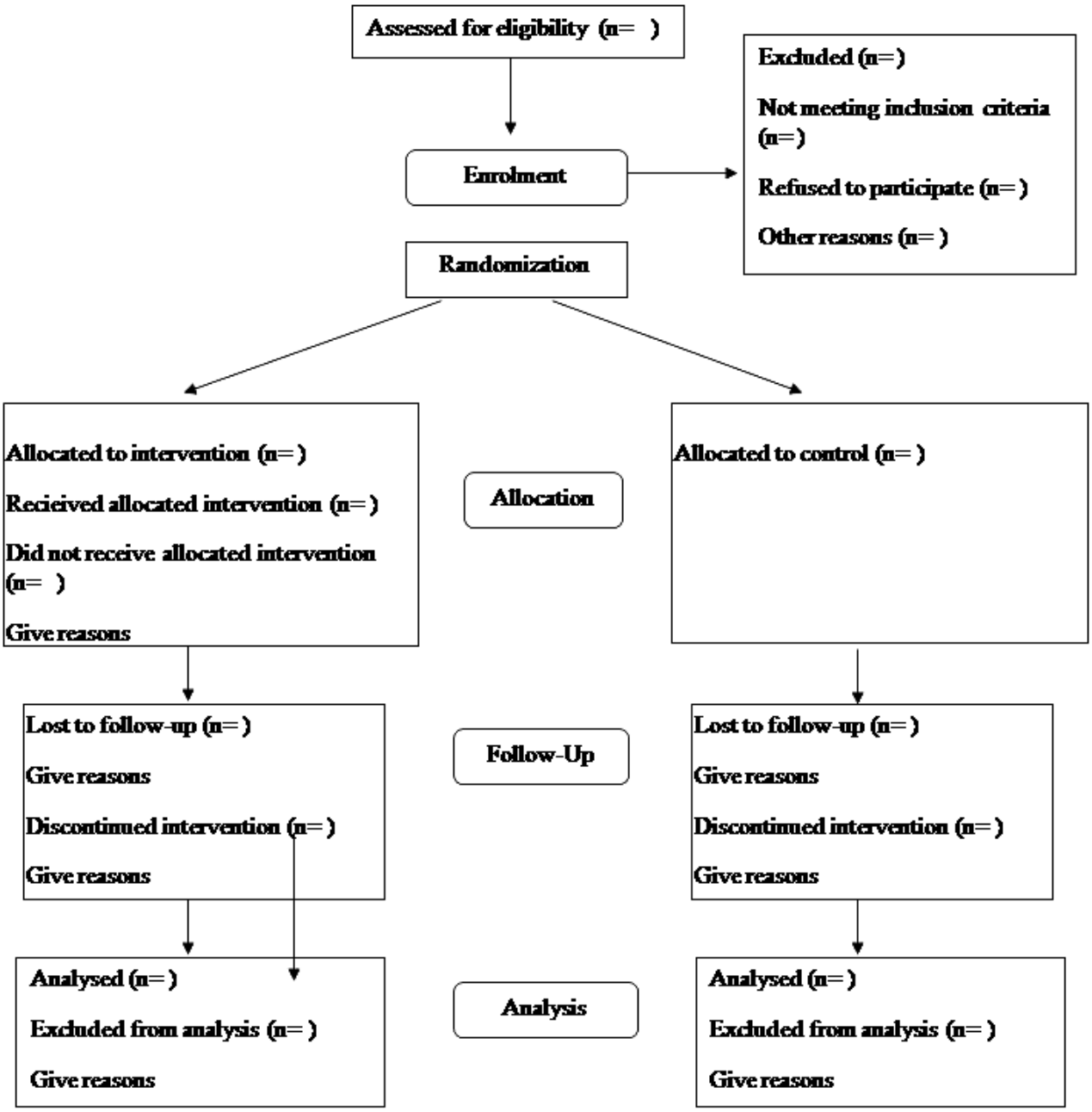
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Table of contents

List of abbreviations

CABG:	Coronary Artery Bypass Grafting
CPB:	Cardiopulmonary bypass
CTU:	Copenhagen Trial Unit
ISF:	Investigator Site File
NYHA:	The New York Heart Association
PCI:	Percutaneous Coronary Intervention
PTCA:	Percutaneous Transluminal Coronary Angioplasty
RPE:	Perceived Extension scale
RMSG:	Respiratory Muscle Stretch Gymnastic

1.0 Introduction and background

Cardiac rehabilitation is an important aspect of recovery after heart surgery. Cardiac rehabilitation programs are advised to provide specific core components of care to optimize cardiovascular risk reduction, reduce disability and promote healthy behaviours (1). It is known that exercise training in cardiac rehabilitation after discharge has a positive effect in patients after coronary artery bypass grafting (CABG) (2-8). However, randomised trials of comprehensive cardiac rehabilitation in the early postoperatively phase is lacking.

1.1 The patient population

In Denmark about 200,000 people have ischaemic heart disease. Treatment of patients with cardiovascular disease cost around 4.6 billion DKK every year (9). From 2007 to 2009 approximately 40,000 patients were hospitalised with cardiovascular disease and approximately 16,000 were diagnosed with ischaemic heart diseases (9). The age distribution shows a characteristically increase in prevalence with cumulative age. The prevalence of angina pectoris in men aged 50 to 59 is approximately 2%, above 60 years it is about 4% and in women above 60 years the prevalence is about 2% (9, 10).

Cardiovascular diseases are the main cause of mortality in Europe accounting for 40% of all deaths in 2008 and 36% in 2010 (11, 12). Furthermore, ischaemic disease was alone responsible for 13% of all deaths in 2010 (11). Annually, cardiovascular disease cause more than 15,000 deaths and significantly reduces quality of life for a large numbers of people in Denmark. Between 2005 and 2008 more than 50% off all cardiac deaths were related to ischaemic heart disease (12). Since the mid-1990s the total mortality rate of ischaemic heart disease has declined in nearly all European Union countries; most remarkably in Ireland, the Netherland's, the United Kingdom, and Denmark (11). In Denmark the mortality rate in ischaemic heart disease has fallen from 121 deaths per. 100.000 inhabitants in 2005 to 77 deaths per. 100.000 inhabitants in 2011 (13). The decrease in mortality is caused by improvements in treatment, prevention and changes in life style (13). The surgical treatment of ischaemic heart disease is CABG. The four heart centres in Denmark performed 1,746 of these surgeries in 2011 and 1,659 in 2010(14). In 2011, the sex distribution was 82% men and 18% women and 39.2% were more than 70 years old (10).

1.1.1 CABG

CABG and catheter-based percutaneous coronary intervention (PCI) with or without stent are alternative approaches to mechanical coronary revascularisation. CABG offers a survival advantage

over medical therapy for high-risk coronary patients (15). A systematic review including 23 randomised trials found that longterm survival did not differ between patients undergoing PCI and CABG (16). The short-term risk of stroke was higher with CABG than with PCI, yet the frequency of angina was lower after CABG than after PCI over 5 years (16). Today CABG is acknowledged as "state of the art" (17). CABG is one of the most frequently performed cardiac surgeries in the western world and the goals of revascularisation for patients with coronary artery disease are to improve survival and/or relieve symptoms. CABG is performed either as an elective or acute procedure. Eighty procent of admissions to departments of cardiac surgery are planned (10).
The standard coronary artery bypass grafting approach is via a median sternotomy. Sources of graft can be the internal mammary artery, the radical artery and/or saphenous vein. Cardiopulmonary bypass (CPB) is being used during the surgery to maintain cardiopulmonary function and tissue perfusion. After the aorta is cross-clamped cardioplegia is administrated to stop the heart and the anastomoses are performed while the heart is stopped. When the anastomoses are finished the cross clamp is removed from the aorta. The intrinsic cardiac rhythm is often spontaneously re-established. After the heart rate is adequate and the blood pressure is confident, the patient is separated from the cardiopulmonary bypass mashine. Epicardial atrial and ventricular pacemaker wires will be inserted (17). Typically 12 to 24 hours after the surgery, the patient is stabilised in the recovery room/intensive care unit and ready to be transported to the cardiac surgical unit (18).

1.1.2 Symptoms and problems related to CABG

It seem that patients undergoing CABG often experience a range of physical and psychological problems and symptoms related to the procedure and the underlying heart disease before, during and after hospitalisation, which negatively can influence the course of treatment and patient's recovery. Lie et al. interviewed 93 patients 2 weeks after surgery and the patients' needs were characterised by a substantial amount of uncertainty and worries related to; what to expect and what was normal for postoperative pain; assessment and sensation of surgical site, different experiences with physical activity/exercise, uncertainty about medications, difficulties with sleep patterns, irritability, postoperative complications, uncertainty about return to work and insufficient information at discharge (19).

1.1.2.1 Anxiety and depression before and after CABG

Patients who have to undergo elective or sub-acute CABG will experience a waiting period of varying length. The waiting period is based on a medical assessment by the physicians. During this time patients may experience symptoms of anxiety and depression which are related to increased severity of chest pain and dyspnoea (20). Furthermore, the waiting period can be extremely stressful for patients (21-23). Many patients find the uncertainty and fear of waiting for CABG more disturbing than their chest pain. This may have long term disabling consequences, as patients adopt a sedentary lifestyle so that normal routines of work and active hobbies are lost, sometimes for ever (24). Data from an observational study of 142 patients undergoing CABG shows that younger patients are more anxious before CABG than older patients (25). Shortly after CABG surgery symptoms of depression are reported and remain evident in around one-fifth of patients one year after surgery (26, 27). In a cross-sectional study of 444 Australian patients it was found that those at risk of persistent mood disturbances after CABG were the young, single, female and those with diabetes (28).

Duits et al examined patterns of anxiety and depression from 2 weeks before CABG to 6 months after surgery in 217 patients. Anxiety and depression was highest before the surgery and decreased significantly 1 week after surgery with no further reductions at 6 months (29). Similar to these results McCrone et al. found that anxiety was common, peaking preoperatively with 38% of patients being anxious. This was reduced to 34% by 2 weeks postoperative, but after 12 weeks no further reductions were observed (30). Anxiety and depression are the most frequently reported symptoms associated with impaired physical functioning and the most frequent problems related to psychosocial functioning between hospital discharge and up to 6 months after coronary artery bypass grafting (31-34). Both anxiety and depression can have a negative effect on quality of life and rehabilitation and up to 5 years after surgery patients with preoperative moderate cognitive-affective depression, could be at risk for sustained feelings of depression (35). Furthermore, depressive symptoms can influence the activities of daily functioning. McKenzie et al. showed significant associations between anxiety and depression and Instrumental Activities of Daily Living functioning (36).

1.1.2.2 Surgical wound and wound infection after CABG

Depressive symptoms are associated with infections, impaired wound healing and poor emotional and physical recovery (33). Patients with ischaemic heart disease who undergo CABG get surgical

wounds, which are located on the median of sternum and either on the lower leg or on the forearm, depending on where the graft vein or graft artery is harvested. In an observational study including 151 patients, 16.6% of patients express various problems like pain, stinging, oozing from incisions and smells related to their wounds (37) . In a study involving 43 patients 19% reported having stinging in both sternal and graft wound (38).

Surgical site infections after coronary artery bypass grafting surgery increases morbidity and mortality (39). The reported incidence of sternal wound infection is between 3.5% and 8% in the US (40, 41) and < 2% in Denmark (42). Using the Society of Thoracic Surgeons National Cardiac Database, Vance et al. analysed 331,429 CABG patients and found major infections in 3.5% of patients. 25.1% of the infections were mediastinitis, 32.6% saphenous harvest site, 35% septicemia, 0.5% thoracotomy and 6.8% multiple sites. Patients with major infections had significantly higher mortality (17.3% versus 3.0%) and longer postoperative length of hospital stay >14 days (47% versus 5.9%) than patients without major infections (40).

1.1.2.3 Pain after CABG

Pain is a common symptom after heart surgery along with fatigue and sleep disturbances. Patients experienced more pain postoperatively after CABG than expected preoperatively even when they were treated with pain medication (43). Pain may be the explanation for the lack of physical activity. In addition a combination of depression and pain seems to influence the functional recovery after coronary artery bypass grafting CABG (44, 45). Pain after CABG is located in the thorax area (84.5 %), in the upper body area; arm(s), shoulder(s), neck or back (43.3%), and leg(s) (35.7%) (46). Mueller et al. examined 200 patients who underwent median sternotomy for open heart for pain intensity in the first seven days postoperatively. There was a statistically significant difference in pain when the three first postoperatively days was compared with seven postoperatively day ($p \leq 0.01$). The maximal pain intensity was higher in the first postoperatively days. The pain distribution did not vary significantly throughout the hospital stay, but the location of the pain did, with more shoulder pain on postoperative day seven (47).

1.1.2.4 Interrupted and insufficient sleep after CABG

Sleeping problems related to CABG are multifarious. Sleeplessness, poor sleep quality and lack of sleep continuity (difficulty falling asleep, restless sleep with frequent nocturnal awakenings and early morning awakenings) are common among patients during recovery after CABG (19, 48). In

the first 4 to 8 weeks after surgery, an increase in daytime sleep and reductions in night time sleep have been found, with the greatest period of disturbance in the first week after surgery (49). Symptoms such as pain, nocturia, impaired sleep cycles, difficulty finding a comfortable position and inability to perform usual routines before going bed appear to be important contributors to poor sleep after cardiac surgery (48). Doering et al. interviewed 89 patients 1 week after discharge and 9% of these patients were complaining because they were not allowed uninterrupted sleep in the hospital due to medication and routine care (50).

1.1.2.5 Respiratory function after CABG

Despite advances in anaesthetic techniques, CABG frequently leads to postoperative pulmonary complications (51). Respiratory complications after CABG include alterations in pulmonary function and gas exchange, reduced ability to cough and may be associated with atelectasis. Atelectasis is common and is associated with reduced lung capacity and respiratory muscle strength. In fact, atelectasis is known to occur during all types of surgery with general anesthesia. Lindberg et al. reported the incidence of atelectasis to be as high as 85% after general anesthesia to lower abdominal surgery (52). Furthermore they showed that the resulting impairment of gas exchange in the postoperative period correlated with atelectasis formation.

Surgical procedures can affect the respiratory muscles. Studies which investigated respiratory muscle strength after CABG demonstrated a reduction in respiratory muscle strength and showed that lung function may be impaired for up to 3 months after CABG (53, 54).

1.1.2.6 Immobilisation before and after CABG

In patients with severe cardiac diseases, physical activity is often reduced, leading to decreased lung volumes and capacities before surgery, which are exacerbated by heart surgery (55). Patients' expectations have been shown to be an important predictor of treatment outcome in a variety of surgical operations (56). The preoperative expectations of patients with cardiac surgery have been shown to be related to quality of life, illness-related disability, physical activity, physical health status, and rehospitalisation after surgery (57). As a consequence of the underlying ischaemic heart disease, patients waiting for CABG can experience lower physical activity in their normal daily activities. Patients have an initial fear that physical activity before surgery can cause a heart attack (58). In the first postoperatively days, patients can be afraid to move themselves while in bed. First of all, they do not want to risk removing various equipment but they also have concern that physical

activity could harm the new operated heart (19). In the following postoperatively days until discharge patients are more physically active e.g. by walking and sitting in a chair and feeling more comfortable in being physical active (50).

1.2 Current care for patients undergoing CABG

Usual care is according to current guidelines and is for patients undergoing CABG divided in two parts; pre-operative time and postoperative time.

Care in the pre-operative time:

Admission interview with nurse on admission day the day before surgery consist of:

- Conversation concerning; health and well-being, treatment, care, observation during hospitalisation.
- Screening for fall, nutrition, sternum scarp.
- Introduction to the ward appliance and the circadian rhythm.
- Information about; fasting procedures, bath, epilering.
- Introduction to; postoperative pain and nausea medication – introduction to pain assessment, postoperative activities.

Consultation with the physiotherapist instructing:

- How to clear the upper respiratory airways after sternotomy,
- How to get out and in of bed.
- How to use a spirometry med positive expiratory pressure after surgery.

After surgery patients arrive to intensive care unit. Usually patients return the following morning to the surgical ward.

Care in the postoperative time:

A number of consultations during the postoperative time regarding:

- Postoperative observation of vital values; blood pressure, pulse, heart rate, temperature, saturation and pain, excretion.
- Introduction to and removing pace wire 3.postoperatively day.
- Reintroduction to; postoperative pain and nausea medication – introducing to pain assessment, mobilisation.
- Nutrition rescreening.
- Conversation with the patient about mental health if needed

Discharge conversation with nurse on the day of discharge consisting of:

- Information on the issues that require attention to after discharge e.g. to care for the scars and prevent and act on sign of infection, pain and various restrictions regarding driving, swimming and lifting.

Consultation with the physiotherapist instructing:

- Directions on management of daily activities with sternotomy after discharge and introduction to Danish health and Medicines Authority recommendations concerning physical activity
- Physical training with other patients who have undergone CABG surgery in the gym

Patients will during the discharge conversation be informed about the possibility of calling the ward if there are changes in conditions. Patients will be convened approximately four weeks after surgery for consultation in the cardiology clinic at their local/regional hospital.

1.2.1 Current cardiac rehabilitation for patients undergoing CABG

Over the past 2 decades, cardiac rehabilitation has become recognized as a significant component in the continuum of care for persons with cardiovascular disease. Cardiac rehabilitation following cardiac surgery includes a number of components; patient assessment, physical activity counselling, exercise training, nutritional counselling, tobacco cessation and psychosocial management. (59). Cardiac rehabilitation programmes are generally divided into 3 main phases; 1) inpatient cardiac rehabilitation (phase 1 cardiac rehabilitation), 2) early outpatient cardiac rehabilitation (phase 2 cardiac rehabilitation) 3) long-term outpatient cardiac rehabilitation (phase 3 cardiac rehabilitation) (1). In The American College Guideline for Coronary Artery Bypass Graft Surgery it is described that cardiac rehabilitation includes; early ambulatory during hospitalisation, outpatient exercise training, and education (17). It is common that the physical part of cardiac rehabilitation for patients undergoing CABG begins 6 to 8 weeks following surgery (17) .

1.3 Trial intervention

SheppHeartCABG-trial uses a 2 x 2 factional randomised controlled design. The trial will be conducted in one Danish Heart Centre. A thorough description can be found in section 6.

Figure 1. SheppHeart^{CABG} trial design

	Exercise training component	No exercise training component
Psycho-educative component	Exercise training, psycho-educative component and usual care	Psycho-educative component and usual care

No psycho-educative component	Exercise training component and usual care	Usual care

1.3.1 Clinical data

1.3.1.1 Cardiac rehabilitation phase 1 for CABG patients

1.3.1.2 Physical intervention

A systematic literature search April 2012 in the databases PubMed, Cinahl and Embase in combination with hand searching reference lists showed one systematic review, seven randomised clinical trials on non-pharmacological interventions targeting physical exercise preoperatively and in the early postoperative period during hospitalisation for CABG patients. Physical exercises in this context consist of either respiratory or aerobe exercises or a combination of both. See appendix 14.4.

The systematic review concluded that there is no evidence of benefit for intensive spirometry in reducing pulmonary complications and in decreasing the negative effect on pulmonary function in CABG patients (60).

Four trials examine the effect of respiratory exercise preoperatively and in the early postoperative period after CABG surgery (61-64). The first examines the use of expiratory positive airway pressure mask in the early postoperative period with the expiratory pressure increased progressively by 3 to 8cm water during 3 to 12 minutes. Respiratory muscle strength 30 days after CABG showed a significantly better recovery in the intervention group compared to the control group ($p<0.01$) (62).

The second trial evaluates the effectiveness of voluntary deep-breathing exercises performed with a positive expiratory pressure early after surgery. The deep-breathing exercises consisted of 30 slow deep breaths performed with a positive expiratory pressure blow-bottle device (+ 10cm). The participants in the intervention group had significantly smaller atelectasis area ($p<0.05$) on 4. postoperative day compared to control group (63). The third examines the effect of inspiratory muscle training pre- and postoperatively. The positive expiratory pressure started equal to 15% of the patients inspiratory muscle strength and was increased incrementally between 15% and 45% based on patients' tolerance in the following days. The intervention showed a significant increase

in inspiratory muscle strength in intervention group and decreasing in usual care group ($p<0.05$). Furthermore there was a significantly decrease in pulmonary function in both groups ($p<0.05$) (61).

The last of the four trials examined the effect of respiratory and physical exercise in pneumonia and peak flow in CABG patients in the early postoperatively time during hospitalisation. One day after extubation there was similar and significant reduction in peak for intervention group as well for control group. However peak flow measurement before discharge returned to baseline values in the rehabilitation group but not in the control group (64).

Two randomised clinical trials examine the effect of physical exercises. One trial examines the effect between 6-minutes walking and 6-minutes cycling. There were found no significant differences between intervention group; 6 minutes-walk distance ($p=0.803$) and 6-minutes cycle work ($p=0.798$) (65). One trial examines the effect between walking exercises and walking/ breathing exercises and a control group. There was a significantly lower 6-minutes' walking distance for the control group compared with the walking exercise group ($p=0.005$) and the walking/breathing group ($p=0.022$) (66).

These trials have a high risk of bias. There are a limited number of participants in some of the trials (61, 62). In one trial 39% participants were unable to commence or complete preoperative baseline assessments (65). Furthermore, not all participants the trials are representative for the CABG population (61, 66).

1.3.1.3 Psycho-social intervention

Furthermore, two systematic reviews and two randomised clinical trial targeting psycho-social intervention in CABG patients was found during the updated literature search January 2013. See appendix 14.5.

Forty-six prospective studies were identifited in a systematic review of pre-operative predictors of post-operative depression and anxiety in individuals who have undergone coronary artery bypass graft surgery. A range of pre-operative predictors of post-operative depression and anxiety were indicated and chief among these are pre-operative depression and anxiety and indicate an early assessment of psychological intervention. (67).

A systematic review of 16 studies (ten descriptive, four quasi-experimental, two experimental) examine the psychological condition of patients who had CABG after discharge and suggest that further examination of anxiety and depression in the postoperative period are need (68).

Patients who experienced high levels of psychological distress before CABG surgery benefited from the psychological intervention provided by an advanced practice nurse providing face-to-face home visits and showed significant improvements in anxiety and depression symptoms with at 6 week and 6 month follow-up in a prospective randomised clinical trial, ($p<0.05$) (69). A randomised clinical trial showed that CABG patients who received massage therapy postoperatively, experience significantly less pain, anxiousness and tension (70). The massage therapy was given on the second and forth postoperative day by a certified massage therapist in 20 min sessions. The control group was offered standard care. Results from studies targeting psycho-social interventions in the early postoperatively time after CABG is promising. However, no randomised trials have been conducted, and evidence is therefore lacking.

1.3.1.4 Mindfulness

Mindfulness is a form of psycho social intervention that offers support for stress-reduction, calm awareness and, self-care through meditation-based exercises. Mindfulness programs have become influential in the form of standardized and structured courses such as Jon Kabat-Zinn´s "Mindfulness-based Stress Reduction" and Mindfulness-based Cognitive Therapy programs. Mindfulness programs have been subject to a range of mechanistic and clinical studies that seem to confirm a general trend of non-specific psychological and physiological improvements across a spectrum of standardized mental health measures, including psychological and physiological well–being, in reducing perceived stress, pain and depression and increasing mindfulness and energy, perceptions of loneliness in older adults and in parallel a down regulation of expression of inflammation-genes (71) It was also found effective in reducing anxiety accompanying cardiovascular disease (72-75). There are no randomised clinical trials in which mindfulness-based stress reduction program is used as an intervention on CABG patients. The effect on sleep and pain observed in other contexts would be highly desirable, but it remains to be shown if this type of intervention is feasible and effective in CABG patients (76, 77) .

1.3.2 Cardiac rehabilitation phase 2 for CABG patients

It seems to be shown that exercise training in the cardiac rehabilitation phase 2 has a positive effect on e.g. cardiopulmonary pulmonary function and quality of life in patients after CABG surgery in

rehabilitation phase 2 (2-8). Furthermore, there is convincing evidence from a randomized study by Belardinelli et al. on the positive effect in peak VO2 ($p < 0.001$) of exercise training in patients after PCI (78); however participation in this study is low, especially in women (79-81).

Evidence show that participation in cardiac rehabilitation programs reduces 5 years mortality by 25% to 46% and recurrent nonfatal myocardial infarction by 31% (82-84) and the positive effects of cardiac rehabilitation related to exercise capacity and quality of life have been well documented, particularly in patients with coronary heart disease and heart failure (85).

1.4 Risk and benefits

A systematic review has analysed 47 studies randomising 10,794 patients to exercise-based cardiac rehabilitation reduced overall and cardiovascular mortality [RR 0.87 (95% CI 0.75, 0.99) and 0.74 (95% CI 0.63, 0.87)] (86). Physical exercises; breathing, cycling, neck and shoulder and physical testing will be performed under supervision by physiotherapist and meets the applicable requirements for safety during training of cardiac patients (87). The 2 x 2 factorial randomised clinical pilot trial is expected to contribute to results, which can improve patients undergoing CABG patients' participation in cardiac comprehensive phase 1 rehabilitation. Additionally, it is believed that the trial can provide a systematic approach to the lacking national consensus on rehabilitation in the rehabilitation phase 1 after CABG. There are no previous reports of risk by psycho-educational interventions. A thorough description is in section 8.2.

1.5 Ethical justification and trial rationale

Only a few number randomised trials and observational studies of non-pharmacological interventions targeted physical exercises and a psycho-social component in the phase 1 period during hospitalisation for CABG patients. Some have been focused on the physical problems and others tried to reduce the psychological impact. Overall, results were diverse. However, none of the prior studies have included a combination of physical exercises and psychosocial interventions. Since recovery after CABG often includes both physical and psychological components, it is plausible to assume that a combination of these could generate more pronounced results. Only few randomised trials in CABG patient in the early postoperative period during hospitalisation exist and these are small only trials with focus on comprehensive rehabilitation after CABG. We therefore considered it appropriate that participants in the control group receive treatment as usual.
It seems to be essential that cardiac rehabilitation is comprehensive, because traditional cardiac rehabilitation has focused on physical training and standardised programmes, however studies

indicate that individualised content and supervised exercise components are a key characteristics for improving outcomes (88). In addition to exercise training, interventions that include patient education yield an improvement in health-related quality of life, a decrease in healthcare costs, and a reduction of psychological symptoms, such as depression and anxiety in patients with chronic heart disease (89).

Trials show a potential for improvements in patient outcomes, however data are sparse in phase 1 comprehensive cardiac rehabilitation for patient undergoing CABG. Furthermore, it is advocated that future investigations give more attentions to the representativeness of the sample. Indeed, study samples should include sufficient females, elderly and patients with comorbidities to be representative.

1.5.1 Informed consent

If the patient, after receiving both verbal and written information decides to participate in the SheppHeartCABG pilot trial, an informed consent form will be signed. Information about the pilot trial is conducted in a room without disruption and patients have the possibility to bring an observer or a relative. Patients are informed of their right to take the time to consider a possible participation in the trial. The original consent form will be stored in the investigator site file (ISF) and a copy provided to the patient. All trial participants are informed that all personal information is confidential. Participants will be informed that they have access to personal documents and records according to current legislation. All trial participants are informed that participation is voluntary and that they have the right to withdraw from the trial without explanation and without consequences for their future treatment. If a trial participant is excluded from the trial, either on the basis of the participant's own choice or the treating physician's judgment, participant will be asked for permission to use already collected data. See section 4 for further details on screening and identification of participants.

1.6. Trial conduct

SheppheartCABG will be conducted in accordance with the protocol after approval by the Copenhagen Trial Unit (CTU), international experts in the field, the Committees on Health Research Ethics in the Capital Region of Denmark**,** the Danish Data Protection Agency and according to good clinical practice guidelines. Substantial amendments to the protocol will not be implemented without the appropriate review and approval of the regional ethics committee and the Danish Data Protection Agency, with the exception of situations where it is necessary to prevent

imminent danger to trial participants. In such cases, the amendment will be reported to the regional ethics committee and the Danish Data Protection Agency as soon as possible.

2.0 Trial objectives and purpose

The objective is to investigate the benefits of a phase 1 cardiac rehabilitation programme, consisting of a psycho-educative component and a physical exercise component. The SheppheartCABG is a pilot trial to test the feasibility of a larger confirmatory trial. The hypotheses to be tested in the larger trial is that a phase 1 cardiac rehabilitation programme including a physical component and a psycho-educative component will improve exercise capacity measured by peakVO_2, mental health and efficacy human outcomes as; quality of life, atelectasis, sleep, anxiety, depression.

3.0 Trial design

3.1 Trial design

SheppHeartCABG is an investigator-initiated randomised clinical pilot trial with a 2 x 2 factorial design. This design has been selected in order to investigate the separate effects of psycho-education and physical exercise. It is our hypothesis, that it is the combined intervention that will have the largest outcome, due to a holistic approach to patient needs. It is a randomised clinical pilot trial with the intension to conduct a larger confirmatory trial.

3.2 Randomisation

Participants will be randomised 1:1:1:1 to usual care or the three experimental intervention groups. Randomisation will be conducted centrally by CTU. The allocation sequence will be computer-generated with a varying block size concealed by the investigators. The allocation will be conducted when investigators login to the web-based 'CTU Online Randomisation System', and select relevant participant information. The participant will hereafter be allocated to one of the four intervention groups (social security number (CPR) and participant number).

3.3 Blinding

Because of the conditions for rehabilitation, it is not possible to blind the staff and patients. However, all physical tests, data collection and administration will be done by blinded staff. Statistical analysis of outcomes and conclusions from these will be blinded.

3.4 Participant timeline

Figure 2. Timeline physical exercises

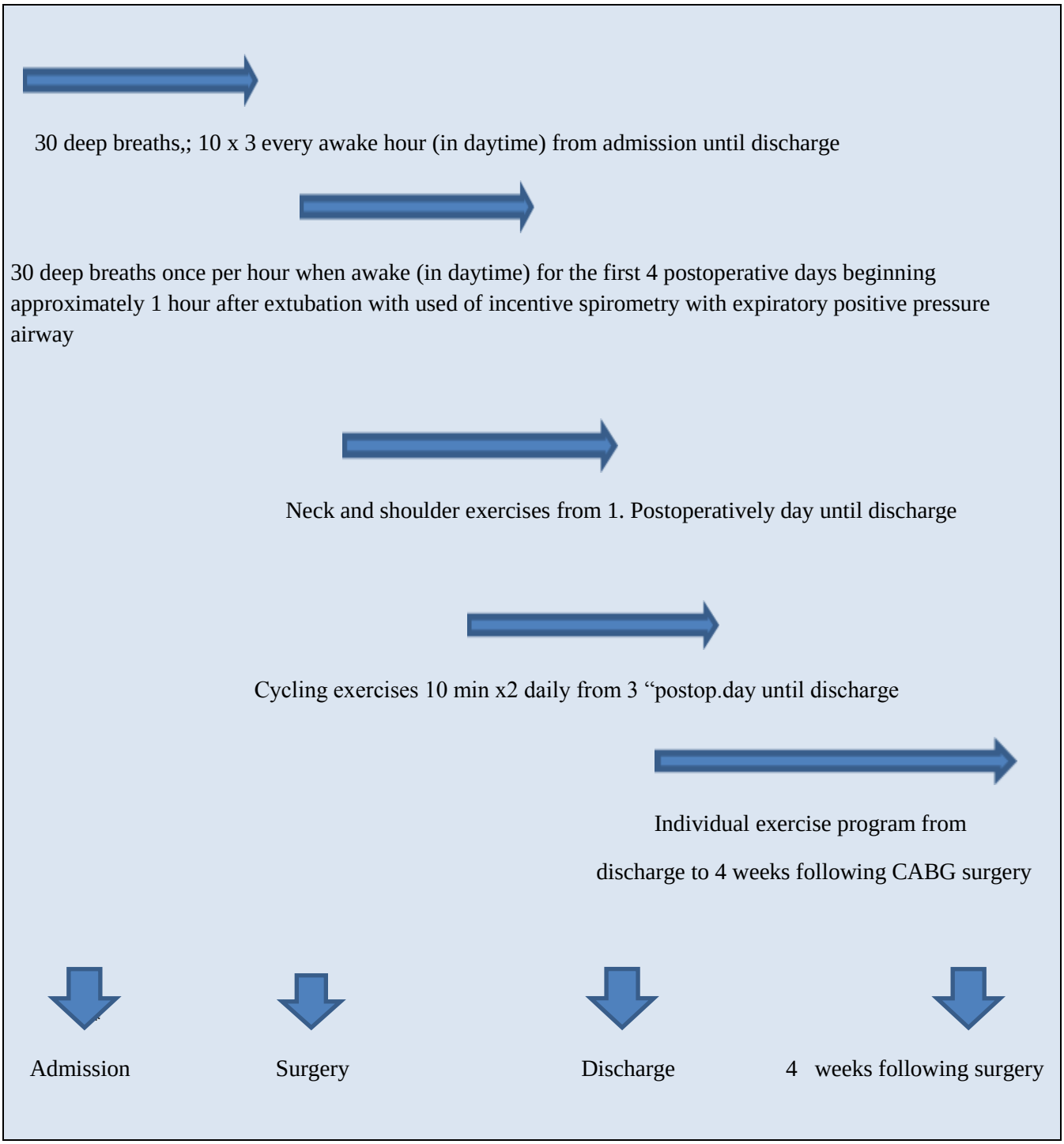
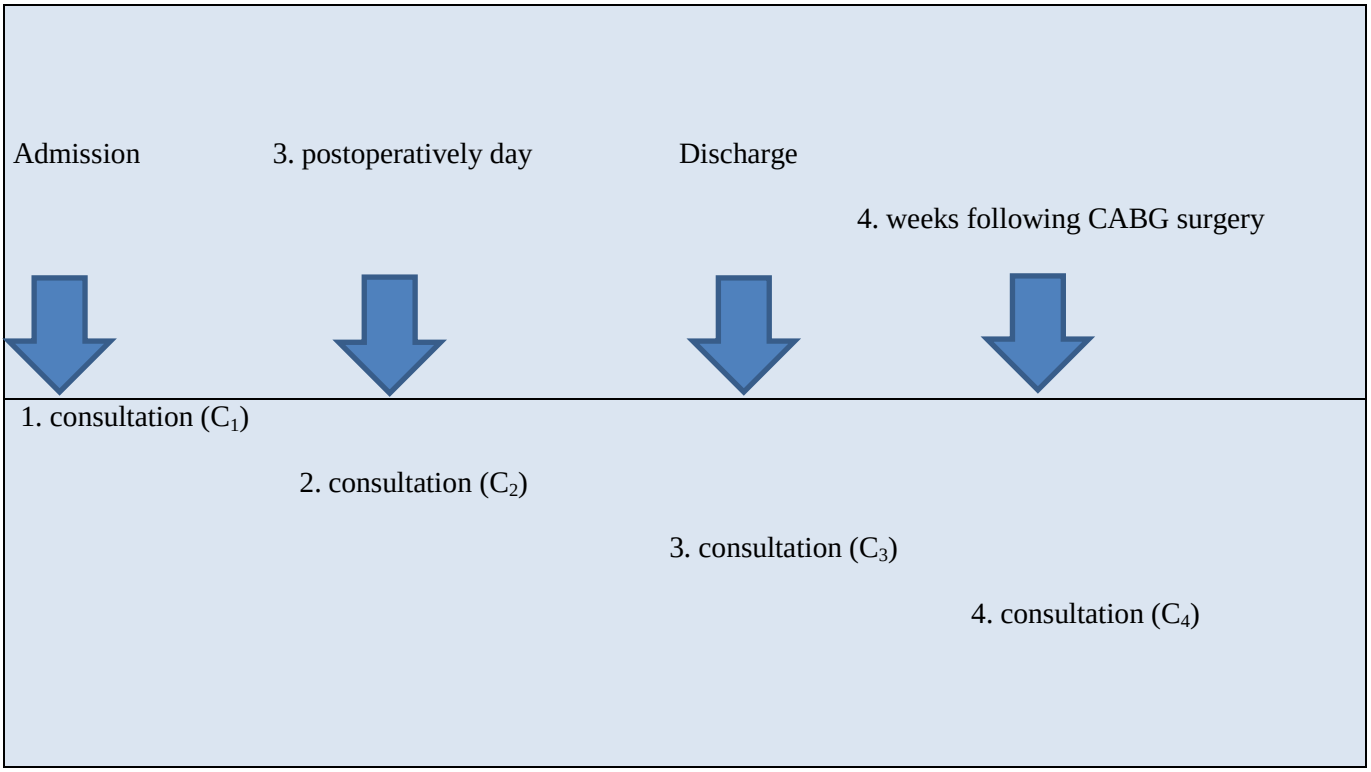

30 deep breaths,; 10 x 3 every awake hour (in daytime) from admission until discharge
30 deep breaths once per hour when awake (in daytime) for the first 4 postoperative days beginning approximately 1 hour after extubation with used of incentive spirometry with expiratory positive pressure airway
Neck and shoulder exercises from 1. Postoperatively day until discharge
Cycling exercises 10 min x2 daily from 3 “postop.day until discharge
Individual exercise program from
discharge to 4 weeks following CABG surgery
Admission
Surgery
Discharge
4 weeks following surgery

Figure 2a. Time line psycho-educative consultations.



4.0 Selection and withdrawal of participants

4.1 Screening and selection

Participants will be identifited consecutively from the waiting list for patients undergoing electiv CABG. Patients who have to undergo CABG will receive approximately one-two weeks before surgery a letter that informs on surgery date and time by mail. The envelope consist furthermore a booklet with general information about heart surgery and the hospitalisation time and written information about the SheppHeartCABG pilot trial. Patients, who on admission day are being transferred from a Cardiological department in another hospital, will receive written information about the SheppHeartCABG pilot trial, when they arrive at the surgical ward. Patients, who are not admitted to in the surgical ward, but are in the Cardiological department at Rigshopsitalet until surgery, will receive written information there.

Patients receive both verbal and written information about SheppheartCABG on the admission day. Patients are informed of their right to take the time to consider a possible participation in the pilot trial. If the patient, after receiving both verbal and written information decides to participate in the

SheppHeart$_{CABG}$ pilot trial, an informed consent form will be signed. If patients are suited and want to participate they will be randomised to either: 1) an exercise component intervention and usual care, or 2) a psycho-educative component intervention and usual care, or 3) these two interventions combined or 4) usual care.

See section 9.1 for further details on screening and identification of participants

4.1 Inclusion criteria

- 18 years or older.
- Persons with ischaemic heart disease referred to elective CABG.
- Speaks and understands Danish.
- Provide written informed consent.

4.2 Exclusion criteria

- Patients at intermediate or high risk according to their cardiovascular status
- Patients with illness limiting the ability to exercise.
- Patients without permanent residence.

4.3 Discontinuation and withdrawal

Participants in the pilot trial can freely withdraw their informed consent at any time and be treated according to the department's standard procedures. Patients will be excluded from the pilot trial if they withdraw their consent and will be informed that withdrawal from the trial will not affect their future treatment. If possible, the reason for withdrawal will be obtained and reported. The patient will be asked to specify what aspects of the pilot trial he/she wishes to withdraw his/her consent from: participation in follow-up examinations, testing, and inclusion of personal data (including survival data) in a database or a register. The patient is not obligated to give reasons for withdrawal.

Pilot trial participants are free to withdraw their informed consent at any time and be treated according to the departments' standard treatment procedures. A patient will be withdrawn from the pilot trial if the participant withdraws his consent and will, in connection therewith, be made aware that termination of the trial will have no implications for his future treatment. Patients who leave the pilot trial will be politely asked for permission to continue to collect data and to use already collected data. If the patient gives permission, he/she will be included in the final analysis. Only if the patient refuses the use of already collected data, all data relating to him/her, will be destroyed.

Discontinuation of the intervention will take place if life threatening arrhythmias or other serious conditions should occur during physical exercise or test of work capacity. The reason for discontinuation of the experimental intervention will be obtained and reported. The discontinued patient will politely be asked for permission to use the data collected before discontinuation, to continue the collection of data relating to the primary effect measure and to later registry and survey based follow-up. On the patient's permission he/she will be included in the final analyses. If permission is not granted all data relating to that particular patient will be destroyed.

5.0 Selection and trial sites and personnel

5.1 Trial sites and setting

SheppHeartCABG will be carried out in Department of Cardiothoracic Surgery at Copenhagen University Hospital, Rigshospitalet. The pilot trial sites will be: the three heart surgery wards and intensive care unit.

5.2 Trial personnel

The pilot trial personnel in SheppHeartCABG are: nurses, physiotherapists and surgeons. Primary responsible physician Daniel Steinbrüchel and Selina Kikkenborg Berg are principal investigators. A physiotherapist with specific knowledge of cardiac rehabilitation initiates the phycial exercise programme. A nurse taught and trained in the psycho-educative conversation and mindfulness will prefere the psycho-educative consultations.

6.0 Trial intervention

This pilot trial will consist of three interventions groups and a usual care group. The three intervention groups consist of; 1) exercise training component alone, 2) psycho-educational component alone and 3) these two combined.

6.1 Physical exercise

The goal of physical exercise is to achieve an improvement in the patients physical work capacity, reduce postoperative atelectasis and to eliminate the fear and uncertainty the patient may feel in relation to physical activity. The physical exercise interventions are based on public health recommendations for physical activity for adults. Furthermore, the interventions are supported by European recommendations for physical training in cardiac patients (59, 85, 90). The physical exercises are divided into three parts; cycling, pulmonary exercises and shoulder / neck exercises. A physiotherapist with specific knowledge of phase 1 and phase 2 comprehensive cardiac rehabilitation after CABG will initiates all physical exercises.

6.1.1 Pre-operative breathing exercise

Participants are encouraged to by the physiotherapist to perform deep breathing exercises consisting of 30 deep breaths one per hour when awake (from pm. 08:00 pm. 22.00) in the period from admission to 4 weeks following surgery (91).

See section 14.1.3 for further details on preoperative breathing exercise.

6.1.2 Postoperative physical exercise

Many factors can contribute to a drop of the exercise capacity early after cardiac surgery compared to the preoperative level (92). Physical exercises for CABG-patients in the first period after surgery must be gentle because of the median sternotomy. Nonetheless exercise training can be started in the postoperative phase 1 (59), but with attention on not making quirky twist and pull movements with chest muscles. This has been extensively described in the ACSM´s Guidelines for Exercise Testing and Prescription (93) . Upper-body training can begin when the chest is stable, i.e., usually after 6 weeks.

Participants will be exercising with an upper with limit ≤ 120 beats pr. minute. This corresponds with a rating of perceived extension scale (RPE) to ≤ 13 on a scale of 6-20 (94) as recommended in guidelines for exercise testing and prescription (93). Recent studies in heart patients showed a good safety profile when exercising up to 80% of maximum capacity (95). Participants are encouraged to exercise moderately, but not exhausting for maximum and safe training effect until 6-8 weeks after surgical procedure (96).

To achieve cardiovascular adjustment the training begins with a warming-up period and ends with a cool-down period, with a gradual downward adjustment of exercise intensity and heart rate, rather than an abrupt end (59). This warm-up phase is a transitional phase that allows the body to adjust to changing physiologic, biomechanical and bioenergetic demands placed on it during the conditioning phase of the exercise session (93). Warming up also improves range of motion and may reduce the risk of injury (97).

6.1.2.1 Cycling exercise

Walking is a frequently employed exercise method in phase 1 cardiac rehabilitation after CABG surgery. An alternative exercise to walking is cycling exercise. Hirschhorn et al. stipulated that stationary cycling with moderate intensity is effective in the restoration of functional exercises

capacity in phase 1 cardiac rehabilitation (65). Cycling can be done whiteout making quirky twist and pull movements in the chest muscles.

The rating of perceived exertion scales Borg RPE Scale® is used to measure the exercise intensity (how hard). In addition the Borg score is a quantitative indicator of perceived exertion with a high degree of reproducibility and closely correlates to heart rate and oxygen consumption during exercises The cycling exercise intensity at Borg RPE Scale® is ≤ 13 on a scale of 6-20 (94). The cycling exercise consists of minimum 10 minutes stationary cycling - alternatively a bed bike - supervised by physiotherapist with a warming-up before and a cool-down period. The cycling exercise will begin the third post-operative day and end on day of discharge with two sessions daily, in the morning and in the afternoon.

See section 14.1.1 for further details on cycling exercise.

6.1.2.2 Pulmonary exercises

Pulmonary function is an important factor with influence on the physical ability. Pulmonary function decreases after open heart surgery (98-101). The surgical procedures and the risk factors involved, such as the median sternotomy, cardiopulmonary bypass, and thoracic manipulation makes change in pulmonary function.

Non-invasive positive pressure has been demonstrated to be an important adjunct to improve gas exchanges and reduce breathing work (102, 103). Improvement of gas exchange in patients who received positive airway pressure (CPAP) application has been observed (104). Voluntary deep-breathing exercise performed with a positive expiratory pressure of 10cm H_2O seems to reduce atelectasis which is commonly seen after cardiac surgery (63).

In the first postoperative days after CABG, there is a reduction in respiratory muscle strength evidenced by the decrease in maximum and expiratory pressures because of the surgery. The use of effective muscle training, performed as three set of ten repetitions, is effective for CABG patients in the immediate postoperatively period for recovery of: maximal inspiratory pressure, maximal expiratory pressure, tidal volume and peak expiratory flow (105). Participants are encouraged to perform breathing exercises consisting of 30 deep breaths once per hour when awake (from pm. 08:00 pm. 22.00) for the first 4 postoperative days beginning approximately 1 hour after extubation. The intervention begins early after extubation therefore it is continuously positive airway pressure

(CPAP) until the patient can cooperate to use a positive expiratory pressure device. There will be an instruction by a physiotherapist at admission day.

See section 14.1.3 for further details on breathing and pulmonary exercises

6.1.2.3 Neck/shoulder exercise

Patients who have undergone CABG have a median sternotomy. They report aching muscles around scapula and a different use of the neck muscles compared to normal. With coughing the patient takes his arm around the chest and supports the sternum while airway clearance. Respiratory muscles stretch gymnastics was originally developed to patient with chronic chronic obstructive pulmonary disease. Respiratory muscles stretch gymnastics can be useful in alleviating muscles aches around the scapula (106).

Neck/shoulder exercises which consist of respiratory muscles strech gymnastics begin on the first postoperative day in sitting and lying position in the patients' room at the ward and continue until discharge. The physiotherapist will introduce the patient pre-operatively in respiratory muscle stretch gymnastics exercises. Participants will perform respiratory muscles stretch gymnastics three times a day; morning, noon and before bedtime.

See section 14.1.2 for further details on breathing and pulmonary exercises

6.1.3 Physical exercise from discharge to phase 2 cardiac rehabilitation

At discharge, together with the patient, the physiotherapist make time plans and prepare an individualised physical exercise protocol, taking into account the patient's clinical condition and physical abilities. This exercise protocol will spread over the period from discharge until phase 2 cardiac rehabilitation begins 6-8 weeks following surgery. The physiotherapist will introduce the exercises so that the patient can perform the exercises sessions independently at home.

The participant must do 30 minutes of daily moderate activity (59). The activity has to be moderate and lie beyond ordinary short-term activities of daily living e.g. walking, gardening. If the 30 minutes is divided, the activity lasts at least 10 minutes. Exercise should be performed at least 3 day a week and for patients with limited exercises capacity it is better to prescribed multiple short sessions (1-10 min) every day in the beginning after discharge.

Sessions are structured with warm up and cool-down activities of 5-10 minutes, including static stretching in light intensity ≤ 10 RPE Borg, aerobic activities will be a component of each exercise

session and precede and follow the conditioning phase. In the beginning the aerobic conditioning phase exercise will initially take about 5-10 minutes, and will gradual increase 1-5 minutes per session per week. The goal for the duration of the aerobic conditionering phase is generally 20-35 minutes per session with intensity RPE Borg of 10-15 (93). Even low-intensity exercises can significantly reduce the physical, social emotional effects of cardiac surgery (107, 108).

See section 14.1.4 for further details on physical exercises after discharge.

6.2 Psycho-education

The goal of the psycho-educative intervention is that the patient learns to interpret and react to relevant physical and psychological symptoms, learn to cope with anxiety and fear, including strategies to manage depressive symptoms and ability to reach out socially.

A trained nurse is responsible for the psycho-educative intervention. The intervention is built on a theoretical basis of the patient-centred approach where the emphasis is on support and education. The conversations are based on a holistic view of the patient and focus on the handling of life and management of heart disease and on having undergone cardiac artery bypass grafting. The intervention is targeted at the modifiable parameters that are reported in patient who undergo cardiac artery bypass grafting. The psycho-educative intervention is divided into two parts; one inspired by RR Parse 'Human Becoming Practice Methodologies' three dimensions (109) and the other is a body scan program as a part of the mindfulness-based stress reduction program (110).

6.2.1 Human Becoming Practice Methodologies´ three dimensions

RR Parse 'Human Becoming Practice Methodologies' three dimensions can be described as: 1. Discuss and give meaning to the past, present and future, 2. Explore and discuss events and opportunities, and 3. Pursuing imagined possibilities. According to this theory there are three ways to alter health: Creative images, see, hear and feel how a situation could be if it was lived in a different way, recognizing personal patterns and value priorities and shed light on the paradoxes by looking at incongruence in a situation and change the view of reality. The nurse is 'truly present' in the process through discussion, silent immersion and reflection. The psycho-educative intervention plus physical exercise was tested in the COPE-ICD trial, with positive effects on psychological well-being (mental health) and general health sub-scale of the SF-36 (89). The theoretical underpinning of the intervention forms the basis for understanding the processes of practice methodology and specific knowledge about heart disease and related symptoms. The supervisor observes and provides feedback in relation to the conversation's methods and goals. The emphasis

on openness in the interviews, and on the nurse's ability to be silently present, while the patient talks, ask questions that encourage reflection, let the patient find answers and solutions and to contribute with knowledge, advice and guidance when demanded and relevant. The training of the nurse takes place prior to the intervention. In practice the intervention will be handled by one nurse with several years' experience in working with patients undergoing coronary artery bypass grafting.

6.2.2 Mindfulness-bases stress reduction

Mindfulness-based stress reduction has been found effective in reducing anxiety accompanying cardiovascular disease (73-75, 110). The most well documented and standardised mindfulness interventions such as Mindfulness-Based Stress Reduction are delivered in the form of a course comprising 8-12 weekly 2-3 hour group meetings, introducing a range of mindfulness practices that participants can continue on their own when the course is completed. However, in many clinical applications, mindfulness programs have been modified and adapted to special needs, situations and resources – for instance, by delivering the mindfulness training in shorter, one-to-one sessions distributed over a shorter time interval, by relying more on audio recorded instructions, and by reducing the number of different mindfulness exercises taught. Such condensed and adapted versions have been shown to have positive short-term effects in several cases. They may be less helpful in establishing an ongoing home practice and long-term effects (a full Mindfulness-based stress reduction course as part of a rehabilitation program may be found to be relevant at a later stage) but with the present pilot trial focus on effective support during the critical period of hospitalisation and surgery recovery, we have formulated a brief mindfulness intervention in cooperation with the Center for Research in Existence and Society, University of Copenhagen. Participants will be encouraged to experiment with the incorporation of the meditation exercises in their daily lives (74).

6.2.3 Consultation

The nurse will conduct consultations with patients individually, and patients are informed that they are welcome to invite spouses/relatives. The consultation will take place in a quiet room and last for about 45-60 minutes. An inspirational guide will form the basis for the consultations. There will be four consultations; admission (C_1), third post-operative day (C_2), day of discharge (C_3) and 4 weeks after discharge (C_4). In the period from discharge and to phase 2 rehabilitation begins, the participants will be given a phone number to the project nurse, who can be contacted in a period on

working days and the project nurse has the opportunity to contact or consult a physician if necessary.

Figure 3. Interview guide psycho-education consultation

A short introduction to the conversations form
A brief medical history
Actual thoughts and questions
Physical and psychical inconvenience as: nausea, pain, anxiety, depression, sleep, fatigue
Family and relationship
Work situation

7. 0 Outcomes

7.1 Efficacy variables

As the interventions either consists of a psycho-educative, physical component or both in combination following explorative outcomes measures has been chosen.

7.1.1 Explorative outcomes

- Physical capacity measured by peak VO2 max using a standardized protocol in accordance with guidelines at discharge and 4 weeks following surgery (90, 111, 112).
- Mental and physical health as measured by the Medical Outcome Study Short Form 36 (SF-36) at admission, at discharge and 4 weeks following surgery (113-116).
- Hospital Anxiety and Depression Scale (117), HeartQoL (118), MFI-20 (119, 120) , B-IPQ (121), EQ-5D (122), IPAQ (123), PSQI (124)., ÖMPSQ (125, 126)

See table 1 for assessment points.

8.0 Safety

8.1 Adverse events and reactions. Definitions.

Adverse event (AE): any undesirable medical event occurring to participant during a clinical trial, which does not necessarily have a causal relationship with the intervention.

Adverse reaction (AR): any undesirable and unintended medical response related to the intervention occurring to participant during a clinical trial.

Serious adverse event (SAE): any adverse event that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect.

Serious adverse reaction (SAR): any adverse reaction that is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect.

Suspected unexpected serious adverse reaction (SUSAR): any suspected adverse reaction which is both serious and unexpected (the nature or severity of which is not consistent with the information available to date) (International Conference on Harmonisation for International conference on harmonisation of technical requirements for registration of pharmaceuticals for human use, 1996).

8.2 Assessment of safety

8.2.1 Psycho educational consultations

There is, as far as we know, no previously risk associated to nursing consultations. If the nurse during the consultations identifies a need for further consultations with professionals, she will encourage the participant to seek help from general practitioner, psychologist or in their usual outpatient setting.

8.2.2 Physical exercise training and testing

Risks associated to exercise training (cycling) and testing is sudden cardiac death associated to ventricular arrhythmias, acute myocardial infarction, and in patients with chronic heart failure, pulmonary edema and deterioration in left ventricular function (127). The last is only found in one study from 1988 (128) and has not subsequently been demonstrated in larger study (6). In a French study of approximately 25.000 patients with ischaemic heart disease, one third having undergone cardiac artery bypass grafting found the risk of cardiac complications at 1:8500 exercise testing and 1:50.000 patient exercise hours (129). Twenty severe cardiac events were reported. 5 were related to exercise testing and 15 were related to exercise training (130, 131). Increasing exercise intensity and age are indicators for risk. Therefore the training intensity will be conducted as moderate to high intensity (less than 80% of VO2 max).

To achieve cardiovascular adjustment the training begins with a warming-up period and ends with a cool-down period, with a gradual downward adjustment of exercise intensity and heart rate, rather than an abrupt end. This cardiovascular adjustment has been shown to reduce the risk of ischemia

and arrhythmia in connection with physical exercise (132, 133). Participants must mainly exercise in an upright position to decrease left ventricular filling pressure and risk of ischemia or heart failure triggered ventricular arrhythmias. When these precautions are respected, both exercise training and exercise testing are considered to possess a low risk for the participants.

Walking exercises is normally the form of exercise which is applied in the early postoperatively period after CABG surgery. Despite early report of the safe use of stationary cycling after CABG stationary cycling is neither recommended in the guidelines, nor customarily selected as mode of exercise in the early postoperatively period during CABG (134). A randomised controlled trial concluded that stationary cycling as a well-tolerated alternative to walking in the early postoperatively period after CABG (65).

Median sternotomy is usually performed as part of CABG and it is commonly performed to secure the sternum during the early postoperatively period (135). Sternal bone healing to attain adequate sternal stability is usually achieved by eight weeks. Therefore upper body movements that exert tension on the sternal wound are avoided during the early postoperatively period.

Pain in neck and shoulder are common after CABG and using respiratory muscle stretch gymnastics a significantly reduced pain around both scapula was showed (p=0.049) (106). Atelectasis is commonly seen after cardiac surgery as a consequence of the surgical procedure. It is demonstrated that pre-operative inspiratory muscle strength is able to prevent pulmonary complications in high-risk CABG patients (odds ratio [OR], 052; 95 % con-fidence interval [CI), 0.30-0.92) and the maintenance of expiratory muscle strength after heart surgery is important in preventing postoperative morbidity (136).

8.3 Assessment and reporting

The pilot trial will be conducted according to the Act. No. 593 of June 14 2011 on Act on Research Ethics Review of Health Research Projects. The investigator will immediately notify the regional ethics committee if there, within the interventions period, occur SAEs, SARs or SUSARs. The report will be accompanied by comments on possible implications for the trial, and notification will be made within 7 days after the investigator has knowledge of the event. In case of serious adverse reactions, which are results of the project, the investigator will provide the regional ethics committee with the information required. Throughout the pilot trial, annual reports including all expected or unexpected adverse events or reactions will be submitted to the ethical committee. Reports will be accompanied by an assessment of the participants` safety. The investigator notifies

the committee within 90 days of completion of the pilot trial. The pilot trial is considered to be finished when the last trial participant has finished the last follow-up assessment. All reporting will be performed on predefined sheets.

8.4 Severity of adverse event

The following variables will be registered when an adverse event happens: Description of the event, beginning and ending of the event, seriousness (mild, moderate, serious), possible causal relation to the intervention and actions taken. This will be registered by a project employee and a physician will be involved if a serious event occurs or if it is required in relation to a moderate adverse event.

9.0 Procedures, assessments and data collection

9.1 Inclusion procedure

Participants in SheppHeartCABG are a patient with ischemic heart disease which have been referred to CABG and speak and understands Danish. The participants have to provide written informed consent. Patients who are at intermediate or high risk according to their cardiovascular status or have illness limiting the ability to exercise will be excluded to participate in SheppheartCABG. As well as patients without permanent residence and no informed consent are excluded.

9.1.1 Screening

Patients will wait to undergo CABG surgery either at home or in a Cardiological department. Patient will be identified and screened consecutively from the current elective CABG waiting list. From the patient record a description of physical capacity will be retrieved. Patients with heart failure similar to The New York Heart Association (NYHA) group I-III and without physical illness which prevents physical exercise are possible participants in the SheppheartCABG pilot trial.

9.1.2 Procedures for informed consent

The participant information including the paper" Trial rights of the individual in a health science research" and copy of brochure "Before you decide" from the Danish Ethic Committee is being send to the patient one-two weeks before surgery together with the letter that informs on surgery date and time and a booklet containing general information about heart surgery and the hospitalisation time. When the consent to take part in verbal information has been given the investigator will encourage the patient to bring relatives at the conversation. The time for verbal information will be planned so it is possible for relative to participate.

This gives the patient and his/her relatives opportunities to read the material in advance and to prepare possible questions. Patients who are transferred from a Cardiological department receive these information papers at admission day. Patients who are at the Cardiological department at Rigshospitalet receive information papers the day before surgery. This group of patients will be given time with their relatives to read the material in advance and to prepare potential questions.

In a secluded and undisturbed room the patient will on the day of admission receive verbal information about SheppheartCABG. In addition, any questions about the written information will be answered. After this the patient will be given time to consider participation in SheppHeartCABG.

If patients accept to participant in SheppHeartCABG they will sign an inform consent.The original consent form will be stored in the investigator site file (ISF) and a copy provided to the patient. All pilot trial participants are informed that all personal information is confidential. Participants will be informed that they have access to personal documents and records according to current legislation. All pilot trial participants are informed that participation is voluntary and that they have the right to withdraw from the pilot trial without explanation and without consequences for their future treatment. If a pilot trial participant is excluded from the pilot trial, either on the basis of the participant's own choice or the treating physician's judgment, the participant will be asked for permission to use already collected data.

9.2. Data collection

Table 1. Data collection.

Demographic and clinical baseline information at inclusion
Age, marital status, occupational status, educational level, gender, height, weight, and nutrional status
Type of heath disease, NYHA-classification, EF, diabetes mellitus, dyslipidemia, smoking, medication, level of activity, number af grafts,

	Baseline inclusion/ admission	**Discharge**	**4 weeks following surgery**
Functional capacity			
Cardiopulmonary exercise testing includes exercise testing by VO_2peak, 6 minutes' walk test, sit and stand test and spirometry.		x	x
Questionnaires			
SF-36	x	x	x
Heart Qol	x		x
HADS	x	x	x
MFI-20	x		x
IPAQ	x		x
B-IPQ	x	x	x
EQ-5D	x		
PSQI	x		X
ÖMPSQ	x	x	X
Blood samples			
Haemoglobin, Sodium, Potassium, Creatinine, Urea, Glukose, Blinded	X		x

LDL-C, Blinded Triglyceriedes cholesterol,			

9.2.3 Demographic variables and clinical characteristics

Demographic variables and clinical characteristics will be collected from patients and from patient records. *See table 1 Data collection.* Data will be registrated by pilot trial staff when informed consent is obtained from the participant.

9.2.4 Questionnaires

The questionnaires in the pilot trial will be completed electronically in the questionnaire system Enalyzer with 'single user', which meets the data legislation for logging. At inclusion, the pilot trial participant will receive an email with a link to a website through which questionnaires can be completed. The e-mail contains a login and password for the trial participant's personal access. The participant has the opportunity to go through the website www.sheppheart.org and login with the log-in and password. If patients do not complete the questionnaire electronically, the material can be sent in paper form and independent trial personnel then enters the responses into the database. The questionnaires will be completed by trial participants at baseline and after the intervention.

9.2.4.1 The MOS 36 Item Short Form Health Survey

The MOS 36 Item Short Form Health Survey (SF-36) is a measure of self-rated health. It uses 36 items to measure 8 components: physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. Scores are calculated for each component and aggregated into two summary scores, a mental component score and a physical component score. Factor analytic studies have confirmed physical and mental health factors that account for 80% to 85% of the reliable variance in the eight scales. Scores range from 0 to 100; higher scores indicate better perceived health (113, 137). With rare exceptions, published reliability statistics have exceeded the minimum standard of Cronbach's alpha 0.70 recommended for measures used in group comparisons in more than 25 studies (113) and most have exceeded 0.80.(138). Reliability estimates for physical and mental summary scores usually exceed 0.90 (139, 140). Experience to date from nearly 400 randomised clinical trials demonstrate that the SF-36 is

very useful for descriptive purposes such as documenting differences between groups or over time and for estimating the relative burden of different medical conditions.

9.2.4 .2 The Hospital Anxiety and depression Scale

The Hospital Anxiety and depression Scale is a 14-item questionnaire that assesses levels of depression and anxiety in medically ill patients. The scale consists of seven questions to assess anxiety and seven questions to assess depression and offers two scores. For each of the questions the respondent chooses from four responses to indicate the frequency/extent to which each applies for the last week. The Hospital Anxiety and depression Scale is a valid and internally consistent measure, with a mean Chronbach's alpha of 0.83 and 0.82 for The Hospital Anxiety and depression Scale-A and The Hospital Anxiety and depression Scale-D respectively (141). Scores of 0 to 7 for either subscale are regarded as normal; 8 to 10 suggests the presence of a mood disorder, and 11 and above suggests probable presence of a mood disorder (142).

9.2.4.3 The HeartQoL questionnaire measures health-related quality of life

The HeartQoL questionnaire measures health-related quality of life in patients with ischemic heart disease, specifically angina, myocardial infarction or ischemic heart failure. The questionnaire consists of 14 items and provides two subscales; a 10-item physical subscale and a 4-item emotional subscale which are scored from 0 (poor The HeartQoL questionnaire measures health-related quality of life) to 3 (The HeartQoL questionnaire measures health-related quality of life better). A global score is available if needed. Asks patients to remember how their heart condition has bothered them in the past four weeks (143). The HeartQoL questionnaire measures health-related quality of life allows clinicians and researchers to (a) assess baseline The HeartQoL questionnaire measures health-related quality of life , (b) make between-diagnosis comparisons of The HeartQoL questionnaire measures health-related quality of life and (c) evaluate changes in The HeartQoL questionnaire measures health-related quality of life in patients undergoing interventions to improve patient HRQL (144). The questionnaire has proven to be a reliable instrument with a Cronbach's alpha between 0.80-0.91 for the global score and each subscale and to be responsive in patients with a wide spectrum of diagnoses (118, 143, 144).

9.2.4.4 EQ-5D

The EQ-5D is a standardised instrument for use as a measure of current health status that provides a simple descriptive profile and a single index value that can be used in clinical and economic evaluation of health care and in population health surveys. The questionnaire covers five

dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The questionnaire consists of a descriptive system produced in a standard layout that enables the respondent to classify his/her health according to the five dimensions and a Visual Analogue Scale that enables the respondent to provide a self-rating of his/her own health (145). In the version of the questionnaire used in this study each dimension is divided into five levels: no problems, some problems, moderate problems, big problems or extreme problems.

9.2.4.5 The Measurement of Fatigue Instrument

The Measurement of Fatigue Instrument is a 20 item self-report instrument designed to measure fatigue. It covers the following dimensions: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation and Reduced Activity (146) . Each item is a statement and the respondent has to indicate to what extent the statement is true using a five level scale. Higher scores indicate a higher degree of fatigue (120). To be sensitive to changes the instruction refers to "the previous days". A confirmatory factor analysis has confirmed that the questions actually described five dimensions Chronbach's alpha was high (mean 0.84). Comparisons between the different groups showed the expected differences (147).

9.2.4.6 The International Physical Activity Questionnaire

The International Physical Activity Questionnaire was developed to measure health-related physical activity in populations. The questionnaire covers four domains of physical activity: work-related, transportation, housework/gardening and leisure-time. The questionnaire also includes questions about time spent sitting as an indicator of sedentary behaviour and refers to the past seven days. In each of the four domains the number of days per week and time per day spent in both moderate and vigorous activity is recorded (123). Practical examples of culturally relevant activities of moderate and vigorous intensity are given.

9.2.4.6 The Brief Illness perception Questionnaire

The Measurement of Fatigue Instrument is a short questionnaire that assesses cognitive and emotional representations of illness on the basis of eight items. The eight items each represent a dimension of the respondent's perception of their own illness. Five items assesses cognitive representations of illness: Consequences, timeline, personal control, treatment control and identity. Two items assesses emotional representations of illness: concern and emotions. The last item assesses illness comprehensibility. The Measurement of Fatigue Instrument has a good test-retest

reliability and concurrent validity and has shown good predictive validity among patients recovering from myocardial infraction (121).

9.2.4.7 The Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index is a self-rated questionnaire which assesses quality and disturbances over 1-month time interval. Nineteen individual items generate seven "component" scores; subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. The sum of scores for these seven components yields one global score. The Cronbach´s alpha of 0.83 obtained for The Pittsburgh Sleep Quality Index components indicates a high degree of internal homogeneity. The Pittsburgh Sleep Quality Index is useful in studying the relation between sleep quality and other variables, such as age, gender and health status (148).

9.2.4.8 The Örebro Musculoskeletal Screening Questionnaire

The original Örebro Musculoskeletal Pain Questionnaire was developed to identify patents at risk of developing persistent back pain problems. In the Örebro Musculoskeletal Screening Questionnaire the questions are formulated such that all musculoskeletal pain is addressed instead of only back pain. The Örebro Musculoskeletal Screening Questionnaire have 25 items, covering days of work, anxiety and tension, depression, pain, activities of daily living related to pain, coping, job satisfaction, fear-avoid-ance beliefs, and patients expectations to recover (125, 126)

9.2.5 Cardiopulmonary physical exercise testing

The physical tests performed by a ergometer cycle test with ergospirometry which made simultaneous measurement of oxygen uptake (VO2), heart rate (HR, beats / min), ventilation rate (VE, l / min), ventilation frequency (VF, number / min), respiratory expirationsratio (RER, CO2/O2 in%), blood pressure (DBP, SBP), physical activity level (METS) and gas exchange (VO2 and VCO2) during progressive loading and in the following recovery period. The test is conducted in outpatient visit. Intensity performed as a ramp protocol (load gradually increases) with the initial workload of 25 W and increased by 12.5 W every minute until exhaustion, usually but not always, is where the patient's oxygen uptake reaches steady state despite additional load. The test follows current standards for cardiopulmonary exercise testing (90).

Before beginning of interventions patient will undergo a cardiopulmonary exercise testing. The cardiopulmonary exercise testing gives functional evaluation of cardiac patients and it is recommended by the exercise Physiology Section of the European Association for Cardiovascular

Prevention and Rehabilitation. The cardiopulmonary exercise testing includes exercise testing by VO2peak, 6 MWT, sit and stand test (30 seconds) and spirometry. The cardiopulmonary exercise test is taking place at discharge and 4 week following surgery. Outcome from physical exercises will be related to VO_2 peak.

10.0 Data handling and record keeping

Individual patient data will be handled as normal data and records will be stored in accordance with Danish Data Protection Agency rules. Anonymous data that is encoded with the individual patient code will be entered into the computerized database KMS and transferred for analysis portal in encrypted mode. This system meets all criteria for the handling of patient data in accordance with the laws on the processing of personal data. All original records are stored at Rigshospitalet for 15 years to allow inspections by competent authorities. Experimental database will be preserved for 15 years and anonymised. After analysis experimental data will be submitted to the Danish Data Archives.

11.0 Statistical plan and data analysis

11.1 Sample size and power

We have no previous information on which we can base our sample size estimation. As the SheppHeartCABG trial is a pilot trial, we will include 60 participants, corresponding to 15 participants in each group (3 interventions: 1 usual). We expect this will be sufficient for obtaining information on the feasibility of a larger confirmatory trial and to give insight in some uncertainties.

11.2 Statistical methods

11.2.1 Significance

Since this is a pilot trial, we will not aim for statistical significant differences. However, we will explore the effect sizes of the interventions, using Cohen's d (REF). Cohen's d will be calculated for all outcome measures, but only for VO_2 max and the Mental Health Component of the SF-36 (both continuous variables) power analysis will be performed to determine the sample size for the larger trials.

11.2.2 Early stopping criteria

Serious adverse events are systematically recorded and reported to the Regional Ethics Committee in the Capital Region. In case of serious adverse events that may yield a safety issue, the trial will be stopped immediately after consultation and report to the regional ethics committee and the responsible physician.

11.2.3 Accountability procedure for missing data/population for analysis

Since this is a pilot trial, the aim is precisely to get insight in uncertainties regarding response rate, drop-out, and missing data. Hence, no specific measures to reduce or account for missing data are taken yet.

12.0 Quality control and quality assurance

To secure the handling of data in the trial an external Data and Security Monitoring Committee will be appointed. They will control the trial according to guidelines for data monitoring committees from European Medicines Agency. The Committee will work under a charter in English for the English speaking members who constitute the Committee.

13.0 Legal and organisational aspects

13.1 Finance and insurance

The idea for the project came from the Heart Centre at Rigshospitalet. The initiators are the project group. The pilot trial will be funded by external funds for research in health sciences. All grants will be payed to the financial office at Rigshospitalet and will be used for salaries for the trial staff. No compensation is given per pilot trial participant and no funding is granted to pilot trial participants or transport expenses. None of the persons responsible for the pilot trial have any financial affiliation with the funds applied for. The participants and the Regional Ethics Committee in the Capital Region will be informed as funding for the trial is achieved. The SheppHeartCABG pilot trial has received a grant from Rigshospitalet, The Heart Centre research foundation on the amount 217.730 kr.

According to the Act on right of appeal and compensation within the National Health Service (Act No. 547 of 24 June 2005) all trial participants are covered by the Patient Assurance Association and will be informed about this prior to inclusion. Sponsors, researchers and trial nurses are covered by the statutory insurance at their respective hospitals.

13.2 Plan for publication, authorship and dissemination

The pilot trial is registered on www.ClinicalTrials.gov before randomisation of patients start. Results of the pilot trial are analysed by an independent statistician, and the results will be interpreted by the steering committee. The conclusion will be prepared in two versions, before the allocation code is broken, with the 2 x 2 trial arms alternately assumed as intervention. Positive, neutral and negative results of the trial will be published. The final manuscripts emanating from the pilot trial will be sent to a ‘peer reviewed’ international journal. Authorship will be allocated using the guidelines for authorship defined by the International Committee of Medical Journal Editors and

depends on the personal involvement. A minimum of one scientific paper are planned based on SheppHeartCABG –Shaping Health in outcomes by exercise training and Psycho-education in Phase 1 for Heart patients. All the articles abstracts as well as the results will be posted on the website www.sheppheart.org .

13.3 Trial timeline

The pilot trial will begin in the middle of August 2013, after approval by the regional ethics committee, with inclusion of the first participants. The trial will end middle of November 2013, the last follow-up in the middle of December 2013, data will be analysis January 2014 and the manuscript will be prepared January – March 2014.

14.0 Appendix

14.1 Physical Exercise protocol

14.1.1 Cycling

Cycling exercise training is conducted in a quiet and shady area of the ward.

Participants will use pulse watches during the cycle training. There will be measured and recorded heart rate and saturation on three scheduled times during exercising. Participants are exercising on stationary cycling with moderate intensity. The subjects are encouraged to train by moderate intensity, but in a way so it is not exhausting for maximum and safe training effect (96).

The rating of perceived exertion scales is used to measure the exercise intensity (how hard). The cycling exercise intensity is at RPE Borg off ≥13 ≤ 15 on a scale of 6-20 (94).

The cycling exercise consists of a stationary cycling session or alternative a bed bike. Time for cycling will be 10 minutes. There will be a warming-up and cool-down period to achieve cardiovascular adjustment with exercise intensity ≤ 10RPE Borg. It has been shown to reduce the risk of ischemia and arrhythmia (132, 133). The subjects to be predominantly work in the upright position to minimize left ventricular filling pressure and the risk of ischemia or heart failure triggered ventricular arrhythmia (132).

The cycling exercise training will be supervised by physiotherapist. The physiotherapist will programme the power on the cycle so it matching RPE Borg off ≥13 ≤ 15 on a scale of 6-20.

The cycling exercise will begin third post-operative day and end on day of discharge. There will be two sessions daily, morning and afternoon.

14.1.2 Neck and shoulder exercises

Respiratory Muscle Stretch Gymnastic (RMSG) is conducted in patients' room at the ward.

RMSG consist of five exercises; body relaxation and four different neck and shoulder exercise developed for use on patients with chronic pulmonary disease (149).

RMSG-1: Whole body relaxation

- Either lying down on a bed or sitting in a chair, contract the muscles of the face, shoulder, back, hands and feet for several seconds. Exhale deeply to relax all the muscles of the body

RMSG- 2: Bending the neck forwards and to both sides

- Raise shoulders for 5 second, the exhale deeply to relax totally
- While pursing the lips, exhale and bend neck to the right to stretch the sternocleidomastoid, and then inhale while bringing neck to original position. Exhale deeply to relax totally
- Repeat above procedure, bending neck to the left.

RMSG-3: Rotating the shoulders, including the pectoralis major and trapezius muscles.

- Gradually rotate shoulders and scapula's forward a few times, the exhale deeply to relax totally.

RMSG-4: Stretching the shoulder girdle and triceps brachii muscle

- Extend arms forward as far as possible, and retain the position for 5 seconds
- While exhaling, return arms to original positions, and relax totally

RMSG- 5: Stretching the triceps brachii and anterior serratus muscles

- While using one hand to protect the wound, place the other hand on opposite shoulder.
- While inhaling, slowly raise elbow vertically to extend the anterior serratus muscle under the armpit
- While exhaling deeply, return arm to original position and relax totally
- Repeat above procedures by changing sides

Pre-operatively the physiotherapists introduce the subjects to respiratory muscle stretch gymnastics. Neck/shoulder exercises begin first postoperatively and contain until discharge. Participants will

perform respiratory muscles stretch gymnastics three times a day; morning, noon and before bedtime.

14.1.3 Breathing and pulmonary exercises

Breathing exercise will take place in the intensive unit care and at patients' room in the ward.

Breathing exercise consist of 30 deep breath once per hour when awake in daytime. Begin at admission and continue until 4 weeks following surgery (63, 91).

Participants are encouraged to perform breathing exercises consisting of 30 deep breaths once per hour when awake in daytime with positive expiratory pressure device. Breathing exercises consist of 3 sessions of 10 breaths with breaks between (63). Because the breathing exercises begin one hour after extubation it can be difficult for the patient to breath sufficiently. Thus, the first treatment is CPAP until the patient is able to breathe through a device with positive expiratory pressure. The nurse/physiotherapist sets the positive expiratory pressure.

Breathing exercise begin approximately 1 hour after extubation until the fourth postoperative days. There will be an instruction by physiotherapist at admission day and repeated after surgery. The physiotherapist will instruct the participant at admission day and by the intensive nurse when the exercise begin.

Breathing exercise will take place in the intensive unit care and at patients' room in the ward.

14.1.4 Physical exercises after discharge

The subject will at discharge receive a physical exercise plan for the period from discharge to the beginning of cardiac rehabilitation phase 2 6-8 weeks following surgery. The physiotherapist will introduce the exercises so the patient can perform the exercises sessions independently at home.

The training will be will be strength training and aerobe training to obtain muscle strength and conditions (150).

Sessions is structured with warm up and cool-down activities of 5 minutes, including static stretching, range of motion and light intensity $\leq$ 10 Borg RPE, aerobic activities will be a component of each exercise session and precede and follow the conditioning phase.

In the beginning the aerobic conditioning phase exercise will initially take about 5-10 minutes, and will gradual increase 1-5 minutes per session and will gradual increase 1-5 minutes per session per

week. The goal for the duration of the aerobic conditionering phase is generally 20-35 minutes per session with intensity RPE Borg of 10-15 (93). Even low-intensity exercises significantly can reduces the physical, social emotional effects of cardiac surgery (107, 108)

The participant must continue with 30 minutes of daily moderate activity. The activity has to be moderate and lie beyond ordinary short-term activities of daily living e.g. walking, gardening. If the 30 minutes is divided, the activity lasts at least 10 minutes.

Exercise should be performed at least 3 day a week and for patients with limited exercises capacity it is better to prescribed multiple short sessions (1-10 min) every day in the beginning after discharge.

Exercise preforming take place at the participants' home.

14.2 Psycho-educative consultations

The psycho-educative intervention is divided into two parts; one inspired by RR Parse 'Human Becoming Practice Methodologies' three dimensions (109) and the other is a mindfulness-based stress reduction program here by a "body scan exercises" (110).

There are five consultations; admission (C_1), third post-operative day (C_2), day of discharge (C_3) and 4 weeks after discharge (C_4). . The consultations take place in a quiet setting in the outpatient clinic and in the ward during hospitalisation and will last approximately 1 hour. 45 minutes for the first part and 15 minutes for the last.

The nurse is able to facilitate contact with or seek advice from a physician if needed.

Parse

Education and information about the disease prepare the patient for excepted symptoms and sensations. Dialogue and shared reflection facilitate strategies for coping with symptoms and experiences associated with the condition for example, anxiety and fear. Cardiac nurse with specific training will perform the psychoeducational intervention,

The consultations focus on managing life after undergoing CABG by establishing a joint approach to disease management and coping strategies using a holistic view. The psychoeducational intervention is inspired by RR Parse 'Human Becoming Practice Methodologies' three dimensions. These a interpreted as

1) Discuss and give meaning to the past, present and future
2) Explore and discuss events and possibilities
3) Move along with envisioned possibilities

According to this theory; there are three ways of changing health; creative imaging, that is to see, hear and feel what a situation might be like if lived in a different way, affirming personal patterns and value priorities and shedding light on paradoxes, that is, looking at the incongruence in a situation and changing the view held of something.
The nurse is truly present in the process though discussions, silent immersion and reflection.

Mindfulness

The core of the mindfulness intervention is the training of a calm open, accepting awareness of the present, the body and the situation, through a system of mediation exercises that are relatively easy to learn.

The brief mindfulness intervention will be focused on the "body scan exercise", an awareness and sequential relaxation practice which is traditionally taught at the beginning of mindfulness programs and which is particularly well suited because it can be performed in a lying position.

A sitting mindfulness exercise will also be introduced, and participants will be able to use the exercises at any time during the day, supported by audio recorded instructions (CD or mp3 player).

14.3 The effect of physical interventions after CABG patients

Author	Year	Population	Type of study	Intervention	Instruments	Results
Freitas et al. (55)	2012	592 partici-pants in seven studies (RCT)	System-atic re-view of seven RCT	Compare the effects of incentive spirometry for preventing postoperative pulmonary complications in	Two reviewers independent-ly evaluated trial quality	No evidence difference between groups in the incidence of any pulmonary complications and functional

				adults undergoing CABG		capacity Needed; powered trial of high methodological rigour to determine if some CABG-patients may derive benefit incentive spirometry
Herdy et al. (59) *Outcomes* Length of ICU stay, days on the ward pneumo-nia.Time until oro-tracheal tube removal, pleural effusion, atelecta-sis, peak flow and change 6-min wal-king di-stance enrol-ment and hospital discharge	2008	Patients waiting at least 5 days for CABG. Interven-tion n= 29. Control group n= 27	RCT	Cardiopulmonary rehabilitation from at least 5 days before CABG until discharge. Program consisted of phase 1 cardiac rehabilitation associated with respiratory physical therapy. Progressed exercise from passive movements to walking and finally to climbing two flights of stairs on the fifth day. Additional	Radiographic reports on admission and 4. postoperatively day. Peak flow measured before surgery and on the day of extubation.	Significant reduction of stay in the ward, markedly reduced in the incidence of pneumonia and AF (relative risk (RR) = 0.2:95% confidence interval [CI] 0.5-0.8). Orotracheal intu-bation shorter in rehabilitation group. Fewer pleural effusions (RR=0.2, 95% CI=0.5-0.8)

				respiratory exercises. Pre- and postoperative cardio-pulmonary rehabilitation Control group: usual care		and atelectasis (RR=0.15, 95% CI=0.03-0.8). Significant reduc-tion in peak flow the day after extu-bation for reha-bilitation group, P <0.05.
Hirschhorn et al,(60) O*utcomes* 6 minu-tes' walk assess-ment, 6 minutes cycle assess-ment and health-related-quality of life – SF 36.	2012	64 patients	RCT	Performed twice daily, moderate-intensity exercise sessions of 10 minutes duration from postoperative day 3 until discharge from hospital. Randomised to stationary cycling or walking exercise intervention groups. 6MWA: 6 minutes walking on a 43.5 m corridor as far as possible while Rating of Perceived Exertion Scales	Preoperative and dis-charge functional exercise capacity and health related quality of life SF-36. Testing on the admission and dis-charge day.	No significant differences between intervention group; 6 min-walk distance p=0.803; 6 min cycle work p=0.798. No significant differences between intervention groups for any aspect of HR-Qol. Moderate-intensity stationary cycling was found effective as moderate

				(RPE) of 3-4 of 10. 6MCA: cycling on an electronically braked cycle ergometer for 6 minutes producing an RPE of 3-4 of 10. Patients completed preoperative and discharge SF-36 while resting between the 6MWA and 6MCA.		intensity walking exercise in the restoration of postoperative functional exercise capacity.
Hirschhorn et al (61) *Outcomes* Sixminu-tes walk distance, vital capacity (VC) and health-related quality of life (as measured by the SF-36 question-naire, rates of indica-tors postope-	2008	RCT	32 patients received standard interven-tion, 31 received walking exercises, 30 patients received walking – breathing exercises.	Standard intervention; preoperative education regarding effects of surgery on long function, body positioning to improve post-operative lung ventilation, huffing/coughing with wound support to facilitate secretion removal.	Six minutes walking assessment, walking/breathing exercises combined with standard program and SF-36v2.	A significant lower 6-minutes' walk distance for the control group compared with the walking exercise group (p=0.005) and the walking/

rative pulmona-ry com-plication.				Walking exercises intervention; Standard preoperative education + education regarding the use of a modified RPE (Borg) scale in relation to twice daily progressive physiotherapy-supervised postoperative walking program. Walking/breathing intervention; Preoperative education as per walking exercises, plus education regarding additional breathing exercises.		breathing group (p=0.022). All sub-scales and physical and mental component summary measures of the SF-36v2 demonstrated significant changes over the period of review. A higher level of burden was noted for all sub-scales, excepting those of "general health" and "mental health" and the MCS at discharge compared with the pre-operatively.
Stein et al. (57) *Outcome*s maximal	2009	Interven-tion n=10	RCT	Intervention 6-day postopera-tive in-hospital program included;	Sub-maximal and maximal functional capacity after	A 6-day program of rehabilitation significantly

inspira-tory and expira-ory pres-sure CABG		Usual care n=10		◦use of expiratory positive airway pressure mask ◦bronchial hygiene techniques ◦progressive distance walking and calisthenics ◦cardiopulmonary training Control group; ◦followed physicians and received routine care assistance not exposed to any speci-fic respire-tory or motor physical intervention.	CABG	attenuated the expected post-operative reduction inspiratory and expiratory muscle strength and improved recovery of functional capacity. Inspiratory muscle strength 30 days after CABG strongly correlated with maximal functional capacity as determined by V_{o2} peak ($p<0.01$). 6- minutes' walk distance was longer 7 days after CABG in intervention ($p<0.05$).
Savci et al (56) *Outcomes* Inspirato-ry	2011	Interven-tion n=22 Control	RCT	Intervention; inspiratory muscle training pre- and	Pulmonary function testing, six minute walk	Significant increasing in inspiratory

muscle strength postoperatively		n=21		postoperatively. Both groups received usual care	test), quality of life and psychosocial parameters	muscle strength in intervention group and decreasing in usual care group ($p<0.05$) and a significantly decreasing in pul-monary function in both group ($p<0.05$).
Westerdahl et al. (58)	2005	Interven-tion=48 Control n=42	Randomi-sed trial (RT)	*Intervention group;* Informed and practiced breathing techniques preoperatively. Started 1 h after extubation perform 30 deep breath once per hour when awake for the first 4 postoperative days in sitting position. It was 3 sets of 10 deep breaths with. -an expiratory resistance of + 10 cm H_2O.	Pulmonary function preoperati-vely and on the fourth postoperative day. Spiral CT on the fourth postoperative day	Intervention group significantly smaller atelectasis area ($p<0.05$) on 4. postoperative day compared to control group.

				Supervised by a physical therapist. *All patients received:* ◦general information about postoperative routines by physical therapist *Control group*: No instruction to any breathing exercises.		

14.4 The effect of psycho social intervention after CABG

Author	Year	Population	Type of study	Intervention	Instruments	Results
McKen-zie et al (62)	2010	257 partici-pants in 46 studies	Systematic review	All studies utilised psychometric assessments. 15 studies just depressive symptoms, 3 symptoms of anxiety exclusively, while 28 studies	The Beck Depression Inventory. The Beck Depression Inventory modified version. The Centre for Epidemio-logical Studies De-	Collective appraisal of the studies indicated that symptoms of depression and anxiety exhibited after CABG surgery are best predicted by preoperative measures The findings indicate a range of preoperative predictors of post-operative depression and

				assessed both.	pression Scale. The State-Trait Anxiety Inventory.	anxiety in CABG. Chief among these are pre-operative depression and anxiety.
Frede-ricks et al (63)	2012	16 studies including 3.783 participants who had CABG and/or valvular replace-ment surgery	Systematic review 10 studies descriptive designs 4 studies quasi-experimental designs 2 studies experimental designs	Purpose: In the presence of anxiety and/or depression, do patients who have had heart surgery engage in self-management behaviours following hospital discharge?		Moderate to severe levels of anxiety and depression exist during the first month of home recovery and appear to have an effect on performance of self-management beha-viours'. Music and relaxation therapy are presented as evidenced based recommen-dations for managing anxiety and depression in patients following heart surgery.
Lie et al. (64)	2007	93 patient	A qualitative mixed method de-sign inte-grating qua-litative and quan-titative approaches	Interview 2 and 4 weeks following surgery	Semistrured inter-view covered experiences of; angina pectoris. discharge medication, sleep pattern, irritability, postopera- tive compli-cations, re-turn to	Two weeks after the patients symptoms and needs were characterised by a substantial amount of uncertainty and worries related to what to expect and what was normal for postoperative pain, assessment and sensation of surgical site, different

					work	experiences with physical activity/exercise, uncertainty about medications, difficulties with sleep pattern, irritability, postoperative complications, uncert-ainty about return to work, and insufficient information at discharge. Four weeks after surgery patients' symptom level was decreased, and they experienced life begin-ning to return back to normal.
Bauer et al. (65)	2010	Intervention n=62 Control n=51	Randomised study	Intervention; massage Control: quiet relaxation	Patients reported measures of pain, anxiety, tension, relaxation, and overall satisfac-tion before and after interventions on days 2 and 4 and also on day 3 (day without an intervention) to identify any potential carry-over effects from day 2 to day 3.	Patients receiving massage therapy had significantly less pain (P <.001), anxiety P <.001), and tension P <.001) on day 2 after the massage compared with before the massage. Similarly, same group also had significantly less pain (P <.001), anxiety (P <.001), and tension (P <.001) after the massage on day 4.

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