Physiotherapy and physical activity in patients undergoing cardiac or lung cancer surgery
Physical Activity
- a medication you need to take daily
Physiotherapy and physical activity in patients undergoing cardiac or lung cancer surgery
Abstract


Cardiovascular diseases are the leading cause of death worldwide. Cardiac surgery is performed to improve prognosis, relieve symptoms and increase functional capacity in patients with cardiac disease. Postoperative pulmonary complications are common after cardiac surgery and a reduced lung function can persist a long time after surgery. A positive association between level of physical activity and lung function has been proposed in both healthy individuals and people with different disabilities. It is not clear if there is an association between level of physical activity and recovery of lung function after cardiac surgery.

Lung cancer is one of the most frequently diagnosed forms of cancer worldwide, and a leading cause of cancer deaths. Surgical resection is the primary approach for curative treatment.

Despite the fact that physical activity has many positive effects on health, patients undergoing lung cancer surgery often report a low level of physical activity. Measuring physical activity is not easy, self-reported physical activity remains the most clinically applicable type of measurement, and a simple and valid questionnaire for screening patients would be valuable.

Patients undergoing lung cancer surgery are often routinely treated by physiotherapists, but this kind of treatment has not been thoroughly investigated.

The purpose of this thesis was to investigate the effect of physiotherapy and physical activity in patients undergoing cardiac or lung cancer surgery.

This thesis include one cohort study of physical activity and recovery of lung function in patients undergoing cardiac surgery, one validation study of two self-reported physical activity instruments in patients undergoing lung cancer surgery, and two randomized controlled trials investigating the effect of physiotherapy for patients undergoing lung cancer surgery.

In study I, patients who remained active or increased their level of physical activity had better recovery of lung function, compared to patients who remained sedentary or reported a lower level of physical activity postoperatively.

In study II, two self-reported physical activity instruments were validated against accelerometer data in patients three and twelve months after lung cancer surgery. Both instruments were found able to identify patients not meeting recommendations on physical activity.

In study III, patients treated by physiotherapists were significantly more active during the first three days after lung cancer surgery, compared to an untreated control group.

In study IV, no between-group differences three months after surgery were found between patients receiving in-hospital physiotherapy compared to an untreated control group. However, the patients in the treatment group reported an increase of physical activity three months after surgery compared to preoperatively, while the patients in the control group did not.

Keywords: Physiotherapy, Physical Activity, Cardiac surgery, Lung Cancer, Randomized Controlled Trial, Thoracic surgery, Physical Function, Lung Function.

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List of papers

This thesis is based on four papers:


Jonsson M, Westerdahl E, Ahlsson A, Hurtig-Wennlöf A. Validation of two self-reported physical activity instruments for patients who have undergone lung cancer surgery. In manuscript.


Abbreviations

6MWT – Six-minute Walk Test
AHA – American Heart Association
AVR – Aortic Valve Repair
BMI – Body Mass Index
CABG – Coronary Artery Bypass Grafting
CI – Confidence Interval
COPD – Chronic Obstructive Pulmonary Disease
FEV1 – Forced Expiratory Volume in one second
FEV% - FEV1 in percent of FVC
FRC – Functional Residual Capacity
FVC – Forced Vital Capacity
IC – Inspiratory Capacity
IPAQ – International Physical Activity Questionnaire
IPAQ-E – International Physical Activity Questionnaire adapted for the Elderly
MET – Metabolic Equivalent
MVPA – Moderate and Vigorous Physical Activity
MVR – Mitral Valve Repair
PA – Physical Activity
PEP – Positive Expiratory Pressure
RCT – Randomized Controlled Trial
TLC – Total Lung Capacity
VATS – Video Assisted Thoracoscopic Surgery
VC – Vital Capacity
WCPT – World Confederation for Physical Therapy
WHO – World Health Organization
Introduction

My career as a physiotherapist started in 2003, and in 2006 I started working at the Department of Cardiothoracic surgery at Örebro University Hospital.

The World Confederation for Physical Therapy (WCPT) has described physiotherapy as a service to maintain or restore movement and functional ability in circumstances where movement and function are threatened by different conditions (1). One important purpose of physiotherapy is to promote health and wellbeing, with emphasis on the importance of physical activity and exercise. As a physiotherapist in the cardiothoracic field, I primarily worked with patients undergoing cardiac or lung cancer surgery. The challenges for physiotherapists at a cardiothoracic surgery department include preventing and treating postoperative pulmonary complications, enhancing postoperative recovery and increasing the level of physical activity.

Shortly after I started working at the cardiothoracic surgery department, I was contacted by Elisabeth Westerdahl, who inquired if I would be interested in participating in a multicenter study she was planning. It sounded interesting and I accepted. During the course of planning and performing the study, I became more and more interested in the field of research, and finally started to work on an application to become a doctoral student, leading to my enrollment at Örebro University in 2012.

I have always been interested in physical activity, and so in the first study I conducted I set out to determine whether there is an association between physical activity and recovery of lung function after cardiac surgery. For my further research, I wanted to evaluate something in the field of cardiothoracic surgery that would be clinically valuable and would increase my own knowledge. As I studied the literature regarding lung surgery patients, I realized that this group of patients had been neglected by research. I decided that the overall aim of my thesis would be to see whether physiotherapy and physical activity could be beneficial for patients undergoing cardiothoracic surgery.

This thesis is representative of my research career, which has involved the field of cardiothoracic surgery, starting with cardiac surgery and proceeding to lung cancer surgery.
Background

Cardiovascular disease

Cardiovascular diseases are a group of disorders of the heart and blood vessels that include coronary heart disease, cerebrovascular disease and congenital heart disease (2). Cardiovascular diseases are the leading causes of death worldwide (2). In Sweden, they are the leading cause of death and one of the most common causes of disability (3).

Behavioral risk factors for cardiovascular disease include unhealthy diet, physical inactivity, tobacco use, and harmful use of alcohol (2). Other risk factors are diabetes, hypertension, high blood lipids, poverty, stress, and hereditary factors (2).

Interventions on a population level that could potentially reduce cardiovascular disease include tobacco control policies, taxation to reduce the consumption of unhealthy foods, improving infrastructure to increase physical activity (such as building walking and cycle paths) and providing healthy school meals to children (2). At the individual level, individual health-care interventions should be provided for those at high risk of developing cardiovascular disease (2).

Secondary prevention of cardiovascular disease includes treatment with medications such as aspirin, beta-blockers, angiotensin-converting enzyme inhibitors and statins (2). There may also be a need for surgical procedures such as balloon angioplasty, heart transplantation, and artificial heart operations, and for the use of medical devices such as pacemakers, prosthetic valves and patches for closing holes in the heart (2). The procedures performed on the patients studied in this thesis are presented in the section “Cardiac surgery.”

Cardiac surgery

Cardiac surgery is performed to improve prognosis, relieve symptoms, prevent ischemic complications, and improve functional capacity (4, 5). There are different types of cardiac surgery. Coronary Artery Bypass Grafting (CABG) is performed in patients with significant stenosis in the left main coronary artery, patients with 3-vessel or 2-vessel disease with significant proximal stenosis of the left anterior descending artery, and patients with single or multi-vessel coronary disease who have a large or moderate area of viable myocardium (4). Aortic valve replacement/repair
(AVR) is performed in patients with symptomatic or severe aortic stenosis or aortic regurgitation, and also in patients with moderate aortic stenosis/regurgitation undergoing CABG or other heart valve surgery (5). Mitral valve repair/replacement (MVR) is performed in patients with symptomatic moderate or severe mitral stenosis or mitral regurgitation) (5), while tricuspid valve repair/replacement is performed in patients with severe tricuspid dysfunction, or in patients with less than severe tricuspid dysfunction undergoing cardiac surgery for other reasons (5). Cardiac surgery is primarily performed via sternotomy, although minimal invasive procedures have become more common recently. The sternotomy can affect postoperative lung function (6). Often the patient is connected to cardiopulmonary bypass, which also affects the lungs (7). It has been shown that CABG significantly reduces the limitations on physical activity in both male and female patients (8).

Postoperative pulmonary complications such as pleural effusion, atelectasis, pneumonia, acute respiratory distress syndrome, and pneumothorax often occur after cardiac surgery (9-19). A reduction of lung function has been shown to persist up to one year after cardiac surgery (20).

Patients undergoing cardiac surgery typically spend the first hours after surgery in an intensive care unit before transferring to a cardiothoracic ward. The length of stay after cardiac surgery has been reported to be around 10 days (21). Pain is common after cardiac surgery and may persist for a long time (22). Pain management during the first postoperative days includes oral and intravenous medication.

**Lung cancer**

Cancer involves the transformation of normal cells into tumor cells in a complex, progressing process (23). Risk factors for cancer include tobacco and alcohol use, unhealthy diet, and physical inactivity (23).

An estimated 1.8 million new lung cancer cases occurred worldwide in 2012, accounting for about 13% of total cancer diagnoses (24). Lung cancer was the most frequently diagnosed cancer and the leading cause of cancer death among males in 2012. Among females, lung cancer was the leading cause of cancer death in more developed countries. In Sweden, some 4000 persons are diagnosed with lung cancer every year, and recently more women than men have received this diagnosis (25).
Known risk factors for lung cancer include smoking and exposure to occupational and environmental carcinogens such as asbestos, arsenic and radon, outdoor pollution, and indoor air pollution from unventilated coal-fueled stoves and cooking fumes (24).

Lung cancer is one of the most preventable cancers. Most lung cancers could be avoided by eliminating the initiation of smoking and increasing smoking cessation among current smokers (24).

**Lung cancer surgery**

Surgical resection, with or without adjuvant chemotherapy is the primary approach for curative treatment of non-small cell lung cancer (26). The surgery can involve either open thoracotomy or video-assisted thoracoscopic surgery (VATS). The most common types of surgery are lobectomy, wedge resection, and pneumonectomy.

One study reported that after lung cancer surgery, 3.6% of patients got pneumonia within 30 days of surgery (27). Factors associated with increased risk of pneumonia were age, previous pneumonia, obesity, alcoholism, and chronic obstructive pulmonary disease (COPD). In the same study, patients undergoing VATS had half the risk compared to patients who underwent open thoracotomy (27). Another study showed that VATS may result in a significant reduction of postoperative pulmonary complications and length of stay (28). Lung cancer surgery has a significant impact on pulmonary function and oxygenation both at two weeks and six months postoperatively, while respiratory muscle strength is not affected (29).

After lung cancer surgery, patients typically spend the first hours in a high-dependency unit before being transferred to a cardiothoracic ward. The length of stay after lung cancer surgery has been reported to be around 7 days (30).

Pain is common after lung cancer surgery. A difference between VATS and thoracotomy has been reported, with VATS resulting in significantly less pain (31). Pain management primarily consists of continuous epidural infusion or locally placed catheters, and supplemental intravenous and oral medications.
Physiotherapy

The WCPT describes physiotherapy as “services provided by physiotherapists to individuals and populations to develop, maintain and restore maximum movement and functional ability throughout the lifespan. The service is provided in circumstances where movement and function are threatened by aging, injury, pain, diseases, disorders, conditions or environmental factors and with the understanding that functional movement is central to what it means to be healthy” (1). The purposes of physiotherapy include promoting health and wellbeing, emphasizing the importance of physical activity and exercise, and preventing impairment due to health and lifestyle factors.

Physiotherapy and cardiac surgery

Physiotherapy is routinely offered during hospitalization to patients undergoing cardiac surgery (32, 33). The in-hospital physiotherapy consists of preoperative information, postoperative mobilization, deep breathing exercises with or without positive expiratory pressure (PEP), coughing with cough assist, range of motion exercises, and postoperative information (32, 33). The aim of the treatment is to prevent or reduce complications such as impaired pulmonary function, impaired thoracic mobility, and pneumonia. Early mobilization after cardiac surgery has been reported to prevent complications, improve functional capacity, and reduce length of stay (34). Deep-breathing exercises have been shown to reduce atelectatic area and improve pulmonary function four days after cardiac surgery (14).

Patient mobility is restricted postoperatively. Heavy lifting and pushing with the arms are prohibited for the first 6-8 weeks after surgery in order not to interfere with the healing of the sternum. The postoperative physiotherapy information aims to reduce the potential fear of movement that may be present after surgery. Patients are also informed about the benefits of physical activity.

Patients undergoing cardiac surgery are often offered cardiac rehabilitation (35). The aim of cardiac rehabilitation is to limit the adverse physiological and psychological effects of cardiovascular disease, reduce the risk of sudden death and reinfarction, increase control of symptom burden, and stabilize or reverse the atherosclerotic process (36). Cardiac rehabilitation has been shown to have many benefits (37).
Physiotherapy and lung cancer surgery

In several centers in the United Kingdom, Australia, and New Zealand, more than 90% of hospital-based physiotherapists routinely treat patients who have undergone thoracic surgery (38, 39). The treatment typically consists of mobilization, shoulder exercises and breathing exercises, and aims to prevent or treat postoperative complications such as impaired lung function, pneumonia, impaired thoracic mobility, and impaired physical function. Another aim of the treatment is to enhance the level of physical activity. Since there has been little evaluation of in-hospital physiotherapy for patients undergoing lung cancer surgery, there is a lack of evidence supporting routine physiotherapy. Some studies suggest that the treatment could decrease pain (40), increase shoulder mobility (40), and increase quadriceps strength (41). No significant effects on pulmonary complications or the six-minute walk test (6MWT) have been found (41-43). None of the studies used an untreated control group to investigate the effect of in-hospital physiotherapy on postoperative level of physical activity.

Pulmonary rehabilitation for 2-4 weeks prior to lung cancer surgery has been reported to improve pre-operative lung function and 6MWT in patients with COPD, both lung function and 6MWT, measured one month postoperatively, were below base-line values (44). Pre-operative exercise may be effective in reducing postoperative complications and length of hospital stay in patients undergoing lung cancer surgery (45, 46), and has been shown to improve exercise capacity and lung function (46).

Postoperative inspiratory muscle training for two weeks after lung cancer surgery may prevent a decline in physical activity level (47). Post-discharge exercise has been reported to increase exercise capacity (48-50) and reduce fatigue (51) although referral to such exercise is currently not part of clinical praxis (38, 39).

Physical activity

Definitions

Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure (52). Sedentary behavior refers to any waking behavior characterized by an energy expenditure ≤1.5 metabolic equivalent (MET) while in sitting or reclined posture (53). One
MET is a unit of sitting/resting oxygen uptake (≈3.5 ml of O₂ per kilogram of body weight per minute) (54). The intensity of physical activity is described as follows by Fletcher et al.: Light intensity = 1.6-2.9 METs, moderate intensity = 3.0-5.9 METs, vigorous intensity ≥ 6.0 METs (54).

**General recommendations**

The most recent and widely referred to recommendations on physical activity come from the World Health Organization (55). It recommends that all adults should, in order to improve health, engage in moderate-intensity physical activity for at least ten minutes at a time, for a total of at least 150 minutes per week, or 75 minutes of vigorous-intensity physical activity, or an equivalent combination of moderate- and vigorous-intensity (55). For additional health benefits, the amount of physical activity should be increased to 300 minutes of moderate-intensity aerobic physical activity or 150 minutes of vigorous-intensity aerobic physical activity per week. The recommendations also include muscle-strengthening activities on at least 2 days per week. Older adults with poor mobility should also perform activities to enhance balance and prevent falls; this should be performed on three or more days per week.

Moderate-intensity activity is described as when heart rate and breathing are raised, but it is still possible to speak comfortably. Vigorous-intensity is described as when the heart rate is higher, breathing is heavier, and conversation is harder (56).

The Physical Activity Guidelines for Americans, published by the U.S. Department of Health and Human Services in 2018 (57) are basically the same as the recommendations from WHO, except for the elimination of the requirement that physical activity be in bouts of at least ten minutes(57).

**Recommendations for patients with cardiovascular disease or cancer**

The Physical Activity Guidelines for Americans states that “Adults with chronic conditions or symptoms should be under the care of a health care provider. People with chronic conditions can consult a health care professional or physical activity specialist about the types and amounts of activity appropriate for their abilities and chronic conditions” (57).
International physical activity guidelines recommend that people with cancer perform at least 150 minutes of moderate intensity physical activity and two to three resistance sessions per week, and avoid extensive sedentary time (58). Less than 60% of people with lung cancer meet these guidelines before treatment, and less than 70% meet the guidelines after treatment (59, 60).

**Effects of physical activity**

Physical activity has well-established health-related effects for both healthy and non-healthy persons (61-68). Being physically active has acute, short-term, and long-term positive effects on health (69).

Patients who are active in the postoperative period after cardiac surgery have shorter hospital stays and a lower number of postoperative complications (65, 70, 71). Physical activity has also been associated with a reduced risk of mortality after heart valve surgery (72).

Long-term lung cancer survivors who report being regularly physically active report better quality of life than those who are more sedentary (73). Further, changing the level of physical activity has been associated with a change in quality of life: increasing the level of physical activity is associated with better quality of life, while reducing the level of physical activity is associated with a reduced quality of life (73). Physical activity has also been positively associated with control of the symptom burden in lung cancer survivors (73).

After lung cancer surgery, limited physical activity is common and is associated with increased length of hospital stay (74). The reasons for the low level of physical activity could include altered respiratory mechanics, pain, and dyspnea. Measurements 6 to 10 weeks after surgery show that patients with lung cancer who have undergone surgery have a lower daily step count than healthy individuals. They also spend more time in prolonged uninterrupted periods of sedentary behavior, and less time in light-intensity physical activity (75). One study from the USA has reported that at a mean of four years after surgery, only 25% of patients are sufficiently active (76) according to the American Cancer Society guidelines for cancer survivors (58). Individuals undergoing surgery for lung cancer have high interest in a physical activity self-management program (77).

Increased physical activity may provide as much mortality reduction as smoking cessation in elderly men (78).
**Physical activity and lung function**

It has been suggested that there is an association between the level of physical activity and lung function in healthy adults (79), older individuals (79), patients with asthma (80), and patients with chronic obstructive pulmonary disease (81, 82). Physical activity is important in maintaining cardiovascular and respiratory function, and change in physical activity is associated with change in cardiorespiratory fitness (81). Levels of physical activity, measured as steps per day, are significantly positively associated with lung function and quality of life in patients with chronic obstructive lung disease (82, 83).

**Measuring physical activity**

There various methods of measuring physical activity can be divided into three groups: 1) Criterion methods (e.g., direct or indirect calorimetry), 2) Objective methods (e.g., pedometers and accelerometers), and 3) Subjective methods (e.g., questionnaires, surveys, or activity diaries).

It has been reported that the ability of objective measurement of physical activity with accelerometers to identify individuals not meeting physical activity recommendations is better than the ability of self-reported measurements (84), although the self-reported measurements are considered easily administrated and hence convenient to use in the clinical setting.

The international physical activity questionnaire (IPAQ) (83) has been used in different countries and different settings and has shown adequate validity and reliability in healthy adults (85-88). Hurtig-Wennlöf et al published a version modified for the elderly, IPAQ-E, which provides acceptable estimates of physical activity in older adults (89).

Statistics Sweden annually produce surveys that examine living conditions in the adult Swedish population (90). Sepp et al. (91) used a category question from the Swedish national survey and observed significant differences in activity counts between groups, indicating that the question may be valid for categorizing people into different categories of activity. The category question will hereafter be called the PA question.
Rationale

Postoperative pulmonary complications are common after cardiac surgery, and reduced lung function can persist for a long time after surgery. A positive association between the level of physical activity and lung function has been proposed in both healthy individuals and people with disabilities. It is not clear whether there is an association between level of physical activity and recovery of lung function after cardiac surgery.

Despite the fact that physical activity has many positive effects on health, patients undergoing lung cancer surgery often report a low level of physical activity. Measuring physical activity is tricky; self-reported physical activity remains the most clinically applicable type of measurement, and a simple and valid questionnaire for screening patients would be valuable when planning interventions.

Patients undergoing lung cancer surgery are often routinely treated by physiotherapists, but this kind of treatment has not been thoroughly investigated.
Aims

The overall aim of this thesis was to investigate the effect of physiotherapy and physical activity in patients undergoing cardiac or lung cancer surgery.

The specific aims for each study were as follows:

Study I: To describe pre- and postoperative self-reported physical activity and lung function in patients undergoing cardiac surgery.

Study II: To validate two self-reported physical activity instruments against accelerometer data in patients who had undergone lung cancer surgery.

Study III: To examine whether physiotherapy during hospitalization after lung cancer surgery has any effect on early postoperative physical activity, physical capacity, and lung function.

Study IV: To examine the effect of in-hospital physiotherapy for patients undergoing lung cancer surgery on postoperative physical capacity, physical activity, and lung function.
Methods

Study participants

Patients in all studies underwent cardiac or thoracic surgery at Uppsala University Hospital (study I) or Örebro University Hospital (Studies I-IV) (Table 1).

The patients included in study I all underwent cardiac surgery at Uppsala University Hospital or Örebro University Hospital, with or without cardiopulmonary bypass. The surgical incision utilized was sternotomy. All patients received premedication and general anesthesia according to clinical routine. Cold blood cardioplegia was used in most cases. The patient’s lungs were kept deflated during aortic occlusion. The pericardium, mediastinum, and occasionally one or both pleura were drained, usually for less than 24 hours after surgery.

In studies II-IV, thoracic surgery was performed either by video-assisted thoracoscopy or open antero-lateral muscle-sparing thoracotomy, according to the surgeon’s preference. At the end of surgery, a single chest tube was placed in the pleural space and connected to a suction device (Thopaz chest drainage system®, Medela, Switzerland or Oasis® dry suction water seal drain, Atrium Europe, The Netherlands). A pressure of -15 cm H₂O was applied. The chest drainage was removed when there was no air leak and the volume of pleural effusion per day was below 300-400 ml. Pain management was primarily delivered by continuous epidural infusion with ropivacaine and sufentanil. Alternatively, locally placed catheters with ropivacaine were used. As a supplement, the patients received intravenous morphine, oral non-steroid anti-inflammation drugs, and paracetamol for as long as needed.
**Study design and participants**

Table 1 Study design and samples

<table>
<thead>
<tr>
<th></th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design</strong></td>
<td>Prospective cohort</td>
<td>Validation study</td>
<td>Randomized controlled trial</td>
<td>Randomized controlled trial</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>283</td>
<td>83</td>
<td>94</td>
<td>107</td>
</tr>
<tr>
<td><strong>Patients</strong></td>
<td>Cardiac surgery</td>
<td>Lung cancer surgery</td>
<td>Lung cancer surgery</td>
<td>Lung cancer surgery</td>
</tr>
<tr>
<td><strong>Time of assessment</strong></td>
<td>Pre-operatively and 2 months postoperatively</td>
<td>3 and 12 months postoperatively</td>
<td>Pre-operatively, during the first three days postoperatively and four days postoperatively</td>
<td>Pre-operatively and three months postoperatively</td>
</tr>
</tbody>
</table>

**Intervention**

In study III and IV, the treatment group received pre- and postoperative physiotherapy while the control group received no physiotherapy. The physiotherapy treatment was available all week with the exception of Sundays. All patients in the treatment group were treated by one of three physiotherapists at the ward. All the physiotherapists were clinically educated to follow the intervention protocol. The treatment was based on the routine treatment provided for patients undergoing cardiothoracic surgery, consisting of early mobilization, breathing exercises and exercises for thoracic and shoulder range of motion.

**Pre-operative information**

On the day of admission, patients in the treatment group received brief (5-10 minutes) individual pre-operative physiotherapy information regarding the importance of postoperative mobilization and mobility restrictions (i.e., free to use arms as much as possible without pain). They also received instructions regarding deep breathing exercises to be performed every waking hour during the first postoperative days, and instruction about coughing/huffing with ipsilateral arm and contralateral hand as support for pain relief: “Put your hand and arm over the wound as support when you cough, huff, or sneeze.”
Postoperative treatment

The treatment group received daily postoperative physiotherapy during their hospital stay. All patients in the treatment group had about the same amount of physiotherapy during the first two postoperative days (20-30 minutes per session). From the third day on, the treatment was individually adapted according to the patients’ status (i.e., patients who were feeling well and deemed adequately active received less time). The treatment consisted of:

*Individually adapted mobilization:* Sitting up in bed or in a chair on the day of surgery. Progressive ambulation in the ward from the first postoperative day, typically from 15 m up to one or two laps around the ward (one lap being approximately 100 m). The patients were instructed to stay out of bed and to walk as much as possible during the day, with or without a walking aid, according to the patients’ needs.

*Exercises for range of motion:* shoulder elevation, shoulder flexion while taking a deep breath, horizontal shoulder abduction with hands at the neck while taking a deep breath, and thoracic rotation. The patients were instructed to perform the exercises twice a day, with five repetitions per exercise, during the first postoperative month.

*Deep breathing exercises:* three series of ten deep breaths, with or without PEP (10 cm H₂O), to be performed every waking hour during their hospital stay. A PEP-device (Rium breathing exerciser; Rium Medical AB, Åkersberga, Sweden) was used to deliver positive expiratory pressure. The patients were instructed to continue the deep breathing exercises after discharge, 4-5 times daily until they could take deep breaths without any pain. The patients were instructed to cough/huff while using their arms as support for pain relief.

*Postoperative information:* prior to discharge the patients received advice regarding physical activity, based on the recommendations from the WHO (55) individually adapted for each patient (Table 2).
Table 2 Physical activity recommendations for patients in the treatment group in study III and IV, based on the recommendations from the World Health Organization

<table>
<thead>
<tr>
<th>Basic recommendations</th>
<th>Perform at least 150 minutes of moderate-intensity aerobic physical activity per week, or at least 75 minutes per week of vigorous-intensity aerobic physical activity.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixing intensities</td>
<td>A mix of moderate- and vigorous-intensity physical activity can be performed to meet the recommendations.</td>
</tr>
<tr>
<td>For how long?</td>
<td>The aerobic physical activity should be performed in bouts of at least 10 minutes.</td>
</tr>
<tr>
<td>Additional health benefits</td>
<td>In order to increase health benefits, the amount of physical activity can be increased above 150 minutes of moderate or 75 minutes of vigorous-intensity physical activity.</td>
</tr>
<tr>
<td>Unable to meet recommendations?</td>
<td>Be as physically active as possible.</td>
</tr>
<tr>
<td>Individually adapted</td>
<td>All advice was given with regard to the patient’s own preferences.</td>
</tr>
</tbody>
</table>

**Measurements**

**Objectively measured physical activity**

Objective measurement of physical activity was made using an accelerometer (ActiGraph, model GT3X+ (Manufacturing Technology Inc., Pensacola, FL, USA).

The patients were instructed to wear the device on the waist at all times, but were allowed to remove it while sleeping, showering or bathing/swimming.

Measurements were made at three times:
1. During the hospital stay, starting in the morning on the first day after surgery (used in studies III and IV).
2. For one week at three months after surgery (used in studies II and IV).
3. For one week at twelve months after surgery (used in study II).

Wear time validation was conducted according to Choi (92). For study IV, minimum wear time per day was set to 600 minutes, and minimum
wear days were set to two days. Cut points according to Barnett (93) were used to calculate sedentary time (0-100 counts), light activity (101-1012 counts) and moderate and vigorous-intensity physical activity (MVPA) (1013 counts and above). All accelerometer data were processed using the designated software (ActiLife version 6.11.9).

**Self-reported physical activity**

**IPAQ-E**
The IPAQ-E (89) was used in studies II-IV to describe the self-reported level of physical activity during the previous week. The mean metabolic equivalent (MET) minutes per week for vigorous, moderate and walking activities is calculated (83, 89). The physical activity level is categorized as follows: High (vigorous-intensity activity on ≥ 3 days and accumulating ≥ 1500 MET-min/week, or ≥ 7 days of any activity accumulating ≥ 3000 MET-min/week), Moderate (≥ 3 days of moderate-intensity activity and/or walking ≥ 30 min, or ≥ 5 days of activity accumulating ≥ 600 MET-min/week), or Low (not reaching either High or Moderate criteria) (83).

**PA question**
In studies I and II, self-reported leisure-time physical activity during the previous month was estimated with the PA question, modified from the Swedish National Institute of Public Health’s national survey (90). The patients report their level of physical activity by choosing one of four categories. The four levels are sedentary, moderate activity, moderate regular exercise and regular exercise (Table 3). The original question asks about physical activity during the last year, the modification in these studies was changing the time frame to one month. The four levels are hereafter called **Sedentary**, **Somewhat active**, **Moderate active** and **Exercise**.
**Table 3** A four-category scale for assessment of self-reported physical activity during the last month

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedentary</td>
<td>You spend most of your time sedentary. You walk or are active in some other way for less than 2 hours per week.</td>
</tr>
<tr>
<td>Somewhat active</td>
<td>You walk or are active in some other way for at least 2 hours per week, usually without sweating.</td>
</tr>
<tr>
<td>Moderate active</td>
<td>You exercise regularly 1-2 times per week, at least 30 minutes per time, with activity that causes you to sweat.</td>
</tr>
<tr>
<td>Exercise</td>
<td>You exercise regularly at least three times per week, at least 30 minutes per time, with activity that causes you to sweat.</td>
</tr>
</tbody>
</table>

The PA question was answered preoperatively (study I) and two months after surgery (study I) or three and twelve months after surgery (study II).

**Physical capacity**

In this thesis, physical capacity refers to functional capacities such as endurance and stamina. In studies III and IV, the 6MWT was used to assess physical capacity preoperatively and three months after surgery. The test was performed in a 25-meter corridor, otherwise following the recommendations from the American Thoracic Society (94). The patients were instructed to walk as far as possible in six minutes. They were informed of time elapsed every minute and no encouragement was given during the test. The use of a walking aid, if needed, was recorded. The output parameter was distance walked.

**Lung function**

Measurements of lung function were performed using Jaeger MasterScreen PFT/Bodybox version 4.6, Spiropharma Cardiopulmonary Diagnostics A/S Denmark for study I.

The lung function tests were conducted pre-operatively, on the day of admission, and two months after surgery, with the patients in a sitting position and wearing a nose clip. The measurements were performed at the Department of Clinical Physiology by experienced medical laboratory technicians, and followed the recommendations of the American Thoracic Society and the European Respiratory Society (95). The highest value of
three correctly performed tests was recorded. Reference values from Quanjer et al. (96) were used.

Variables used were forced expiratory volume in one second (FEV1), vital capacity (VC), forced vital capacity (FVC), total lung capacity (TLC), functional residual capacity (FRC), residual volume (RV) and inspiratory capacity (IC).

In studies II-IV, lung function was assessed using a hand-held spirometer (The MicroLab Cat No ML3500, MicroMedical, Kent, England), according to the recommendations of the American Thoracic Society and the European Respiratory Society (95).

Variables used were FEV1, FVC and FEV1 in percent of FVC (FEV%).

Dyspnea

In studies III and IV, perceived dyspnea was measured using the Modified Medical Research Council dyspnea scale (97), where the patients rate dyspnea from 0 (no dyspnea) to 4 (breathless when washing/getting dressed).

Pain

In studies III and IV, pain intensity was measured using a numeric rating scale (98) at rest, while taking a deep breath and when coughing. The scale ranged from 0 (no pain) to 10 (worst imaginable pain).

Statistical analysis

The SPSS version 15.0 software package (SPSS Inc., Chicago) was used for the statistical analysis in study I. Analyses in studies II-IV were performed using IBM SPSS Statistics 25 (IBM Corporation, Armonk, New York) and Stata 14.2 (StataCorp LLC, College Station, Texas).

For all analyses, a two-sided p-value <0.05 was considered statistically significant.

In study I, pre-operative and postoperative values for self-reported leisure-time physical activity were compared using the Wilcoxon signed rank test.

Demographic data were analyzed using descriptive statistics. The pulmonary function values two months postoperatively were expressed as a percentage of the pre-operative values.
For patient characteristics in studies II-IV, continuous data was summarized as mean ± standard deviation or median with corresponding interquartile range. Categorical data were presented as numbers and percentages. Normality of data was assessed with the Shapiro-Wilk test. Log transformation of skewed distributions was applied if necessary.

In study II, Spearman’s rank correlation coefficient was used to assess correlations between self-reported and objectively measured physical activity. Divergence between observed and statistically expected number of patients in the different levels of physical activity was tested with the chi2 test.

Differences between the groups in studies III and IV were tested using the Student’s t-test for normally distributed continuous variables, and the Mann-Whitney U test for continuous variables with skewed distribution. Differences of categorical variables were tested using the chi2-test.

In study III, differences in physical activity between the groups during the first three postoperative days were examined using a linear regression model with group allocation as fixed factor, adjusting for surgery time and duration of pleural drainage.

In study IV, missing data were imputed using a multiple imputation method for postoperative 6MWT, pre- and postoperative IPAQ-E, and postoperative accelerometer data. Age, sex, body mass index, length of surgery, duration of pleural drainage, length of stay, and pre-operative 6MWT were used as predictors for multiple imputations. Five imputed datasets were used when comparing the variables with missing values, and the average of the statistics or p-values was used for statistical inference. Differences within the groups between pre-operative and postoperative were tested with the Wilcoxon signed rank test.
Ethical considerations

All studies were conducted according to the Declaration of Helsinki. All measurements were non-invasive. Any potential risk of participation in the studies was considered to be very small, and outweighed by the potential benefits for future patients receiving evidence-based treatment.

Study I was approved by the Regional Ethical Board (Dnr 2007/160) and written informed consent was obtained from each patient and the study. Participation in the study was voluntary and the patients were allowed to withdraw from the study at any time without giving any reason. The study was registered at ClinicalTrials.gov (NCT01282671).

Studies II-IV were approved by the Regional Ethical Board (Dnr 2013/199) and written informed consent was obtained from each patient. Participation in the studies was voluntary and the patients were allowed to withdraw from the studies at any time without giving any reason.

The control group in the randomized controlled trial received the same routine treatment regarding surgery, pain management and nursing as the treatment group. Had a surgeon in the ward judged that a patient in the control group was in need of physiotherapy, the study protocol would have been broken and the patient would have been treated accordingly. This was not necessary in any of the cases. Registration: ClinicalTrials.gov (NCT01961700).
Results

In summary, the main findings of this thesis are:

- Patients who remained active or increased their level of physical activity two months after surgery had significantly better recovery of lung function compared to those who remained sedentary or reported a lower level of physical activity in the months after cardiac surgery.
- The PA question and the IPAQ-E were able to identify patients with an insufficient level of physical activity after lung cancer surgery.
- Patients undergoing lung cancer surgery who were treated by a physiotherapist during the in-hospital phase were significantly more physically active during the first three days after surgery.
- There were no statistically significant between-group differences three months after lung cancer surgery when comparing patients treated by physiotherapists during the in-hospital phase with untreated patients. The patients treated by physiotherapists did however report a higher level of physical activity three months postoperatively compared with preoperatively, while the patients in the control group reported no change in level of physical activity.

Physical activity and lung function

Study I included 283 patients with a mean age of 67 ± 10 years (Table 4). All patients underwent elective cardiac surgery (isolated CABG (n = 100), AVR and/or MVR (n = 135) or combination CABG and valve repair (n = 48)). Before surgery, the lung function for the whole sample was within the normal range (VC 91 ± 15% and FEV1 90 ± 17% of predicted values). The lung function, measured two months after surgery, decreased for the whole sample (FEV1 was 93 ± 11% and FVC 94 ± 11% (p<0.001) of preoperative values).

The 52 patients who reported being sedentary preoperatively had significantly lower lung function than more active patients (FVC 84 ± 15% vs. 89 ± 15% of predicted values, p<0.05). Compared to preoperative activity, 113 patients (40%) reported higher level of physical
activity postoperatively (p<0.001), 38 patients (13%) a lower level, and 132 patients (47%) reported the same level as before surgery.

The sample was dichotomized into two groups according to change in level of physical activity:, 230 patients (81%) remained active or had become more active two months after surgery while 53 patients remained sedentary or reported a lower level of physical activity postoperative than pre-operative. The more active patients had significantly better recovery of lung function than those being less active (VC (94 ± 11% of preoperative value vs. 91 ± 9%, p = 0.03), TLC (96 ± 11% vs. 90 ± 11%, p = 0.01), and IC (94 ± 14% vs. 88 ± 19%, p = 0.008)). There were no baseline differences between the groups.

**Validation of two self-reported physical activity instruments**

In study II, the sample consists of patients from a randomized controlled trial who provided accelerometer measurements and data on self-reported physical activity (Table 4).

A majority of the patients described themselves as *Somewhat active* or *Moderate* active, both three and twelve months after surgery. Accelerometer data revealed that most of the time was spent in sedentary.

There were statistically significant correlations between both instruments and time spent in light physical activity, time spent in MVPA, steps per day and counts per day, measured three and twelve months after surgery. The correlations were stronger for the higher intensities of physical activity, and generally stronger for the measurements 12 months after surgery as compared to three months after surgery.

More than statistically expected of the patients in *Sedentary* and *Low* were under the cut-points of 30 minutes of MVPA/day and 4600 steps/day, while more than expected of the patients in *Exercise* and *High* were above the cut-points.

**Short-term effect of in-hospital physiotherapy**

Study III included a total of 107 patients (Table 4). Thirteen patients were excluded because they were discharge before third postoperative day (n=10) or due to technical errors in accelerometer data (n = 3). The study group consisted of 94 patients (treatment group n = 50, and control group n = 44). Of these, 24 patients in the treatment group and 16 in the control
group did not perform postoperative assessment of 6MWT, spirometry, dyspnea, or pain, but did have accelerometer data and were assessed for physical activity level. Of those in the treatment group who did not complete all steps, eight were discharged before postoperative day 4, were unable to perform (n = 15), or lacked of staff support (n = 1). In the control group, five were discharged before postoperative day 4 (n = 5), or were unable to perform (n = 11).

At baseline, the randomization process yielded no major differences between the groups regarding age, gender, body mass index (BMI), physical function (6MWT), lung function, self-reported physical activity or dyspnea. The groups were comparable regarding type of surgery, but there were significant differences in length of surgery and length of stay. There was a significant correlation between duration of pleural drainage and length of hospital stay (r = 0.61, p < 0.001).

During the first three postoperative days, patients in the treatment group reached significantly more counts (2010 (1508) vs 1629 (1146), mean difference 495 [95% CI 44-1109]), after adjusting for length of surgery and duration of pleural drainage) compared to the control group. In terms of steps per hour the results were 49 (47) vs 37 (34), mean difference 14 [95% CI 3-30], after adjusting for length of surgery and duration of pleural drainage).

For patients available for the follow-up test on the fourth postoperative day (treatment group n = 26, control group n = 28), there were no significant differences between the groups regarding 6MWT, spirometric values, pain, or dyspnea.

**Long-term effect of in-hospital physiotherapy**

A total of 107 patients were included in the study (Table 4). There were no statistically significant differences between the groups, except for gender and length of surgery. The treatment group had a higher proportion of males and a longer time in surgery.

The 6MWT for the whole sample was 92% of predicted values (99). When comparing the pre- and postoperative 6MWT, there was a statistically significant decrease of 12 m (95% CI 0.3-23.5, p = 0.045) for the whole sample three months postoperatively. No differences in 6MWT between the groups were found. There were no statistically significant differences in lung function, pain, or dyspnea.
Self-reported physical activity, assessed by the IPAQ-E category, increased in the treatment group from pre-operatively to three months after surgery ($p = 0.047$), while no difference was present in the control group ($p=0.87$). There was no statistically significant difference between the groups pre- or postoperatively.

There were no statistically significant differences between the groups in physical activity measured by accelerometer three months after surgery.

Distance in 6MWT was significantly correlated with physical activity measured by accelerometer three months after surgery (steps per day: $r = 0.507$, $p < 0.001$).

No statistically significant correlation between objectively measured physical activity during hospital stay and three months after surgery was found.

### Table 4 Descriptive data for the samples in studies I-IV

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study I (n=283)</th>
<th>Study II (n=83)</th>
<th>Study III (n=94)</th>
<th>Study IV (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)(n)</td>
<td>231/52</td>
<td>36/47</td>
<td>45/49</td>
<td>47/60</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67 ± 10</td>
<td>68 ± 8</td>
<td>68 ± 8</td>
<td>68 ± 8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27 ± 4</td>
<td>26 ± 4</td>
<td>26 ± 4</td>
<td>26 ± 4</td>
</tr>
<tr>
<td>Never smoked/ex-smoker/current smoker (%)</td>
<td>44/51/5</td>
<td>19/56/8</td>
<td>19/62/13</td>
<td>23/69/15</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>2.9 ± 1</td>
<td>2.3 ± 1</td>
<td>2.3 ± 1</td>
<td>2.3 ± 1</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>3.9 ± 1</td>
<td>3.4 ± 1</td>
<td>3.4 ± 1</td>
<td>3.4 ± 1</td>
</tr>
<tr>
<td>Length of surgery (minutes)</td>
<td>216 ± 71</td>
<td>127 ± 52</td>
<td>128 ± 47</td>
<td>128 ± 51</td>
</tr>
</tbody>
</table>

Data presented as numbers (n), percent (%), or mean ± SD. BMI = body mass index, FEV1 = forced expiratory volume in one second, FVC = forced vital capacity.
Discussion

In the present thesis it was found that patients scheduled for cardiac surgery who reported being sedentary preoperatively had lower lung function than more active patients. Patients who remained active or increased their level of physical activity two months after cardiac surgery had better recovery of lung function than patients who remained sedentary or reported a lower level of physical two months postoperatively.

Patients undergoing lung cancer surgery spent the majority of their time being sedentary, both at three and twelve months after surgery. Both the PA question and IPAQ-E seems to give valid information on level of physical activity.

Patients undergoing lung cancer surgery who received physiotherapy during the in-hospital phase were significantly more physically active during the first three days than patients not receiving physiotherapy.

There were no statistically significant differences in physical capacity, objectively measured physical activity, lung function, pain or dyspnea three months after lung cancer surgery between patients receiving physiotherapy during hospital stay and patients not receiving physiotherapy. However, patients receiving physiotherapy showed a significantly increased level of self-reported physical activity three months after surgery compared to preoperatively, whereas the patients in the control group reported no change in level of physical activity.

Association between physical activity and lung function

In study I, the lung function for the whole sample was significantly lower two months after surgery compared to preoperatively. Sedentary patients presented with lower lung function than more active patients. In addition, patients who remained active or increased their level of self-reported physical activity showed a better recovery of lung function than patients who remained sedentary or reported a lower level of physical activity compared to pre-operatively. Supporting these results, physical activity has been positively associated with lung function in healthy adults (79), older individuals (79), patients with asthma (80), and patients with chronic obstructive pulmonary disease (81, 82).

Impaired lung function could lead to postoperative pulmonary complications, which in turn could lead to increased morbidity and mortality. For patients with high age or pulmonary disease, even a small
decrease in lung function might be clinically relevant, and our results indicate a positive effect of being physically active in the first postoperative months, adding to the well-established positive cardiovascular effects of physical activity.

It has been reported that patients undergoing cardiac surgery increase their level of physical activity one year after surgery (8, 64, 100). This is supported by our results; the patients reported being more active two months after surgery, compared to preoperatively. The improved level of physical activity might be due to the surgery having positive effect on functional status, that is, the patients have improved ability to be physically active. Being able to be more physically active might lead to improved quality of life, lower incidence of cardiac events, and reduced mortality.

The fact that sedentary patients in our study presented with lower lung function than the active patients is consistent with previous results, showing that sedentary men have lower lung function compared to active men (101). Our results indicate that sedentary patients have reduced lung function after cardiac surgery, which emphasizes the importance of enhancing level of physical activity in these patients.

### Validation of two self-reported physical activity instruments

In study II, the PA question and the IPAQ-E were validated against accelerometer data for patients 3 and 12 months after lung cancer surgery.

There were moderate correlations between the instruments and accelerometer derived data on time in MVPA. For time in sedentary and light intensity physical activity, the correlations were low. This means that the instruments have better ability to describe physical activity in higher intensities, while their ability to describe low intensity physical activity and sedentary behavior is weak. The results in our study were similar to those presented by Hurtig-Wennlöf et al. (89).

The cut-point of 4600 steps/day, as proposed by Tudor-Locke (102) as a minimum for people with disabilities in order to meet the recommended levels of physical activity from the WHO, would probably be appropriate for the patients in this study, being an aged population that has undergone lung cancer surgery. Both instruments were able to identify patients not meeting physical activity guidelines; less than statistically expected of the patients in the Sedentary or Low groups reached the cut-points of 30
minutes of MVPA/day or 4600 steps/day. While more than expected of the patients in the Moderate active, Exercise and High groups reached the cut-points. Similar to our results, the IPAQ-E has been shown being able to identify inactive individuals in an elderly sample (89).

For patients in the Somewhat active (PA question) and Moderate active (IPAQ-E), a more thorough evaluation of level of physical activity would be necessary to be able to identify patients who are not meeting the recommended levels of physical activity. This evaluation may include interviewing the patients.

**Short-term effect of in-hospital physiotherapy**

In study III, we found that patients undergoing lung cancer surgery and treated by physiotherapists during their hospital stay are significantly more physically active for the first three days after surgery compared to an untreated control group. To our knowledge, this is the first study to investigate the effect of in-hospital physiotherapy on the level of physical activity.

We found two studies reporting on in-hospital physical activity after lung cancer surgery (74, 103). Agostini et al. (74) reported low physical activity, with a median of 170 steps on the second day after surgery and 223 steps on the third day. Our patients were somewhat more active, with a median of 659 and 805 steps on the second and third day respectively. In contrast, the patients in the study by Esteban et al. (103) were actually very active, with a mean of 7275 steps on the second day and 8943 steps on the third day. The corresponding results from our patients were 974 and 1041 steps. There are some differences in methodology, Esteban et al. (103) used a pedometer placed at the waist, Agostini et al. (74) used Sensewear, a motion sensor placed on the upper arm, and we used the Actigraph GT3X+ accelerometer placed at the waist. Patients in the other two studies were all treated by physiotherapists, like the patients in our treatment group. Esteban et al (103) excluded patients undergoing pneumonectomy; these patients were not excluded in the study by Agostini et al. or our study. These methodological differences might explain some, but not all, of the disparity in reported physical activity.

There were no significant differences between the groups in 6MWT, spirometry or pain measured on the fourth postoperative day. A lack of difference in 6MWT between patients receiving physiotherapy and a control group has been reported earlier (41), supporting the results in our
The physical activity performed by the patients in the ward might have been at too low an intensity to show an effect on exercise capacity measured by the 6MWT. However, adding early postoperative exercise to routine physiotherapy did not improve exercise tolerance (104). Further, the short duration of the treatment (four days) might not be enough to show results on the 6MWT. Considering the internal missing data due to early discharge or inability to perform the test, the small sample size contributes to the uncertainty regarding these results.

Pleural drainage has been shown to have a negative impact on 6MWT, lung function and pain (105, 106), but this was not further evaluated in this study.

The group receiving physiotherapy remained at the hospital for a longer period. The reason for this remains unclear, but it seems unlikely that the physiotherapy treatment would have an impact on the length of stay. In a clinical setting, length of stay is dependent on factors other than the patient’s physical status. Length of stay is an important outcome but is hard to evaluate due to many contributing factors. In our study, there was a significant correlation between duration of pleural drainage and length of stay. Differences in length of stay after lung cancer surgery have also been linked to older age, male gender and comorbidities such as chronic obstructive pulmonary disease (107). One study suggests that high-intensity rehabilitation during hospital stay may reduce length of stay, however, duration of pleural drainage was not reported in that study (108). In our study, there was a significant difference in length of surgery between the groups, and this could potentially affect the length of stay. Length of surgery has been associated with postoperative complications after pulmonary lobectomy (109), and postoperative complications have been associated with length of stay (110).

Medical patients admitted to hospital spend more than 80% of the time lying in bed (111), and patients who have undergone lung cancer surgery spend the majority of their time in hospital being sedentary (74). The patients in our sample were also quite inactive. Physical activity in lung cancer surgery patients has been described from six weeks up to six months after surgery. The data show that only about 25% of the patients are sufficiently active after surgery compared to recommendations for cancer survivors (76), and these patients are more sedentary and less active than healthy controls (75).

The patients in our study experienced a low level of physical activity, despite which they were deemed fit for discharge. This could indicate a
need for outpatient physiotherapy, which may potentially increase exercise capacity (48). Despite the potential benefits of pulmonary rehabilitation, referral to such rehabilitation is rare (38). One important role the physiotherapist could play during the in-hospital phase could be informing patients about the benefits of, and referring interested patients to, pulmonary rehabilitation.

It is not clear whether it is important to be physically active in the early postoperative period, but it seems likely that it would be beneficial to get a good start. Our results indicate that physiotherapists could play an important part in helping patients to be physically active in the early postoperative period.

**Long-term effect of in-hospital physiotherapy**

In study IV we found no significant differences in physical capacity, measured with the 6MWT three months after surgery, between patients receiving physiotherapy during the in-hospital phase and untreated patients.

Neither did we find any significant differences between the groups in objectively measured physical activity, lung function, pain, or dyspnea. However, the patients in the treatment group had a significantly increased level of self-reported physical activity three months after surgery compared to pre-operatively, while the patients in the control group reported no change in level of physical activity. However, there were no statistically significant between-group differences.

As far as we know, this is the first study measuring the effect of in-hospital physiotherapy on the level of physical activity between a treatment group and an untreated control group according to a protocol similar to routine care.

In-hospital physiotherapy showed no statistically significant effect on 6MWT three months after surgery in study IV. The treatment that was delivered during the hospital stay was focused on preventing postoperative pulmonary complications and enhancing the level of physical activity. Although it included walking and ambulation, the emphasis was not on exercise, and the intensity of the walking might have been too low to have an impact on the 6MWT. Also, the treatment was delivered over a rather short time (4-5 days), which might have been too short. Further, the 6MWT for the whole sample was normal pre-operatively, which makes it unlikely that there would be a large increase for the patients.
postoperatively. Thus the study may have lacked the power to detect significant differences between the groups.

The level of physical activity has been shown to deteriorate from pre-operative to two months postoperatively for patients undergoing lung cancer surgery (112). The fact that the patients in the treatment group in our study reported an increase in level of physical activity is interesting and calls for further research in larger trials. The lack of significant difference between groups could possibly be due to the relatively small number of patients in the study.

With a possibly new cancer diagnosis, patients may be unable to comprehend other information. It has been reported that the timing of an intervention is crucial for adherence (113), and it has been suggested that interventions should be offered to patients when they have completed first-line treatment (113). Some patients see the cancer as an opportunity for behavior change and a trigger to start exercising (114). Even a little information on physical activity can help to increase the level of physical activity in older adults (115). It has been reported that patients would like to receive information about how to cope with recovery in general (116) and specifically about physical activity (76). The length of stay after lung cancer surgery in our study was only 4-5 days, and it could be difficult for patients to comprehend the information regarding the importance of physical activity when given so close to the surgery, especially since the majority of the patients were diagnosed with cancer. Future studies with the aim of increasing the level of physical activity could preferably place the intervention some time after diagnosis and first line treatment.

We found a statistically significant correlation between 6MWT and objectively measured physical activity three months after surgery, supporting the results of Granger et al. (59), who found a strong correlation between 6MWT and steps per day. The 6MWT has been shown to be a predictor of survival in lung cancer patients (117), and deteriorates after lung cancer surgery (112). In our study there was a statistically significant deterioration in 6MWT of 12 meters three months postoperatively compared to pre-operatively for the whole sample. Although this change was statistically significant, it fails to reach the point of clinically important difference, which has been suggested as being between 22 and 42 meters (118).
Methodological considerations

Study I is the first study investigating an association between physical activity and recovery of lung function. It would have been valuable to objectively measure level of physical activity, i.e. with the use of accelerometers; such a study is currently being planned.

Studies III and IV are the first randomized controlled trials evaluating the effect of in-hospital physiotherapy on objectively measured level of physical activity for patients undergoing lung cancer surgery, both during the immediate postoperative period, and three months after surgery.

There was more missing data than expected for the 6MWT and spirometry four days after lung cancer surgery, to a large part due to patients being discharged prior to the measurements. In hind-sight, the value of these measurements as early as four days postoperatively may be questioned. A follow-up visit 2-4 weeks postoperatively might have been more reasonable.

It would have been valuable to perform objectively physical activity measurement preoperatively; however, the patients present at the thoracic surgery ward a short time after decision of surgery, making it difficult to perform such a measurement. Future studies should however consider objective measurement of pre-operative level of physical activity.

In studies III and IV, all patients undergoing elective surgery for confirmed or suspected lung cancer were included, and we found no difference between the treatment group and the control group in terms of physical capacity. Future studies should evaluate the effect of physiotherapy in high-risk patients, such as older patients or patients with comorbidities. Evaluation of treatment at higher intensity would also be interesting to perform.

The design in the RCT was single-blinded, and there is also a risk of a spill-over effect, that is, the patients spent their in-hospital time in a ward together with patients undergoing cardiac surgery, who all followed a clinical pathway that included early mobilization and ambulation. Since the patients are treated in a mixed setting, this potential bias is probably impossible to prevent.
Clinical implications

The results in study I imply that physical activity is beneficial for patients after cardiac surgery; this could be used as an argument when giving these patients advice regarding postoperative physical activity. Future studies could investigate the association between objectively measured physical activity and recovery of lung function after cardiac surgery, taking preoperative level of physical activity in consideration, trying to describe causation.

The physical activity category instruments, the PA question and the IPAQ-E, could be used clinically to screen the level of physical activity in patients undergoing lung cancer surgery. Identifying those who do not reach the recommended level of physical activity would be beneficial when planning physical activity enhancing interventions for these patients. Which instrument to use will depend on the setting. The PA question is quick to answer and does not need any processing of the data and might be the best instrument in the clinical setting, while the IPAQ-E, since being used internationally in previous studies, might be a better choice in research.

The results in studies III and IV imply that physiotherapy during the in-hospital phase may have positive effects on physical activity after lung cancer surgery. It would be interesting to perform a qualitative study, examining patients’ experiences of in-hospital physiotherapy before and after lung cancer surgery, with the aim of providing a treatment desirable for the patients.

It would be important to identify patients with a low level of physical activity and evaluate whether physiotherapy may have a positive effect in this group, for patients undergoing cardiac as well as lung cancer surgery.

It is clear that the level of physical activity is low after lung cancer surgery, and there is a need to find ways of improving this. The question of when and how an intervention should be tailored remains to be answered.
Conclusions

- An increased level of physical activity compared to the pre-operative level was reported as early as two months after cardiac surgery. Our data show that there is a significant positive association between physical activity and recovery of lung function after cardiac surgery. The relationship between objectively measured physical activity and postoperative pulmonary recovery needs to be further examined to verify these results.

- After lung cancer surgery, patients describe themselves as somewhat active, while accelerometer data shows that the majority of the time is spent being sedentary. Both the PA question and the IPAQ-E seem to give valid information on the level of physical activity, and could be used to identify patients who would benefit from intervention aiming at increasing the physical activity level.

- Patients receiving in-hospital physiotherapy showed an increased level of physical activity during the first days after lung cancer surgery, compared to an untreated control group. However, no effects on the six-minute walk test or spirometric values were found. The clinical importance of an increased physical activity level during the early postoperative period needs to be further evaluated.

- No differences in functional capacity or lung function three months after lung cancer surgery were found between patients receiving in-hospital physiotherapy and an untreated control group. There was no statistically significant difference between the groups regarding objectively measured physical activity. However, self-reported physical activity increased in the treatment group from pre-operative to three months after surgery, while there was no difference in the control group.
Sammanfattning på svenska


Fysisk aktivitet har flera positiva effekter på hälsa, både hos friska individer och personer med olika former av funktionsnedsättningar, bland annat på lungfunktion. Världshälsoorganisationen (WHO) rekommenderar att alla vuxna är fysiskt aktiva, med aktivitet på måttlig intensitetsnivå, minst 150 minuter per vecka, alternativt 75 minuter av fysisk aktivitet med hög intensitet. Aktivitet med måttlig eller hög intensitet kan också kombineras för att nå rekommendationerna. Personer med lungcancer når sällan rekommendationerna från WHO.

I undersökningen visade sig att patienter som var aktivare eller rapporterade en högre aktivitetsnivå postoperativt hade bättre återhämtning jämfört med patienter som skilde sig från de aktivare patienterna. Denna information kan vara av vikt för att identifiera patienter som kan vara i behov av interventioner som syftar till att öka fysisk aktivitetsnivå.

Det övergripande syftet med den här avhandlingen var att undersöka effekten av fysisk aktivitet och fysioterapi hos patienter som genomgått hjärt- eller lungcancer kirurgi.

I det andra delarbetet undersöktes sambandet mellan fysisk aktivitet och återhämtning av lungfunktion efter hjärtkirurgi. Resultatet visade att de patienter som var stillasittande eller rapporterade en lägre aktivitetsnivå postoperativt hade sämre återhämtning jämfört med patienter som antingen bibehöll eller ökade sin aktivitetsnivå.

I det tredje delarbetet undersöktes effekten av fysioterapi under sjukhusvistelsen i samband med lungcancer kirurgi med avseende på fysisk
aktivitet under de första tre dagarna. Patienterna i behandlingsgruppen var mer aktiva än patienterna i kontrollgruppen.

Det fjärde delarbetet undersökte mer långsiktiga effekter av fysioterapi under sjukhusvistelsen i samband med lungcancerkirurgi. Inga skillnader mellan behandlingsgrupp och kontrollgrupp hittades. Patienterna i behandlingsgruppen rapporterade dock en högre aktivitetsnivå tre månader postoperativt jämfört med preoperativt, medan patienterna i kontrollgruppen inte rapporterade någon förändring av aktivitetsnivå.
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