Lung Function, Respiratory Muscle Strength and Effects of Breathing Exercises in Cardiac Surgery Patients

CHARLOTTE URELL
Dissertation presented at Uppsala University to be publicly examined in B:42, BMC, Husargatan 3, Uppsala, Friday, March 1, 2013 at 09:15 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

Background: Breathing exercises are widely used after cardiac surgery. The duration of exercises in the immediate postoperative period is not fully evaluated and only limited data regarding the effects of home-based breathing exercises after discharge from hospital have been published.

Aim: The overall aim of this thesis was to evaluate the effects of deep breathing exercises with positive expiratory pressure (PEP) and describe lung function and respiratory muscle strength in patients undergoing cardiac surgery.

Participants and settings: Adult participants (n=131) were randomised to perform either 30 or 10 deep breaths with PEP per hour during the first postoperative days (Study I): the main outcome was oxygenation, assessed by arterial blood gases, on the second postoperative day. In Study III, 313 adult participants were randomly assigned to perform home-based deep breathing exercises with PEP for two months after surgery or not to perform breathing exercises with PEP after the fourth to fifth postoperative day. The main outcome was lung function, assessed by spirometry, two months after surgery. Studies II and IV were descriptive and correlative and investigated pre and postoperative lung function, assessed by spirometry, and respiratory muscle strength, assessed by maximal inspiratory pressure, and maximal expiratory pressure.

Results: On the second postoperative day, arterial oxygen tension (PaO$_2$) and arterial oxygen saturation (SaO$_2$) was higher in the group randomised to 30 deep breaths with PEP hourly. There was no improved recovery of lung function in participants performing home-based deep breathing exercises two months after cardiac surgery, compared to a control group. Subjective experience of breathing or improvement in patient perceived quality of recovery or health-related quality of life did not differ between the groups at two months. Lung function and respiratory muscle strength were in accordance with predicted values before surgery. A 50% reduction in lung function was shown on the second postoperative day. High body mass index, male gender and sternal pain were associated with decreased lung function on the second postoperative day. Two months postoperatively, there was decreased lung function, but respiratory muscle strength had almost recovered to preoperative values.

Keywords: Breathing exercises, Cardiac surgery, Deep breathing, Lung function, Oxygenation, Physical therapy, Positive expiratory pressure, Spirometry, Respiratory muscle strength

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List of Papers

This thesis is based on the following studies, which are referred to in the text by their Roman numerals.

I Urell C, Emtner M, Hedenström H, Breidenskog M, Tenling A, Westerdahl E.

II Urell C, Westerdahl E, Hedenström H, Janson C, Emtner M.

III Westerdahl E, Urell C, Jonsson M, Bryngelsson I L, Hedenström H, Emtner M.
Home-Based Deep Breathing Exercises Performed Two Months Following Cardiac Surgery – A Randomised Controlled Trial. Submitted

IV Urell C, Emtner M, Hedenström H, Westerdahl E.
Respiratory Muscle Strength in Cardiac Surgery Patients Submitted

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<td>ABG</td>
<td>Arterial blood gases</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
</tr>
<tr>
<td>ATS</td>
<td>American Thoracic Society</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>CABG</td>
<td>Coronary artery bypass grafting</td>
</tr>
<tr>
<td>CG</td>
<td>Control group</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>CPAP</td>
<td>Continuous positive airway pressure</td>
</tr>
<tr>
<td>ERS</td>
<td>European Respiratory Society</td>
</tr>
<tr>
<td>FEV₁</td>
<td>Forced expiratory volume in 1 second</td>
</tr>
<tr>
<td>FRC</td>
<td>Functional residual capacity</td>
</tr>
<tr>
<td>FVC</td>
<td>Forced vital capacity</td>
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<tr>
<td>HRQoL</td>
<td>Health-related quality of life</td>
</tr>
<tr>
<td>IC</td>
<td>Inspiratory capacity</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive care unit</td>
</tr>
<tr>
<td>IR-PEP</td>
<td>Inspiratory resistance positive expiratory pressure</td>
</tr>
<tr>
<td>IS</td>
<td>Incentive spirometry</td>
</tr>
<tr>
<td>MEP</td>
<td>Maximal expiratory pressure</td>
</tr>
<tr>
<td>MIP</td>
<td>Maximal inspiratory pressure</td>
</tr>
<tr>
<td>NRS</td>
<td>Numeric rating scale</td>
</tr>
<tr>
<td>NIV</td>
<td>Non-invasive ventilation</td>
</tr>
<tr>
<td>NYHA</td>
<td>New York Heart Association classification</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>Arterial carbon dioxide tension</td>
</tr>
<tr>
<td>PaO₂</td>
<td>Arterial oxygen tension</td>
</tr>
<tr>
<td>PEP</td>
<td>Positive expiratory pressure</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>SaO₂</td>
<td>Arterial oxygen saturation</td>
</tr>
<tr>
<td>SpO₂</td>
<td>Peripheral oxygen saturation</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SF-36</td>
<td>Short form 36</td>
</tr>
<tr>
<td>TG</td>
<td>Treatment group</td>
</tr>
<tr>
<td>VC</td>
<td>Vital capacity</td>
</tr>
</tbody>
</table>
Introduction

Coronary heart disease is one of the most common causes of morbidity and mortality globally (1, 2). Although cardiac surgery is an effective treatment for patients with advanced coronary heart disease, it carries a risk for serious non-cardiac complications, such as pulmonary impairments, sepsis, stroke, renal impairments, deep sternum infections, and gastrointestinal complications, all of which prolong the length of hospital stay (3). Pulmonary impairments are the single greatest non-cardiac complications and the causes are multifactorial (3-5). In the early postoperative period, lung function, measured as vital capacity (VC) and forced expiratory volume in one second (FEV₁), is usually decreased by 35-60% (6-9), and a 6-13% decreased lung function can persist for four months (10). In the first postoperative days a reduced lung function can contribute to impaired gas exchange (11, 12) and respiratory muscle strength decreases during the first days after surgery (13): however, little data on respiratory muscle function months after surgery is reported.

Breathing exercises are widely used in postoperative care for preventing postoperative pulmonary impairments, such as decreased lung volumes, atelectasis, decreased oxygenation and pneumonia, and are used in different ways and through a variety of devices and techniques (12, 14-18). In Sweden, deep breathing exercises with positive expiratory pressure (PEP) is a common postoperative treatment (19), however, it is unclear whether different duration and frequencies affect lung volumes and oxygenation levels.

The challenge of this thesis was to contribute to the increasing knowledge in how to prevent and reduce the negative effects of pulmonary impairments after cardiac surgery by deep breathing exercises with PEP and to describe lung function and respiratory muscle strength in cardiac surgery patients.
Background

Postoperative pulmonary impairments and risk factors

Cardiac surgery increases the risk of postoperative pulmonary impairments (4, 20). The definition of postoperative pulmonary impairments is still unclear, but atelectasis, pleura effusion, pulmonary oedema, bronchospasm and pneumonia are reported as pulmonary impairments (21). Clinical manifestations of postoperative pulmonary impairments range from arterial hypoxemia to acute respiratory distress syndrome (22). In the first postoperative week 67-100% of patients have areas of atelectasis (17, 23) and the prevalence of pneumonia is reported to be 3-12% after cardiac surgery (21, 24).

Several risk factors, classified as preoperative-, perioperative- and postoperative are involved in causing pulmonary impairments, but the pathogenesis is complex and not completely understood.

Preoperative risk factors for postoperative pulmonary impairments include general disability, infections in the respiratory passage, lung disease, smoking, older age (>80 years), overweight (Body Mass Index, BMI >25), diabetes mellitus, malnutrition and dehydration (25, 26). Although chronic obstructive pulmonary disease (COPD) is conventionally associated with increased postoperative morbidity and mortality after cardiac surgery, this association has been challenged (27-29). Postoperative pulmonary impairments are two-fold greater in current smokers than in non-smokers and their hospital stay is prolonged (30) and after cardiac surgery obese patients suffer more pulmonary impairments than non-obese patients (25).

Perioperative risk factors for postoperative pulmonary impairments include median sternotomy incision, dissection of internal mammary artery, hypothermia for myocardial protection, the use of cardiopulmonary bypass, and general anaesthesia (31-34). After sternotomy, changes in the chest wall configuration can reduce chest wall compliance for up to three months postoperatively (35). The retrieval of the internal mammary artery, which typically necessitates pleural dissection, may also contribute to pulmonary impairment (36). Topical cooling for myocardial protection causes phrenic nerve dysfunction followed by diaphragm paralysis (33, 37) and almost all anaesthetics generate a reduction in functional residual capacity (FRC) and negatively influence oxygenation (38). One reason for reduced FRC is loss
of respiratory muscle tone, which allows the elastic forces of the lungs to pull the chest wall (39). Mucociliary clearance is also affected by the general anesthesia, intubation and analgesia.

Postoperative risk factors for postoperative pulmonary impairments include immobilisation, pain, pain analgesics and, hyperhydration (40, 41). A supine position during intubation results in decreased FRC and an upward shift of the diaphragm, relaxation of the chest wall, altered chest wall compliance, and a shift in blood volume from the thorax to the abdomen. A combination of these factors results in a mismatch in ventilation-perfusion (32). Sternal pain is commonly reported during hospital stay (31, 41, 42) and a worsening of pain correlates with decreased lung function and maximal inspiratory pressure (MIP) during the first postoperative days (41). Pleural drain is an important cause of postoperative pain and shorter duration of pleural drain renders a shorter length of stay in the intensive care unit (ICU) (43).

Lung function
Lung function variables measured in this thesis were vital capacity (VC), forced vital capacity (FVC), inspiratory capacity (IC), forced expiratory volume in one second (FEV1), functional residual capacity (FRC), and total lung capacity (TLC). Lung volume is used synonymously.

The majority of patients undergoing cardiac surgery have almost normal lung function preoperatively (44). In comparison to preoperative values, a mean reduction in lung function is reported to be 35-60% in the first postoperative week (8, 9, 45). Reduced lung function contributes to impaired gas exchange (46). There is an inverse correlation between atelectatic area and arterial oxygenation (PaO2) during the first (11) and second (23) postoperative days. Lung function gradually recovers, but even four months after cardiac surgery a reduction of preoperative values with 6-13% is reported (10). Although lung function decreases after cardiac surgery, it is unclear whether breathing exercises can influence lung function several months postoperatively.

Respiratory muscle strength
Evans et al. (47) suggest a maximal inspiratory pressure (MIP) greater than 50 cm H2O is normal, whereas, in the “Statement on Respiratory Muscle Testing (48), a MIP above 80 cm H2O usually excludes patients with clinically relevant inspiratory muscle weakness, e.g. dyspnea. According to Evans et al. (47), maximal expiratory pressure (MEP) values greater than 60 cm
H₂O are considered normal for producing an effective cough. The majority of cardiac surgery patients have both MIP and MEP above these recommendations before surgery (13, 44, 49). The first week after cardiac surgery, a 35% reduction is reported, compared to preoperative values (44), and 18 months after surgery recovered values of MIP and MEP are reported (50), but the relation between lung function and respiratory muscle strength is unclear.

Physiotherapy treatment in the postoperative period

After cardiac surgery, physiotherapy treatment during hospital stay often consists of early mobilisation, breathing exercises, instruction in efficient coughing techniques and an active range of motions for the shoulder girdle and upper back (19, 51).

Breathing exercises are widely used in postoperative care in hospitals to prevent postoperative pulmonary impairments and their effects (7, 12, 18, 52). The main purpose of different breathing exercises during the postoperative period is to increase lung volume. During the hospital stay, common breathing exercises/techniques for patients with spontaneous breathing include; deep breathing (17), incentive spirometry (IS) (53, 54), breathing exercises with PEP (12, 23), inspiratory resistance-positive expiratory pressure (IR-PEP) (17, 55, 56) and non-invasive ventilation (NIV) (8, 57).

The forced expiratory technique and coughing aimed at mucus clearance are used in a clinical setting but are insufficiently evaluated after cardiac surgery. In Sweden, during hospital stay, mobilisation and breathing exercises with PEP are the first choices of therapy after non-complicated cardiac surgery (19). As no single breathing exercise during the postoperative period has proven superior, there is a lack of consensus regarding the most appropriate breathing exercises (8, 52, 57, 58). As there is limited evaluation of breathing exercises after discharge (50) it is unclear whether breathing exercises, several months after surgery, can influence decreased lung function.

Deep breathing exercises with PEP

Deep breaths are an important part of normal breathing. In clinical practice patients do not naturally sigh and yawn after surgery, probably because of pain. Deep breathing with post-inspiratory pause increases FRC, which in turn increases alveolar stability, can justify the use of deep breaths for the prevention of atelectasis (59). Following cardiac surgery, deep breathing exercises are often recommended for reducing areas of atelectasis and improving oxygenation (23).
The use of PEP in postoperative care specifically aims at increasing lung volume and facilitating mucus clearance. Although the physiological effects of PEP are unknown, the potential increase in FRC is considered essential (60). Deep breathing and PEP can also be used as a mucus clearance technique. As deep breathing increases lung volume, it promotes an effective forced expiratory technique or cough manoeuvre. PEP is purported to promote movement of mucus in patients with cystic fibrosis (61), but data on the function of PEP as a mucus clearance technique in postoperative care are limited.

Different devices for PEP breathing are used in clinical practice; a mask or a mouthpiece is connected to either a resistance nipple to create positive pressure during expiration, or a blow bottle system in which the resistance is created by a water seal. The pressure achieved depends on how the manoeuvre is performed, the applied resistance, and the patient’s expiratory flow. In postoperative care, expiratory resistance is often regulated to achieve 5-20 cm H2O.

Deep breathing exercises with PEP can be performed in different ways. In this thesis the purpose of the breathing exercises with PEP was to increase lung volumes and to facilitate the following deep breath. The deep inhalation was to create a larger lung volume than normal tidal breathing and the holding of the breath after maximal inhalation aimed at improving the possibility of increased gas exchange. Furthermore, PEP during exhalation aimed to stimulate the diaphragm into a favourable position.

Deep breathing exercises with PEP performed every hour during the first four postoperative days after cardiac surgery increase lung function (12) and IS in combination with PEP reduce the incidence of pneumonia and length of hospital stay (62). A six-day postoperative rehabilitation program with PEP breathing in combination with walking training is reported to increase respiratory muscle strength, measured as MIP and MEP, after cardiac surgery (63). However, the recommendations on duration and frequency of breathing exercises differ in both studies and clinical practice.

**Duration and frequency of breathing exercises**

The duration of treatment sessions range from 4 to 40 minutes (6, 55, 56, 58, 62, 64, 65), and there is a lack of evidence for how long after surgery the breathing exercises should continue. The number of breaths range from 5 to 30 breaths per hour (12, 14, 23, 66) and the frequency of daily sessions ranges from once an hour to once a day (6, 12, 23, 66).

The optimal duration and frequency of breathing exercises after surgery has not been fully investigated, thus, it is unclear if deep breathing exercises
with PEP performed after the fourth to fifth postoperative day can influence lung function.

Rationale for this thesis

Approximately 6000 adults undergo open cardiac surgery every year in Sweden (2). Postoperative pulmonary impairments are the most common non-cardiac complication after cardiac surgery and increase both morbidity and mortality.

Breathing exercises are widely used in the postoperative care for preventing or/and treating already developed impairments. Hourly deep breathing exercises with PEP have positive effects on lung function and oxygenation during hospital stay after cardiac surgery. The optimal duration of breathing exercises is unknown and instructions concerning how long patients should continue the breathing exercises after discharges vary within clinical practice.

As impaired lung function occurs in the first postoperative days after cardiac surgery, the factors that might affect lung function should be investigated in an attempt to identify plausible threats to lung function. Furthermore, respiratory muscle strength decreases in the first postoperative week, but it is unknown when patients regain muscle strength after cardiac surgery and if respiratory muscle strength correlates with lung function two months after surgery.

The hypotheses of the present thesis were:

- a higher rate of deep breathing exercise with PEP during the first postoperative days increases oxygenation and lung function
- deep breathing exercises with PEP, performed during the first two postoperative months, decrease pulmonary impairment and improve patient-perceived quality of recovery and health-related quality of life
- age, obesity, smoking, airflow obstruction, and pain negatively influence lung function on the second postoperative day
- respiratory muscle strength and lung function are decreased two months postoperatively
Aims

The overall aim of this thesis was to evaluate the effects of deep breathing exercises with positive expiratory pressure (PEP) and to describe lung function and respiratory muscle strength in patients undergoing cardiac surgery.

The specific aims were:

Study I
To determine the effect of 30 versus 10 deep breaths hourly, while awake, with a PEP-device, on oxygenation and lung function, during the first two days after cardiac surgery.

Study II
To investigate the pre-, peri-, and postoperative factors influencing lung volumes, measured by spirometry, on the second postoperative day after cardiac surgery.

Study III
To evaluate the effectiveness of home-based deep breathing exercises performed with a PEP-device during the first two months after cardiac surgery.

Study IV
To describe respiratory muscle strength, measured as maximal inspiratory pressure and maximal expiratory pressure, before and two months after cardiac surgery.
Methods

Design
This thesis consists of four studies. In Study I 131 patients participated, of which 107, who performed lung function testing, participated in Study II. Study III consisted of 313 participants, of which a subgroup of 36 was included in study IV. In Studies I, II, and IV the participants were recruited from Uppsala University Hospital, Uppsala, Sweden. In Study III, the participants were recruited from Uppsala University Hospital and from Örebro University Hospital, Örebro, Sweden. The Regional Ethical Review Board in Uppsala, Sweden approved the studies (Studies I-II Dnr: 2007/044 and Studies III-IV Dnr: 2007/160). Participants were given verbal and written information about the study and informed consent was obtained from each participant. The study design, sample size, main outcome measures and time of assessment are outlined in Table 1.
Table 1
Overview of study design, sample size, main outcome measurements and time of assessments in Studies I-IV

<table>
<thead>
<tr>
<th></th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
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<tbody>
<tr>
<td><strong>Design</strong></td>
<td>RCT</td>
<td>Descriptive</td>
<td>RCT</td>
<td>Descriptive</td>
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<tr>
<td></td>
<td></td>
<td>Correlative</td>
<td></td>
<td>Correlative</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>131</td>
<td>107</td>
<td>313</td>
<td>36</td>
</tr>
<tr>
<td><strong>Main outcome measurements</strong></td>
<td>Arterial blood gas (PaO₂, SaO₂, PaCO₂) Lung function (VC, FVC, FEV₁, IC) Sternal pain</td>
<td>Lung function (VC, FVC, FEV₁, IC, FRC, TLC) Sternal pain</td>
<td>Lung function (VC, FVC, FEV₁, IC, FRC, TLC) Patient-perceived quality of recovery Health-related quality of life Subjective experience of breathing SpO₂ Thoracic excursion</td>
<td>Lung function (VC, FEV₁, IC) Sternal pain Subjective experience of breathing SpO₂</td>
</tr>
<tr>
<td><strong>Time of assessments</strong></td>
<td>Preoperative and 2nd postoperative day</td>
<td>Preoperative and 2nd postoperative day</td>
<td>Preoperative and 2 months after surgery</td>
<td>Preoperative and 2 months after surgery</td>
</tr>
</tbody>
</table>

FEV₁ = Forced expiratory flow in one second, FRC = Functional residual capacity, FVC = Forced vital capacity, IC = Inspiratory capacity, PaO₂ = arterial oxygen tension, PaCO₂ = arterial carbon dioxide tension, RCT = Randomised controlled trial, SaO₂ = arterial oxygen saturation, SpO₂ = Peripheral oxygen saturation, TLC = Total lung capacity, and VC = Vital capacity
Participants and settings

To be eligible for participation in the four studies, participants had to be >18 years, scheduled for coronary artery bypass grafting (CABG) or valve surgery, and literate in Swedish. Participants were not included if they had angina at rest before surgery (Studies I-II). Furthermore, the participants were excluded after randomisation (Studies I-II) if they were postoperatively artificially ventilated for >15 hours or used continuous positive airway pressure (CPAP) treatment, received aorta balloon treatment, or had a pneumothorax requiring drainage treatment.

For Studies III and IV, patients who had an emergency operation, previous cardiac or lung surgery, kidney failure requiring dialysis or were participant in other ongoing studies were not included. Criteria for not being randomised (Studies III-IV) were intubation time > 24 hours, ICU time > 72 h, severe hemodynamic impairment, pulmonary or neurological complications, requiring dialysis, sternum related infections, sternum instability, mental health disorders, or other complications that could affect the patient’s opportunity to participate in the study (perform deep breathing exercises, spirometry examination and/or respiratory muscle test). Exclusion from the study was determined by the study manager (physical therapist) at each hospital in consultation with the cardiothoracic surgeon or cardiothoracic anaesthesiologist. The recruitment processes for the randomised trials (Studies I and III) are presented in the flow charts in Figure 1 and 2.

Reasons for participant withdrawal after randomisation in Study I were arterial needle out of order and too tired for spirometry (Figure 1). Reasons for participant withdrawal after randomisation in Study III were haemodynamic instability (n=3), pericardial or pleural effusion (n=5), sternal instability/infection (n=2), pain (n=1), cough (n=1), fatigue (n=5), other morbidities (n=2), failure to cooperate (n=1), and unwillingness to participate in the follow-up (n=24).

The characteristics of the participants analysed in Studies I-IV are presented in Table 2.
Figures 1 and 2. Recruitment process for the randomised trials (Studies I and III). *For causes of lost to follow-up in Study III, see text. ABG = arterial blood gas.
**Table 2**

Background characteristics of participants in Studies I-IV, mean ±SD, min-max and number (%).

<table>
<thead>
<tr>
<th></th>
<th>Study I n=131</th>
<th>Study II n=107</th>
<th>Study III n=313</th>
<th>Study IV n=36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, (years)</td>
<td>69 ± 9</td>
<td>68 ± 9</td>
<td>67 ± 10</td>
<td>67 ± 10</td>
</tr>
<tr>
<td>Age, (years) min-max</td>
<td>37 - 86</td>
<td>37 - 86</td>
<td>24 - 89</td>
<td>37 - 83</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>33 (25)</td>
<td>21 (20)</td>
<td>58 (18)</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>98 (75)</td>
<td>86 (80)</td>
<td>255 (82)</td>
<td>32 (89)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27 ± 4</td>
<td>27 ± 4</td>
<td>27 ± 4</td>
<td>27 ± 4</td>
</tr>
<tr>
<td><strong>NYHA</strong></td>
<td></td>
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</tr>
<tr>
<td>I-III A, n (%)</td>
<td>92 (71)</td>
<td>72 (67)</td>
<td>263 (84)</td>
<td>27 (77)</td>
</tr>
<tr>
<td>IIIB-IV, n (%)</td>
<td>26 (20)</td>
<td>20 (19)</td>
<td>23 (7)</td>
<td>7 (20)</td>
</tr>
<tr>
<td>Airflow obstruction, n (%)</td>
<td>16 (12)</td>
<td>14 (13)</td>
<td>108 (35)</td>
<td>8 (22)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>21 (16)</td>
<td>19 (18)</td>
<td>63 (20)</td>
<td>8 (22)</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never, n (%)</td>
<td>64 (49)</td>
<td>55 (51)</td>
<td>135 (43)</td>
<td>20 (55)</td>
</tr>
<tr>
<td>Stopped, n (%)</td>
<td>55 (42)</td>
<td>44 (41)</td>
<td>162 (52)</td>
<td>15 (42)</td>
</tr>
<tr>
<td>Current, n (%)</td>
<td>12 (9)</td>
<td>9 (8)</td>
<td>12 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG, n (%)</td>
<td>55 (42)</td>
<td>54 (50)</td>
<td>106 (34)</td>
<td>16 (45)</td>
</tr>
<tr>
<td>Valve, n (%)</td>
<td>61 (47)</td>
<td>53 (50)</td>
<td>153 (49)</td>
<td>20 (55)</td>
</tr>
<tr>
<td>CABG+valve, n (%)</td>
<td>14 (11)</td>
<td>0 (0)</td>
<td>54 (17)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pleura space entered, n (%)</td>
<td>61 (47)</td>
<td>58 (56)</td>
<td>176 (56)</td>
<td>21 (62)</td>
</tr>
</tbody>
</table>

*Airflow obstruction= FEV₁/(F)VC <0.70 in Studies II-IV, defined as a diagnosis of asthma or COPD in Study I, BMI=Body Mass Index, CABG= Coronary Artery Bypass Grafting, NYHA= New York Heart Association

Note: when numbers in the columns do not add to n or 100%, there is an internal dropout in the background data.*
Surgery, postoperative care and physiotherapy

All participants received general anaesthesia and artificial ventilation with a positive end-expiratory pressure of 5-12 cm H₂O. During anaesthesia and after surgery, all patients inspired oxygen with a concentration of 35-80%. After extubation, all participants received supplemental oxygen (1-5 litres) for maintaining arterial oxygen saturation (SaO₂) above 90%. The participants underwent aortic-, mitral- or tricuspidal valve replacement, CABG, or a combination of these: in Studies II and IV, no participants underwent combination surgery. All participants were administrated analgesics for pain and care according to standard routines at Uppsala University Hospital and Örebro University Hospital.

Preoperatively, the physiotherapists orally informed all participants about the importance of early postoperative mobilisation, deep breathing exercises with PEP, and daily active exercises of the shoulder girdle and upper back. The participants met the physiotherapist once or twice daily during the first postoperative days in hospital. All participants were mobilised according to clinical routine: assisted to sitting as early as possible after surgery and were sitting out of bed and/or standing on the first postoperative day, walking in the room or a short distance in the corridor on the second postoperative day, and walking a longer distance in the corridor on the third postoperative day. Before discharge, all participants were orally informed about the importance of starting physical activity gradually.

Study groups, procedures, and intervention

Studies I-II

Preoperatively, sealed envelopes were used to randomly allocate the participants either to a treatment group (TG) or a control group (CG) for performing deep breathing exercises with PEP with two different durations hourly in the two first postoperative days. The deep breathing exercises with PEP started approximately one hour after extubation and continued during daytime until the morning of the second postoperative day. The TG was instructed to perform 30 deep breaths with PEP hourly (three sets of 10 consecutive deep breaths) and the CG was instructed to perform one set of 10 consecutive deep breaths with PEP hourly. Each set was documented in the medical records by the nursing staff.
Studies III-IV

On the fourth postoperative day participants were randomly allocated, either to a treatment group (TG) or a control group (CG), through sealed envelopes. From the fourth to fifth postoperative day, the TG was instructed to continue with 30 deep breaths with PEP (three sets of 10 consecutive deep breaths) five times a day for two months. The CG was instructed to end the deep breathing exercises with PEP after the fourth to fifth postoperative day. All participants were contacted at home by telephone one month postoperatively. The TG documented each training session in an exercise diary and was contacted and coached by a physiotherapist ten days after surgery for coaching of the breathing exercises.

Deep breathing with PEP

The participants were informed preoperatively by a physiotherapist at the Cardiothoracic Surgery Department, about the deep breathing exercises with PEP. All participants practiced the technique preoperatively together with the physiotherapist. A mouthpiece connected to a three-way valve was used as the PEP-device (“Breathing exerciser”, Rium Medical AB, Åkersberga Sweden) (Figure 3). Preoperatively, expiratory resistance nipples were tested, with a manometer (Figure 3) to create an expiratory pressure of 10-15 cm H₂O. The participants were instructed to perform the exercises in a sitting position, if possible, to perform slow maximal inspirations followed by a two-second inspiratory hold, and a slightly activated expiration through the PEP-device. To minimise the risk of airway closure, the participants were instructed to ending the expiration approximately above FRC.
Figure 3.
Mouth piece with nipple and manometer in the PEP-set (“Breathing exerciser”, Rium Medical AB, Åkersberga Sweden).
Measurements

**Spirometry (Studies I-IV)**

In **Studies I and II**, lung function (VC, FVC, FEV₁, IC) was measured preoperatively and on the second postoperative day with a portable dynamic spirometry (Cardio Perfect dynamic spirometry, Welch Allyn, New York, USA). The measurements were performed at the bedside by two physiotherapists, who were unaware of the participant’s group allocation. The equipment was volume-calibrated every morning prior to measurement. The participants were in a sitting position and used a nose clip. The highest value of three technically satisfactory manoeuvres was retained for VC, FVC and FEV₁, and the mean of three values was used for IC. The highest value of VC and FVC was used for VC in **Study II**.

In **Studies III and IV**, lung function (VC, FVC, FEV₁, IC, functional residual capacity (FRC) and total lung capacity (TLC)) was performed preoperatively and two months postoperatively with a Jaeger MasterScreen PFT/Bodybox (Intramedic AB, Bålsta, Sweden). The measurements were taken at the Department of Clinical Physiology, Uppsala University Hospital and Örebro University Hospital by medical laboratory technicians, who were unaware of the participant’s group allocation. The equipment was calibrated every morning prior to measurements, and during calibration room temperature and barometric pressure were updated. The highest value of three technically satisfactory attempts was retained.

The spirometry was standardised as described in American Thoracic Society/European Respiratory Society (ATS/ERS) "Standardization of spirometry" (67, 68). Predicted values for lung function were related to age, sex, height, and weight in some variables, according to the reference values reported by Hedenström et al. (69, 70).

**Arterial blood gas (Study I)**

On the second postoperative day, arterial blood gas samples were drawn from arteria radialis. The participants had been without supplementary oxygen and did not perform the deep breathing exercises with PEP for at least 10 minutes before measurement. The analyses were performed immediately after the blood gas samples were taken. Arterial oxygen tension (PaO₂), arterial carbon dioxide tension (PaCO₂), and arterial oxygen saturation (SaO₂) were evaluated through ABG analyses (ABL 725, Triolab Sollentuna, Sweden) by a nurse at the Department of Cardiothoracic Surgery,
Uppsala University Hospital, and who was unaware of the participant’s group allocations.

**Respiratory muscle strength (Study IV)**

Maximal respiratory muscle strength (measured as MIP and MEP, expressed in cm H$_2$O) was measured preoperatively and two month postoperatively. The measurements were performed at the Department of Clinical Physiology at Uppsala University Hospital by medical laboratory technicians. The participants were in a sitting position and used a mouthpiece. The participants were instructed to hold the mouthpiece tightly in the mouth to prevent air leakage. MIP was measured near residual volume after a maximal exhalation and MEP was measured near TLC after maximal inhalation. The highest value from three technically acceptable manoeuvres was recorded. The inspiratory- and expiratory muscle tests were standardised as described in ATS/ERS Statement on Respiratory Muscle Testing (48) and assessed by Jaeger Respiratory drive/Muscle strength (Intramedic, Bålsta, Sweden). Predicted values for MIP and MEP were adjusted for age and gender (47).

**Sternal pain (Studies I-IV)**

Sternal pain was quantified on a numeric rating scale (NRS) (71) on the second postoperative day (Studies I-II) and two months after surgery (Studies III-IV). The NRS rates were from 0 (no pain) to 10 (the worst imaginable pain). In Studies I and II the participants rated their sternal pain at rest, while taking a deep breath, while performing deep breathing exercises with PEP, while coughing, and while moving from lying to sitting. In Studies III and IV, the participants rated their pain at rest, while taking a deep breath and while coughing. The validity of NRS for pain intensity has good sensitivity with expected pain intensity change (72).

**Patient-perceived quality of recovery (Study III)**

Patient-perceived quality of recovery was assessed through a Swedish version of quality of recovery score (QoR-40), which is designed to measure the patient’s recovery after surgery and anaesthesia. QoR-40 was measured on the fourth postoperative day and two months after surgery. The QoR-40 is a self-administrated 40-item score measuring five dimensions: physical comfort, emotional status, physical independence, psychological independence and pain. Each item is rated on a five-point Likert scale (for positive items: 1=none of the time, 5=all of the time: for negative items, the scoring was reversed). The possible score on QoR-40 is from 40 (extremely poor quality of recovery) to 200 (excellent quality of recovery) (73, 74). The validity,
reliability, and clinical acceptability of QoR-40 are reported to be good in patients undergoing surgery and general anaesthesia (74).

**Health-related quality of life (Study III)**

Health-related quality of life (HRQoL) was measured through a Swedish version of Short Form-36 (SF-36) (first version) both preoperatively and two months after surgery (75-77). The SF-36 compromising 36 items across eight dimensions: physical functioning (PF), role limitation due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitation due to emotional problems (RE) and mental health (MH). The responses to each question within one dimension are combined to generate a score from 0 to 100, with higher scores indicating better health. In addition, the questionnaire comprises two main domains physical health (PF, RP, BP, GH) and mental health (VT, SF, RE, MH). SF-36 is a self-administrated questionnaire and is widely used in various countries (78). The Swedish version of SF-36 has good reliability and construct validity across general populations (75). Furthermore, SF-36 has established reliability and validity for patients with coronary artery disease (79).

**Subjective experience of breathing and oxygen saturation (Studies III and IV)**

The participants were asked to describe their breathing ability two months after surgery compared to their preoperative breathing ability (improved, unaltered or impaired) (Studies III-IV). Two months postoperatively, the participants in the treatment group in Study III, were asked to score their subjective benefit and/or discomfort of the breathing exercises performed during the postoperative period. Answers were recorded on an arbitrary scale from 0 (not at all) to 3 (very much). The participants were asked to give information on assumed respiratory tract infections/pneumonia and antibiotic treatments during the study period.

Saturation of peripheral oxygen (SpO₂) was measured by a handheld pulse-oximetry (Rad-5v Handheld, Masimo, Irvine, USA) with a probe on the participant’s finger preoperatively and two months after surgery in Studies III and IV.

**Thoracic excursion (Study III)**

Thoracic excursions were measured with a tape (marked in mm) around the circumference of the chest to provide a measure of chest expansion or mobility preoperatively and at two months after surgery. Thoracic excursions were
measured at the level of the xiphoid process, performed with the participants standing with their hands placed on their head and given the instructions ‘Breathe in maximally and make yourself as big as possible’ and ‘Breathe out maximally and make yourself as small as possible’ (80). Thoracic excursion measured as difference in size of thorax between inspiration and expiration was recorded. This method of measuring thoracic excursion is shown to be reliable in healthy volunteers (81).

Demographic and descriptive data were collected from medical record or reported by the participant.
Statistical analyses

All tests were two-sided and considered statistically significant if p<0.05. An overview of the statistical methods used in the studies is presented in Table 3. Sternal pain, quantified with NRS, was considered as ordinal data and therefore, analysed by non-parametric statistics. HRQoL, measured as SF-36, was analysed by parametric statistics.

<table>
<thead>
<tr>
<th>Statistical methods</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
</tr>
<tr>
<td>Sample size calculation</td>
<td>x</td>
</tr>
<tr>
<td>Descriptive statistics</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>x</td>
</tr>
<tr>
<td>Median (min-max)</td>
<td>x</td>
</tr>
<tr>
<td>Distribution of data</td>
<td></td>
</tr>
<tr>
<td>Histogram</td>
<td>x</td>
</tr>
<tr>
<td>Kolmogorov-Smirnov test</td>
<td>x</td>
</tr>
<tr>
<td>Parametric statistics</td>
<td></td>
</tr>
<tr>
<td>Chi-square test</td>
<td>x</td>
</tr>
<tr>
<td>Unpaired Student’s t-test</td>
<td>x</td>
</tr>
<tr>
<td>Paired Student’s t-test</td>
<td>x</td>
</tr>
<tr>
<td>Pearson’s product moment correlation</td>
<td>x</td>
</tr>
<tr>
<td>Multiple regression analyses</td>
<td>x</td>
</tr>
<tr>
<td>Analyses of variance (ANOVA)</td>
<td>x</td>
</tr>
<tr>
<td>Non-parametric statistics</td>
<td></td>
</tr>
<tr>
<td>Mann-Whitney U test</td>
<td>x</td>
</tr>
<tr>
<td>Wilcoxon sign rank test</td>
<td>x</td>
</tr>
<tr>
<td>Kruskal-Wallis test</td>
<td>x</td>
</tr>
<tr>
<td>Spearman’s rank correlation test</td>
<td>x</td>
</tr>
</tbody>
</table>

*SD* = Standard deviation
Sample size calculation

To obtain a power of 80% in Study I, a sample size of 63 participants in each group was needed to detect a difference of 0.5 kPa in PaO₂ between groups, assuming an SD of 1 kPa. The mean difference between groups in Study I was based on absolute values of PaO₂, on the second postoperative day.

To obtain a power of 80% in Study III, a sample size of 160 participants in each group was needed to detect a 10% difference in FEV₁, assuming a SD of 25% two months after surgery. The mean difference between groups in Study III was based on the relative change (postoperative value in % of preoperative value) in each group.

Descriptive statistics

In all studies, descriptive statistics were used for demographic data. Continuous variables were presented as mean and standard deviation (SD). For ordinal data, the median, minimal and maximal values were presented. For nominal data, absolute or relative numbers (%) or both were described. The distribution of data, was evaluated with the Kolmogorov-Smirnov test and histograms.

Parametric statistics

Chi-Square tests were used when analysing groups of nominal data at baseline (Studies I and III). Unpaired Student’s t-test was used in Studies I and III when analysing continuous variables between treatment and control group, and in Study II when calculating the stratified analyses between two subgroups (Gender, BMI >25 versus ≤ 25). In Studies II, III and IV, paired Student’s t-test was used for analyses of paired observations of continuous variables. The univariate analyses of continuous data in Studies II and IV were calculated with Pearson’s product moment correlation. In Study II, dependent variables were postoperative VC, FEV₁ and IC and independent variables were both pre-, peri- and of postoperative character. If an independent variable was associated with impairment in VC, FEV₁ or IC in the univariate analyses with a p≤0.1, it was included in the forward multiple regression analyses in Study II. The dependent variable in Study IV was postoperative MIP and the independent variables were age and BMI. ANOVA was used to analyse differences between more than two subgroups (age and pain groups) in Study II.
Non-parametric statistics

Mann-Whitney U test was used to analyse ordinal data between groups in Studies I and III, Wilcoxon sign rank test was used for analysing of paired observations of ordinal data (Study III), and Kruskal-Wallis test was used for analysing differences between different age groups and sternal pain (Study II). Correlation between ordinal data variables was assessed by Spearman’s rank correlation test (Studies II and IV).
Results

Lung function (Studies I-IV)

Preoperative lung function in Studies I-IV was in accordance with, or just below predicted values, and did not differ between treatment and control groups in Studies I and III. On the second postoperative day after cardiac surgery, less than 40% of predicted lung function was restored (Figure 4). Decreases in VC, FEV$_1$ and IC were approximately 50% of preoperative values (VC 1.64 l, FEV$_1$ 1.20 l and IC 1.40 l) (Study II).

![Figure 4](image)

Lung function, percent of predicted values, preoperatively and on the second postoperative day, mean ± SD, (n=107).

$FEV_1$ = forced expiratory volume in 1 second, $IC$ = inspiratory capacity, $VC$ = vital capacity
Lung function values on the second postoperative day did not differ between the treatment group performing 30 deep breaths with PEP hourly and the control group performing 10 deep breaths with PEP (Study I).

In the multivariate analyses, male gender and high BMI were associated with low postoperative IC (expressed as % of predicted) on the second postoperative day (Study II) (Table 4): this indicated that 33 % of the variance in IC, was explained by gender and BMI. Age was the only variable explaining the variance for VC (Table 4).

**Table 4**
The variables significantly associated with postoperative lung function (expressed as percent of predicted), (n=107). Multivariate analyses.

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>VC B (95% CI)</th>
<th>FEV₁ B (95% CI)</th>
<th>IC B (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male versus female</td>
<td>ns</td>
<td>ns</td>
<td>-20.0 (-25.8,-14.2)</td>
</tr>
<tr>
<td>BMI (kg)/length m²</td>
<td>ns</td>
<td>ns</td>
<td>-0.86 (-1.51,-0.21)</td>
</tr>
<tr>
<td>Age/10 years</td>
<td>3.17 (0.72,5.62)</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

R² 0.07 0.09 0.33

*B=regression coefficient, BMI= Body Mass Index, CI= confidence interval, FEV₁= forced expiratory volume in 1 second, IC= inspiratory capacity, ns= non significant, R²= adjusted R square, VC=vital capacity*

Two months postoperatively, a small (6%, VC, Study III) decrease was found in lung function compared to preoperative values (Study III: VC p < 0.001, Study IV: VC p=0.009). Two months postoperatively, lung function values did not differ between the treatment group performing deep breathing exercises with PEP for two months after surgery and the control group that did not perform any breathing exercises (Study III).

Two months after surgery, a low positive correlation (r=0.35, p=0.04) between lung function (IC) and inspiratory muscle strength (MIP) was found (Study IV).
Arterial blood gas (Study I)

A difference was found in PaO$_2$ and SaO$_2$ between the participants performing 30 deep breaths with PEP and the group performing 10 deep breaths with PEP hourly during the two first days after surgery (Table 5).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment group n=63</th>
<th>Control group n=68</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO$_2$ (kPa)</td>
<td>8.9 ± 1.7</td>
<td>8.1 ± 1.4</td>
<td>0.004</td>
</tr>
<tr>
<td>PaCO$_2$ (kPa)</td>
<td>5.4 ± 0.6</td>
<td>5.5 ± 0.7</td>
<td>0.678</td>
</tr>
<tr>
<td>SaO$_2$ (%)</td>
<td>92.7 ±3.7</td>
<td>91.1 ± 3.8</td>
<td>0.016</td>
</tr>
</tbody>
</table>

PaCO$_2$ = arterial carbon dioxide tension, PaO$_2$ = arterial oxygen tension, SaO$_2$ = arterial oxygen saturation

Respiratory muscle strength (Study IV)

Maximal respiratory muscle strength, measured as MIP and MEP, was in accordance with predicted values both preoperatively and two months after surgery: no decrease in respiratory muscle strength between pre- and postoperative values was found (Table 6).

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Two months after surgery</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIP</td>
<td>78 ± 24 (87 ± 25)</td>
<td>73 ± 22 (81 ± 23)</td>
<td>0.19 (0.22)</td>
</tr>
<tr>
<td>MEP</td>
<td>122 ± 33 (108 ± 28)</td>
<td>115 ± 38 (101 ± 30)</td>
<td>0.18 (0.15)</td>
</tr>
</tbody>
</table>

MEP = maximal expiratory pressure, MIP = Maximal inspiratory pressure
Sternal pain (Studies I-IV)

Coughing was the most painful activity both two days and two months after surgery (Table 7). Two months after surgery, median sternal pain at rest was 0 (Table 7). No differences between groups were found, on either the second postoperative day (Study I), or two months after surgery (Study III).

On the second postoperative day, more pain during mobilisation from lying to sitting was associated with more pronounced decrement in lung function (VC $r=0.33, p=0.001$) (Study II).

Table 7
Sternal pain, measured by NRS, median (min-max) in Studies I-IV.

<table>
<thead>
<tr>
<th></th>
<th>Study I n=131</th>
<th>Study II n=107</th>
<th>Study III n=313</th>
<th>Study IV n=36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two days after surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At rest</td>
<td>0.5 (0-7)</td>
<td>0.2 (0-7.2)</td>
<td>0 (0-7)</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>Deep breathing</td>
<td>3 (0-9)</td>
<td>3 (0-9)</td>
<td>1 (0-7)</td>
<td>0 (0-4)</td>
</tr>
<tr>
<td>PEP breathing</td>
<td>2 (0-9)</td>
<td>2 (0-9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Coughing</td>
<td>4.5 (0-10)</td>
<td>4.5 (0-10)</td>
<td>2 (0-9)</td>
<td>1 (0-8)</td>
</tr>
<tr>
<td>Mobilisation</td>
<td>3.5 (0-10)</td>
<td>3.8 (0-10)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

$NRS=$ Numeric Rating Scale

Patient-perceived quality of recovery, health-related quality of life (Study III) and subjective experience of breathing (Studies III-IV)

The quality of recovery improved in both treatment and control groups (Study III) from base line at fourth postoperative day to two months after surgery ($p<0.001$), but there was no difference between the groups ($p=0.92$). There was improvement in five of the eight aspects of health-related quality of life two months after surgery (Study III), compared to preoperative val-
ues, but no differences between the treatment and the control groups were found (p=0.14-0.74).

Experience of breathing ability improved two months after surgery compared to before surgery, in approximately 50% of the participants (Studies III-IV).

In the treatment group, 72% experienced subjective benefit from the exercises, 5% found no benefit and 23% of participants had no opinion. Discomfort related to the breathing exercises was reported by 2% to a high degree and 17% to some extent. The adverse experience given were related to increased pain and dizziness (Study III).

Oxygen saturation (Studies III, IV), thoracic excursion (Study III), and postoperative pulmonary infections (Study III)

Oxygenation, measured as SpO2, was above 97% both before surgery and two months postoperatively (Studies III and IV) and there was no difference between treatment and control groups in study III (p=0.66).

There were no differences regarding thoracic excursion, either within groups from pre- to two months postoperatively, or between groups at the two-month follow-up (p=0.55) (Study III).

Two months after surgery, 13 participants in the treatment group and 15 participants in the control group reported respiratory infection or pneumonia after surgery (p= 0.60). The self-reported use of antibiotic treatment for respiratory infection/pneumonia was n=6 in the treatment group, and n=13 in the control group (p= 0.07) (Study III).

In Study I, compliance with the breathing exercises did not differ between the treatment and control groups, and on average, 65 ± 5% of the possible sessions were carried out. In Study III, the participants in the treatment group reported they performed the breathing exercises 4 ± 3 times (min-max 3-5) a day postoperatively and each session consisted of 23 ± 12 (min-max 3-60) breaths.
Discussion

Participants performing 30 deep breaths with a PEP device hourly had higher PaO$_2$ and SaO$_2$ than participants performing 10 deep breaths with a PEP device hourly the two fist days after cardiac surgery. Participants who continued the breathing exercises for two months after surgery had no positive effects on lung function, oxygenation, HRQoL, quality of recovery or subjective breathing ability, compared to a control group without breathing instructions after the fourth to fifth postoperative day.

Preoperatively, lung function and respiratory muscle strength were in accordance with predicted values. Two days after surgery, the lung function was reduced to 50% of preoperative values and two months after surgery a small, 6%, reduction of preoperative values was found. Two months after surgery, respiratory muscle strength was in accordance with predicted values.

Effects of deep breathing exercises with PEP

The deep breathing exercises with PEP used in this thesis, were considered to slow down expiration and increase lung volume, and might have prevented or reduced airway collapse. However, there is scarce scientific evidence that breathing exercises with PEP are superior to other breathing exercises in patients undergoing abdominal or thoracic surgery (82). A combination of initial deep inspiration with an expiratory resistance could possibly extend the time with higher lung volume, which may help expand and maintain alveolar and airway patency and re-expansion of atelectasis, as previously demonstrated in the in-hospital phase (12, 23). After cardiac surgery the PEP technique has been combined with incentive spirometry (IS) with positive outcomes on lung function, a 6-minute walking distance, and postoperative pulmonary impairments as well as dyspnea and HRQoL (SF-36) both one, and 18 months after cardiac surgery (50, 62).

The hypothesis in Study I was that a duration of 30 deep breaths (treatment group) with PEP hourly during the two first days after surgery increased oxygenation and lung function, compared to 10 deep breaths hourly (control group). This statement was based on a previous study in which 30 deep
breaths with PEP reduced the atelectatic area and improved the lung function compared to no deep breathing exercises during the first days after cardiac surgery (12). As expected, the treatment group had higher levels of oxygenation than the control group. The duration of 10 and 30 deep breaths with PEP was chosen according to ordinary routines in Sweden (19). Although the absolute difference in PaO$_2$ between the groups was 0.8 kPa and the impairment could be considered small, it could be important because it was positioned in the steep part of the oxygen dissociation curve. Thus, the difference was considered clinically relevant. Alveolar recruitment and re-expansion of lung tissue, due to a longer period at higher volumes, could be a possible explanation as of why an intensified intervention can increase oxygenation. Rothen et al. (83) demonstrate instant re-expansion of collapsed lung tissue with one VC manoeuvre in anaesthetised subjects, however arterial oxygenation can be influenced by non-pulmonary factors, such as cardiac output and efficiency of hypoxic pulmonary vasoconstriction, even if this was not the focus of the present study.

Although oxygenation (PaO$_2$, SaO$_2$) differed between the groups in Study I, lung function did not differ. One explanation could be the dynamic spirometry measured maximal lung function capacity (VC, FVC, FEV$_1$, IC) but oxygenation reflected the volume patient breaths within each breath (tidal volume). A second explanation could be hyperhydration, which might influence oxygenation but not the lung function. A third explanation could be reduced reliability of the spirometry, which requires cooperation from the participants.

Currently, there is no scientific documentation of how long after the surgery patients should continue breathing exercises, or which kind of breathing exercises are most beneficial: the recommendations between hospitals vary (19). The aim of Study III was to evaluate the effectiveness of home-based deep breathing exercises performed with a PEP device during the first two months after cardiac surgery. The hypothesis was deep breathing exercises performed during the first two months after cardiac surgery would decrease pulmonary impairments and improve patient-perceived quality of recovery and HRQoL. The results from the present study indicated home-based deep breathing exercises two months after cardiac surgery had no effect on pulmonary impairments and improve patient-perceived quality of recovery and HRQoL, compared to a regime without breathing exercises after the fourth to fifth postoperative day.

Two studies have evaluated breathing exercises performed after discharge (50, 62). Haeffener et al. (62) and Ferreira et al. (50) have evaluated incentive spirometry (IS) combined with PEP from the first postoperative day to one month postoperatively and found improvement in lung function (62),
sensation of dyspnea after 6 minute walking test, and improved HRQoL, measured as the physical dimension of SF-36 (50). The positive effects achieved in the studies by Haefeler et al. (62) and Ferreira et al (50) could be attributed to the use of IS, which helps the patient visualise the inspiratory volume. However, Hirschorn et al. (84) found no effects of a walking/breathing exercise intervention on vital capacity or HRQoL four weeks after discharge.

Deep breathing exercises in the early postoperative period have positive effects on atelectasis (12, 23), oxygenation (23), lung function (12) and length of in-hospital stay (18). As a gradual spontaneous recovery of lung function occurs after surgery, breathing exercises might not provide any additional effect two months after surgery. The gradual increase in daily activities expected after cardiac surgery might also lower the effects of breathing exercises. An increased frequency or intensity in exercises is likely to be more efficacious, but as 150 breaths a day were performed if the patients followed the instructions, the recommendation of frequency was considered feasible. However, subgroups of patients who are not able to be as physically active as recommended, i.e. patients with a lung disease, smoking history, advanced age, or obesity need to be investigated.

Two months postoperatively, there was improvement in five of the eight aspects of SF-36 in both groups (Study III) compared to preoperative values. However, there were no differences between the treatment and control groups after two months for HRQoL (Study III). These results are in accordance with healthy people of the same age (77). Although physical and mental components of HRQoL (SF-36) are reported to improve from before surgery to three months postoperatively in cardiac surgery patients (85), further studies are needed to investigate the relationship between HRQoL and lung function in these patients.

Compliance with the breathing exercises

During the two first days after surgery (Study I), compliance with breathing exercises did not differ between the groups: on average, 65 ± 5% of the possible sessions were carried out. The participants were instructed and reminded to perform the breathing exercises every hour they were awake. If a participant was unable to perform the deep breathing exercises, or had a feeling of sickness, a member of the staff returned to the patient 15 min later to coach the participant to perform the breathing exercises again. With this kind of supervised treatment, an expected high level of compliance was found. The most common reason for not performing the breathing exercises was tiredness. One limitation might be the non-control of the intensity of the
deep breaths. Even though participants had sternal pain in the first days after surgery compliance with the breathing exercises was good.

In Study III, the participants were supposed to perform the breathing exercises at home for two months. The participants stated they had performed the deep breathing exercises 4 ± 3 times a day postoperatively and each session had consisted of 23 ± 12 breaths. Almost all participants in the treatment group reported the breathing technique was easy to perform. One reason for the lack of effect of the home-based exercises may be compliance with the breathing exercises. Even though participants in the treatment group documented compliance with treatment in an exercise diary, the overall extent of individual training was not possible to monitor. The breathing exercises might have had an effect if they were actually performed according to the protocol. On discharge, participants were instructed in the deep breathing performance but they were not supervised on how to perform the deep breathing exercises at home, and this might contribute to the lack of differences between the groups. Unsupported home-based training could be difficult to comply. In home-based pulmonary rehabilitation programs for patients with COPD 23-31% of participants drop out (86). In Study III, all participants in the treatment group were contacted by telephone by a physical therapist 2 times during the treatment period. In a study by Ferreira et al (50), the patients were weekly contacted by telephone during the study period, in order to emphasize the importance of executing the exercises. Telephone supporting appeared to be an effective strategy to improve adherence in home-based cardiac rehabilitation (87). In the future, telemedicine could perhaps help to individualise the breathing exercises for participants.

Preoperative lung function and respiratory muscle strength

Preoperative lung function in the present studies was in accordance with predicted values (69, 70). The importance of preoperative lung function on the development of postoperative pulmonary impairment is unclear. Mortality rate associated with cardiac surgery is not influenced by the presence and severity of airflow obstruction in patients with COPD, but the incidence of pneumonia and length of hospital stay increase in patients with severe airflow obstruction (28, 88).

For respiratory muscle strength, MIP was 87% and MEP was 108% (expressed as percent of predicted value before surgery) (47). Previous studies have reported similar preoperative values for MIP (13, 44) but lower levels for MEP (13, 44, 49). The variation in MEP values between studies could be
due to differences between the groups studied and the way in which the tests were performed. Few data is reported about the impact of respiratory muscle strength in the preoperative period (49). Rodrigues et al. (49) report an association between MIP or MEP below 70% of predicted value (89) and the need for prolonged invasive mechanical ventilation after cardiac surgery. In elective thoracotomy and laparotomies of the upper abdomen preoperative respiratory muscle strength above 75% of predicted values (89) appears to be protective against postoperative pulmonary complications (90). However, further studies are needed to investigate whether preoperative respiratory muscle strength can be used to identify risk patients for postoperative pulmonary impairments.

Although it is possible to increase the respiratory muscle strength preoperatively in cardiac surgery patients (91-93), the postoperative benefits are unclear. In addition, it is unclear whether inspiratory muscle training (IMT) for patients with verified inspiratory muscle weakness would be more beneficial than for patients without muscle weakness. Thus, further studies investigating if, how, and in which cardiac surgery patients, preoperative IMT would be of benefit are needed.

Postoperative lung function and respiratory muscle strength
Reduced lung function affects gas exchange, and there is an inverse correlation between atelectasis area and arterial oxygenation (PaO₂) during the first postoperative days after cardiac surgery (11, 12). Pulmonary impairments after cardiac surgery create problems and are an important cause of postoperative morbidity.

On the second postoperative day, the 50% decrease in lung function was in accordance with previous studies (8, 9). The causes of reduced lung function are multifactorial and involve a combination of surgery, anaesthesia, immobilisation and pain (31-33, 36). The levels of sternal pain in the first postoperative days were lower than reported in previous studies (31, 40, 42), possible because of the individual pain analgesics regime and early mobilisation. Postoperative pain may be associated with changes in the thorax mechanism, although changes in thoracic excursion were not evaluated on the second postoperative day. Increased sternal pain was associated with more pronounced decrement in lung function, which was in accordance with another study (41).
Even though lung function was decreased two months after cardiac surgery, respiratory muscle strength was not. There was a non-significant reduction in MIP and MEP to 94% of preoperative values. In the early postoperative period, decrement in respiratory muscle strength is reported: Riedi et al. (94) demonstrate an 11% reduction in MIP five days after surgery, and Morsch et al. (44) report a 36% reduction of MIP six days after surgery, compared to preoperative values. One month after cardiac surgery, Stein et al. (63) evaluated a six-day rehabilitation program and found almost recovered MIP. One explanation for the reduced respiratory muscle strength in the early postoperative period after cardiac surgery might be sternal pain, which affects the possibility of performing the muscle strength test properly. The finding of recovered respiratory muscle strength two months after cardiac surgery agreed with results one and 18 months after surgery (50, 63); however, it is still unclear if, and how, muscle strength is affected by surgery. One explanation for the recovery of muscle strength at the two month follow-up might be decreased sternal pain levels or an assumed less sedentary behaviour. A positive correlation between the level of activity in daily life and respiratory muscle strength is reported in healthy elderly population (95). Participants had less pain at the two month follow-up, however, physical level or sedentary behaviour was not assessed.

Although, there was a small reduction in respiratory muscle strength (6%), and the values were in accordance with predicted values at the two months follow-up. This decrease was not statistically significant, but might be useful when treating patients with severe lung function impairment or other morbidities.

The low correlation between MIP and VC, FEV₁, IC, two months after surgery supported respiratory muscle strength and lung function are interrelated: a linear association between MIP and FVC is also reported in healthy men (96) and patients two weeks after cardiac surgery (97). However, further studies are needed to investigate the relationship between lung function and respiratory muscle strength.

Methodological considerations

In evaluation the effects of breathing exercises the focus was primarily on lung function and oxygenation, as in previous studies (7, 12, 13, 18, 62, 98). For practical reasons, lung function was evaluated at the bedside with dynamic spirometry (Study I). However, with dynamic spirometry, FRC could not be measured, which might have been the most important parameter to measure, as it might reflect the normal breathing in each breath. Furthermore, the evaluation of oxygenation through arterial blood gas (ABG), was
chosen because this is a direct measure of PaO\textsubscript{2}, SaO\textsubscript{2}, and PaCO\textsubscript{2} (Study I). ABG was measured two days after cardiac surgery and compared between the groups. ABG before surgery was not practical, as the arterial needle was inserted before surgery when sedation already started. As the between-individual difference in ABG is small, only postoperative measurement was considered appropriate.

Puls-oximetry was chosen to measure SpO\textsubscript{2}, as both the pre and postoperative SpO\textsubscript{2} values were measured outside of the ICU (Studies III and IV). Pulse-oximetry is accurate in the 70-100% saturation range, where readings do not usually vary more than 1-2\% from the measurements obtained by blood gas analysis (99). An uncertainty, of magnitude of 2\%, in the 80-100\% SpO\textsubscript{2} interval has been reported (100).

The reference values chosen for lung function were developed by Hedenström et al (69, 70) and are used in Sweden: these values are based on gender, age and height, and weight in some variables (69, 70).

The reference values for MIP and MEP (Study IV) were based on Evans et al (47), who combined results from other published reference values (89, 101-103) to obtain one regression equation for MIP and one for MEP depending on age, but separate for gender. However, it is important to consider that “normal values” differ between different reference values particularly with MIP and MEP where the normal range is wide (48).

The first and second days after cardiac surgery are critical, and avoiding a return to mechanical ventilation is important. Mobilisation in bed and to sitting and walking is vital for preventing pulmonary impairment in the immediate postoperative care (104). Breathing exercises are important for recovery especially for immobilised patients, and maybe necessary for a quicker rehabilitation. Therefore, evaluation of the duration of deep breathing exercises with PEP on the second postoperative day was chosen (Study I).

In studies III and IV, home-based breathing exercises and respiratory muscle strength were evaluated. As both lung function and respiratory muscle strength are influenced by postoperative pain and restricted thoracic movement (31, 35, 41) and because the healing of the sternum these values were evaluated two months postoperatively.

**External validity**

Participant characteristics in the four studies were similar to the Swedish population of cardiac surgery patients (2): therefore the external validity of
the results were considered to be good. In international studies (6, 49, 62) the samples included younger adults and a greater part of smoking participants. In all four studies, the seriously unwell patients were not included, as the aim was to describe and evaluate deep breathing exercises with PEP in uncomplicated patients, and the selection should be representative. As none of the studies was designed to evaluate subgroups additional studies are required to study groups of special interest.

Clinical implications and further research

The findings from these studies suggest a higher duration of deep breathing exercises with PEP in the first days after cardiac surgery to improve oxygenation. Therefore, duration of 30 deep breaths is recommended as a part of standard care for elective cardiac surgery patients, in addition to mobilisation in the first postoperative days. In clinical practice, and to improve the compliance, the staff has an important role in reminding patients to perform the breathing exercises every hour, it is recommended that each session is recorded in a diary. The breathing exercises with PEP were well tolerated and PEP is a cheap breathing device to use.

The home-based breathing exercise program was also well tolerated, but did not demonstrate any difference in lung function, oxygenation, HRQoL, quality of recovery or subjective breathing ability, compared to a control group two months after cardiac surgery. Further studies are needed to investigate the effects of breathing exercises after discharge, as contraindicative results of home-based breathing exercises have been presented (50, 62). Further studies of subgroups i.e. patients with lung disease, smoking history, advanced age, or obesity would be beneficial for evaluating whether postoperative home-based breathing exercises are beneficial for these groups. Improvements in anaesthesiological and surgical techniques may result in shorter hospital stay (105) and therefore a greater responsibility for the rehabilitation is likely to be home-based. The growing number of older and chronically ill patients is a challenge to surgery and postoperative rehabilitation, and further research should be designed to identify patients who would benefit the most from breathing interventions after discharge.

High BMI and pain are risk factors for decreased lung function on the second postoperative day: therefore, patients with high BMI should receive extra attention during postoperative care. As pain is related to a larger decrease in postoperative lung function, optimal pain relief is important.

Cardiac surgery patients have respiratory muscle strength in accordance with predicted values both before and two months after surgery. Two months
after surgery, there is a low correlation between maximal inspiratory strength and lung function. However, further studies are needed to investigate whether patients with low respiratory muscle strength benefit from inspiratory muscle training and for further analysis of the relationship between respiratory muscle strength and lung function.
Conclusions

• After cardiac surgery, performing 30 deep breaths hourly with PEP during the first two postoperative days improves oxygenation more than performing 10 deep breaths with PEP hourly.

• Home-based deep breathing exercises with PEP performed five times a day (30 breaths every session) for two months after cardiac surgery does not improve lung function, oxygenation, health-related quality of life, quality of recovery, or subjective breathing ability.

• Lung function is decreased by 50%, and is less than 40% of predictive values on the second postoperative day after cardiac surgery. Patients with high BMI are a risk group for decreased postoperative lung function and pain is related to a larger decrease in lung function two days after surgery.

• Respiratory muscle strength is not impaired either before or two months after cardiac surgery. Two months postoperatively, there is a low correlation between maximal inspiratory muscle strength and lung function.
Lungfunktion, andningsmuskelstyrka och effekter av andningsövningar hos personer som genomgår hjärt-kirurgi

Sjukgymnastiska insatser i vården av patienter som genomgår hjärtkirurgi handlar om att förebygga och lindra effekterna av de lungfunktionsned-sättningar som uppstår i samband med operationen. Mobilisering lyfts ofta fram som förstahandsalternativ och till detta adderas andningsövningar, framför allt under den första postoperativa perioden.

En av de vanligast förekommande andningsövningarna, i det postoperativa förloppet, i Sverige, är djupandningsövningar med motstånd på utandningen (Positive Expiratory pressure, PEP). Det är oklart med vilken duration, under de första postoperativa dagarna, andningsövningarna bör utföras. Inte heller är det klart hur länge patienterna bör fortsätta utföra andningsövningar efter de fyra första postoperativa dagarna.

Lungfunktionen är nedsatt initialt efter det kirurgiska ingreppet men också flera månader efteråt. Andningsmuskelstyrkan har rapporterats vara nedsatt den första veckan efter operationen men endast ett fåtal studier har studerat andningsmuskelstyrkan i efterförloppet efter hjärtoperation.

Det övergripande syftet med avhandlingen var att utvärdera effekten av djupandningsövningar med PEP och beskriva lungfunktion och andningsmuskelstyrka hos personer som genomgått hjärtkirurgi.

I det första delarbetet utvärderades effekten av olika duration av djupandningsövningar med PEP de två första dagarna efter operationen. I delarbete II beskrivs lungfunktionen samt faktorer som påverkat lungfunktionen två dagar efter operationen. I delarbete III utvärderades effekten av djupandningsövningarna med PEP utförda från och med den 4-5:e postoperativa dagen och under två månader. I delarbete IV studerades andningsmuskelstyrkan före och två månader efter operationen.
De huvudsakliga fynden i de två randomiserade delarbete

na (I och III) var att 30 djupa andetag med utandning mot motstånd (PEP) varje vaken timme, förbättrar PaO\textsubscript{2} och SaO\textsubscript{2} i jämförelse med om 10 djupa andetag med PEP genomfördes varje vaken timme under de två första dagarna efter operationen. En högre duration av djupandningsövningar med PEP kan rekommenderas de två första dagarna efter hjärtkirurgi till patienter som genomgår elektiv hjärtkirurgi.

Vidare kunde ingen skillnad i lungfunktion, SpO\textsubscript{2}, hälsorelaterad livskvalitet, återhämtning efter operation eller upplevelse av andningen påvisas hos den grupp som fortsatt med andningsövningarna efter den fjärde postoperativa dagen och två månader framöver i jämförelse med en icke-behandlad kontrollgrupp. Fler studier behövs för att utvärdera effekterna av andningsövningar efter att patienterna har lämnat sjukhuset, eftersom motstridiga resultat har rapporterats.

De huvudsakliga fynden i de två deskriptiva delarbete

na (II och IV) i avhandlingen visar att personer som genomgått elektiv hjärtkirurgi har en sänkt lungfunktion med 50 % och att endast 40 % av de förväntade värdena återstår två dagar efter operationen. Personer med högt BMI eller smärta från bröstbenet har en mer uttalad lungfunktionsnedsättning än andra. Vidare påvisar resultaten att andningsmuskelstyrkan är i nivå med de förväntade värdena både före och två månader efter operationen. En svag korrelation mellan andningsmuskelstyrka och lungfunktion påvisades två månader postoperativt.
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References


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