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Changes in Health-Related Quality of Life During Rehabilitation in Patients With Operable Lung Cancer: A Feasibility Study (PROLUCA)

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Abstract

Introduction: Surgical resection in patients with non–small cell lung cancer (NSCLC) may be associated with significant morbidity, functional limitations, and decreased quality of life. **Objectives:** The objective is to present health-related quality of life (HRQoL) changes over time before and 1 year after surgery in patients with NSCLC participating in a rehabilitation program. **Methods:** Forty patients with NSCLC in disease stage I to IIIa, referred for surgical resection at the Department of Cardiothoracic Surgery RT, Rigshospitalet, were included in the study. The rehabilitation program comprised supervised group exercise program, 2 hours weekly for 12 weeks, combined with individual counseling. The study endpoints were self-reported HRQoL (Functional Assessment of Cancer Therapy–Lung, European Organization for Research and Treatment in Cancer–Quality of Life Questionnaire-QLQ-C30, Short-Form-36) and self-reported distress, anxiety, depression, and social support (National Comprehensive Cancer Network Distress Thermometer, Hospital Anxiety and Depression Scale, Multidimensional Scale of Perceived Social Support), measured presurgery, postintervention, 6 months, and 1 year after surgery. **Results:** Forty patients were included, 73% of whom completed rehabilitation. Results on emotional well-being ($P < .0001$), global quality of life ($P = .0032$), and mental health component score ($P = .0004$) showed an overall statistically significant improvement during the study. **Conclusion:** This feasibility study demonstrated that global quality of life, mental health, and emotional well-being improved significantly during the study, from time of diagnosis until 1 year after resection, in patients with NSCLC participating in rehabilitation.

Keywords
lung cancer, exercise, rehabilitation, NSCLC, HRQoL

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Introduction

Health-related quality of life (HRQoL), including physical, psychological, and social functioning, has become an important topic in clinical oncology during and after treatment for lung cancer.[1] Furthermore, many randomized controlled trials include HRQoL measures as a valid and useful endpoint in addition to the traditional clinical outcomes of, for example, mortality and morbidity.[2] As predictor of survival, HRQoL reflects how patients with lung cancer experience the impact of the cancer disease and its treatment on their quality of daily living, thus making HRQoL an important clinical outcome.[3-6]

Kurtz et al[7] describe the connection between physical symptoms as a result of the disease combined with subsequent treatment and decline in physical function and its

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effect on emotional well-being. They find that the severity of cancer-related symptoms, restrictions in social functioning, and radiation treatment were the primary predictors of depressive symptoms in elderly lung cancer patients during the first year after diagnosis. As a result, early identification of psychosocial difficulties in patients with non–small cell lung cancer (NSCLC) is recommended.[7] Lowery and colleges also hypothesize that the decline in HRQoL in post-surgical NSCLC survivors reflects a decline in the physical component more than a decline in the emotional component of HRQoL.[8]

Factors negatively associated with HRQoL following lung cancer surgery include the extent of resection,[9] postoperative pain,[10] degree of comorbidity,[10] distressed mood,[11] and fatigue.[12] Cerfolio and Bryant observed that pneumonectomy leads to worse HRQoL than lobectomy and that preoperative HRQoL is an important predictor of postoperative HRQoL.[13]

Despite a history of lung cancer, most cancer survivors appear to believe that they have good to excellent health, and although many lung cancer survivors already practice behaviors associated with a healthy lifestyle, there are still many who do not and who may need help in selected areas.[14] Engaging in physical activity among lung cancer survivors is particularly low during the early posttreatment period. Lung cancer survivors who currently meet physical activity guidelines report better quality of life in multiple domains than less active individuals, but as most lung cancer survivors do not meet physical activity guidelines, they may benefit from interventions promoting regular physical activity.[1]

The overall aim of this feasibility study was to investigate the safety and feasibility of preoperative and early postoperative rehabilitation in a nonhospital setting, with a focus on exercise, in patients undergoing surgery for lung cancer. Sommer et al[15] recently reported on this topic. The aim of this article is to present HRQoL changes over time before and 1 year after surgery in the same population of patients with NSCLC participating in a rehabilitation program.

Methods

Patients and Settings

The Perioperative Rehabilitation in Operation for LUng CAncer (PROLUCA) feasibility study included 40 patients. The inclusion criteria were the following: biopsy-proven diagnosis of NSCLC, scheduled for surgery with curative intention, at least 18 years of age, World Health Organization performance status 0 to 2,[16] resident of the City of Copenhagen or a surrounding municipality, able to read and understand Danish, and approval by the primary surgeon. The exclusion criteria were the following: presence of metastatic disease or surgical inoperability, diagnosis of lung cancer not verified pathologically, severe cardiac disease, and contraindications to maximal exercise testing as recommended by the American Thoracic Society and by exercise testing guidelines for cancer patients.[17,18]

Procedure

The study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement for nonpharmacologic interventions and the World Medical Association Declaration of Helsinki.[19,20] Written informed consent was obtained from all patients prior to initiation of the study procedure. The study was approved by the Danish National Committee on Health Research Ethics (File No. H-3-2012-028) and the Danish Data Protection Agency (File No. 2007-58-0015).

The study comprised a 4-arm, randomized feasibility design. Patients were referred from 2 medical departments to the Department of Cardiothoracic Surgery, Rigshospitalet.

Baseline assessment included physical tests and patient-reported outcomes and was performed at the Copenhagen Centre for Cancer and Health. HRQoL was assessed at the following 5 time points:

1. Baseline assessments completed as close to the time of diagnosis as possible
2. Presurgery assessments completed the day before surgery
3. Postintervention assessments completed 2 to 14 days after the last exercise session
4. Six-month assessments completed as close as possible to 26 weeks after surgery
5. One-year assessments completed as close as possible to 52 weeks after surgery

Group Allocation (Randomization)

Following the successful completion of baseline assessments, patients were randomized and allocated, on an individual basis, to 1 of the 4 exercise intervention groups, as described in the study protocol by Sommer et al.[21] Around half of the patients initiated the postoperative exercise 2 weeks after surgery and the other half 6 weeks after surgery.

The intention-to-treat analysis included all randomized participants in their randomly assigned allocations. The intervention group assignment was not altered based on the participant's adherence to the randomly allocated study arm. Patients who were lost to follow-up were included in the analysis (intention-to-treat).

Postoperative Exercise Training Protocol

The postoperative exercise intervention was a part of the rehabilitation services available at a rehabilitation center,

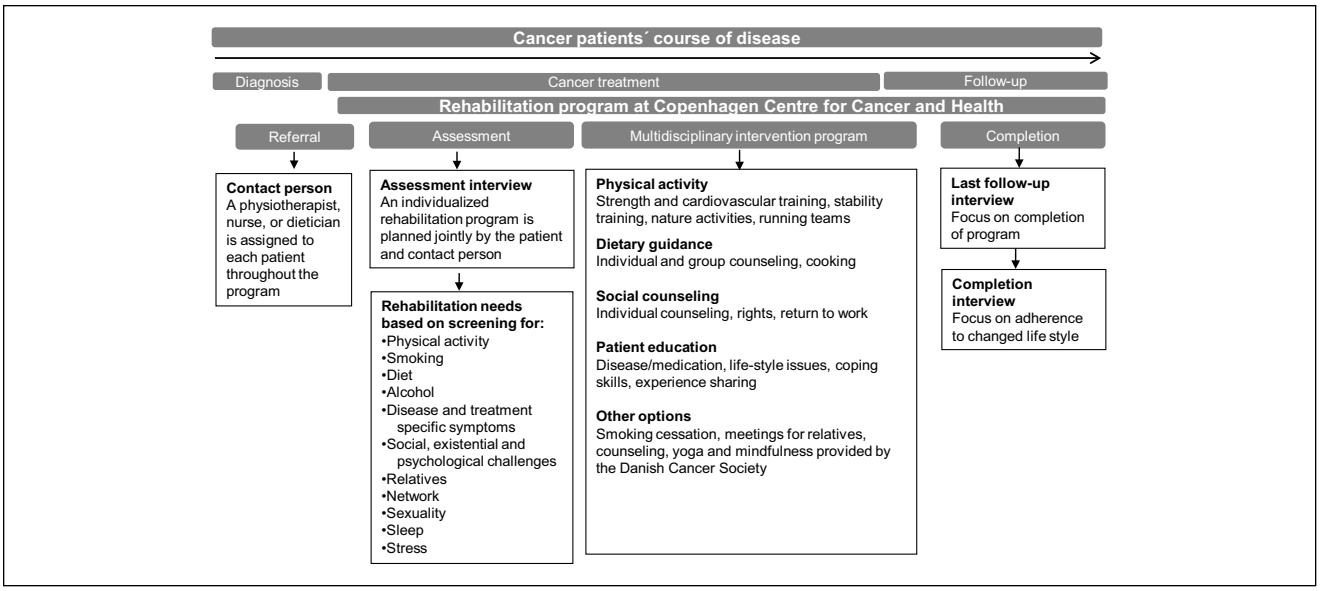

Figure 1. Rehabilitation services available from diagnosis to follow-up at the rehabilitation center.

described in Figure 1. Every participant was initially screened for rehabilitation needs using a professional rehabilitation guide covering the following topics: disease specific, social, network, relatives, psychological, existential, diet, smoking, alcohol, physical activity, sexuality, sleep, and stress. The theoretical framework of the rehabilitation guide was based on World Health Organization on International Classification of Functioning,[22] Bandura's self-efficacy theory,[23] and Miller's motivational interviewing.[24] The exercise intervention consisted of 24 group-based exercise sessions combined with 3 individual counseling sessions and 3 group-based lessons in health-promoting behavior. If the patients had special needs in terms of smoking cessation, nutritional counseling, or patient education, this was also offered as part of the rehabilitation. The postoperative exercise consisted of individually tailored, supervised strength exercise and group-based cardiorespiratory exercise twice a week (60 minutes/session) on nonconsecutive days for 12 weeks, for a total of 24 sessions.

Sommer et al[15] describe the details of the exercise intervention and the physiological results of the PROLUCA feasibility study.

Adherence Considerations

To maximize adherence, several strategies were employed: telephone-based follow-up, free parking in front of the center, and remuneration for transport expenses. A high degree of scheduling flexibility allowed patients to perform tests at a convenient time to allow space for competing demands such as medical appointments, work, and family commitments.

Patient-Reported Outcomes

Patient-reported outcomes included HRQoL, symptoms and side effects, anxiety and depression, well-being, distress, lifestyle, and social support, which were measured at 5 time points: baseline, presurgery, postintervention, and 6 months and 1 year after surgery. HRQoL was assessed using the integrated system of the European Organization for Research and Treatment in Cancer (EORTC), which is often used in cancer patients participating in international clinical trials and devised through collaborative research. The EORTC QLQ (Quality of Life Questionnaire) C30 assesses patient symptoms and HRQoL in cancer patients.[25] Symptoms and side effects were further assessed using the EORTC-QLQ-LC (Lung Cancer) 13, which is an additional page to the EORTC-QLQ specifically designed to cover a wide range of lung cancer patients varying in disease stage and treatment modality.[26] EORTC measures single items, and the scoring scale ranges from 0 to 100. A high score for a functional scale represents a high/healthy level of functioning, and a high score for the global quality of life represents a high HRQoL. However, a high score for a symptom scale/item represents a high level of symptomatology or problems.[25,26] A difference of 5 to 10 points in the scores represents a small change, 10 to 20 points a moderate change, and greater than 20 points a large clinically significant change from the patient's perspective.[27]

HRQoL was also assessed using the Functional Assessment of Cancer Therapy–Lung (FACT-L) scale. FACT-L contains 4 subscales for physical well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), and functional well-being (7 items), while

the 7-item FACT-L lung cancer subscale (LCS) assesses symptoms commonly reported by lung cancer patients (eg, shortness of breath, loss of weight, tightness in chest). The trial outcome index (TOI) is derived by adding scores on the physical well-being and functional well-being subscales to the lung cancer subscale.[28] All FACT-L items are rated on a 5-point Likert-type scale ranging from 0 = "Not at all" to 4 = "Very much," and scores range from 0 to 24 (emotional well-being), 0 to 28 (other 4 subscales), 0 to 84 (TOI), and 0 to 136 (total score).[29,30] Higher scores represent better quality of life or fewer symptoms.[28] General well-being was assessed using the 36-item Short Form Health Survey (SF-36) version 1, standard recall (4 weeks). SF-36 includes 8 scales measuring general health with 2 summary scales: physical and mental component scales.[28,31] Psychological well-being was assessed using the Hospital Anxiety and Depression Scale (HADS), which has 14 items designed to measure general anxiety and depression in patients with physical illness.[32] The National Comprehensive Cancer Network (NCCN) Distress Thermometer is a validated measure of distress and consists of a single item, with responses ranging from 0 to 10.[33] The NCCN Distress Thermometer was used to assess distress, and the Multidimensional Scale of Perceived Social Support (MSPSS) was used to assess social support. MSPSS is a 12-item scale that uses a 7-point Likert-type scale ranging from 1 = "Very strongly disagree" to 7 = "Very strongly agree." The scale yields 3 subscale scores for family, friends, and significant others, in addition to a total score, which is verified with a confirmatory factor analysis.[34] In addition to the MSPSS questionnaire, 7 questions on support from other cancer patients were collected. In other cancer studies, the above-mentioned validated instruments were found appropriate and easy to administer.[33,35-37]

Statistical Analysis

Repeated-measures analysis of variance was performed using the MIXED Procedure, SAS/STAT software, version 9.3. The clustered nature of the data was taken into account by specifying a heterogeneous autoregressive (1) covariance structure. The overall effect of time was evaluated using an F test. Estimated scale mean scores are reported as mean with corresponding 95% confidence intervals (CIs) and compared to reference data when available. We used Danish reference data for the EORTC QLQ-C30[38] and the SF-36.[39] For smoking, alcohol, and physical activity habits we used logistic, Poisson, and multinomial logistic regression models, respectively. The clustered nature of the data was taken into account using generalized estimating equations,[40,41] as implemented in the GENMOD procedure in SAS/STAT software, version 9.3. Wald tests were used to evaluate changes over time.

Results

Study Population and Baseline Characteristics

A total of 180 patients referred for surgery were screened for eligibility, 124 of whom were eligible. Forty patients (32%) were included and randomized in accordance with the flow chart shown in Figure 2. Table 1 shows the characteristics of the 40 patients included in the study. The mean age was 68 years, 15% were currently employed, and the majority were retired (Table 1). The most frequent comorbidities were hypertension, dyslipidemia, rheumatic disease, and chronic obstructive pulmonary disease (COPD). Five patients had no comorbidity, and 16 patients had more than 2 comorbidities. At baseline, 70% were ex-smokers and 25% were currently smoking. Eleven patients reported that their level of alcohol consumption was above 7 units per week for females and above 14 units per week for males, which is the maximum weekly intake recommended by the Danish National Board of Health. Five patients reported they were sedentary before time of diagnosis. Nine patients (22%) underwent thoracotomy, and 31 (78%) patients had video-assisted thoracic surgical resection (VATS). Thirteen (33%) received postoperative (adjuvant) chemotherapy. The extent of resection was lobectomy (83%), pneumonectomy (2%), bilobectomy (5%), wedge resection (8%), and VATS segmental resection (2%).

The 2 most frequent reasons given by patients for not attending the study were either logistical problems or concerns about the coming surgery (Figure 2).

Dropouts

Eleven patients dropped out during the intervention, primarily due to lack of motivation or due to side effects to adjuvant chemotherapy. There was no difference between completers and dropouts regarding demographic data, stage of disease, or type of surgery.

Changes in Health-Related Quality of Life

The FACT-L emotional well-being showed a statistically significant improvement across the 5 time points (Figure 3A, $P < .0001$). The results from FACT-L lung cancer subscale, TOI, and the total score also showed a statistically significant improvement across the 5 time points (Figure 3B, $P = .0421$; Figure 3C, $P = .0376$; and Figure 3D, $P = .0163$). The EORTC-QLQ-C30 functional scales showed increasing levels of global quality of life and emotional well-being (Figure 4A, $P = .0032$, and Figure 4B, $P = .0006$). Results from the SF-36 showed improvements for the mental health component score (Figure 5A, $P = .0004$) and for the domain scores for role physical function, vitality, and mental health during the study period (Figure 5B,

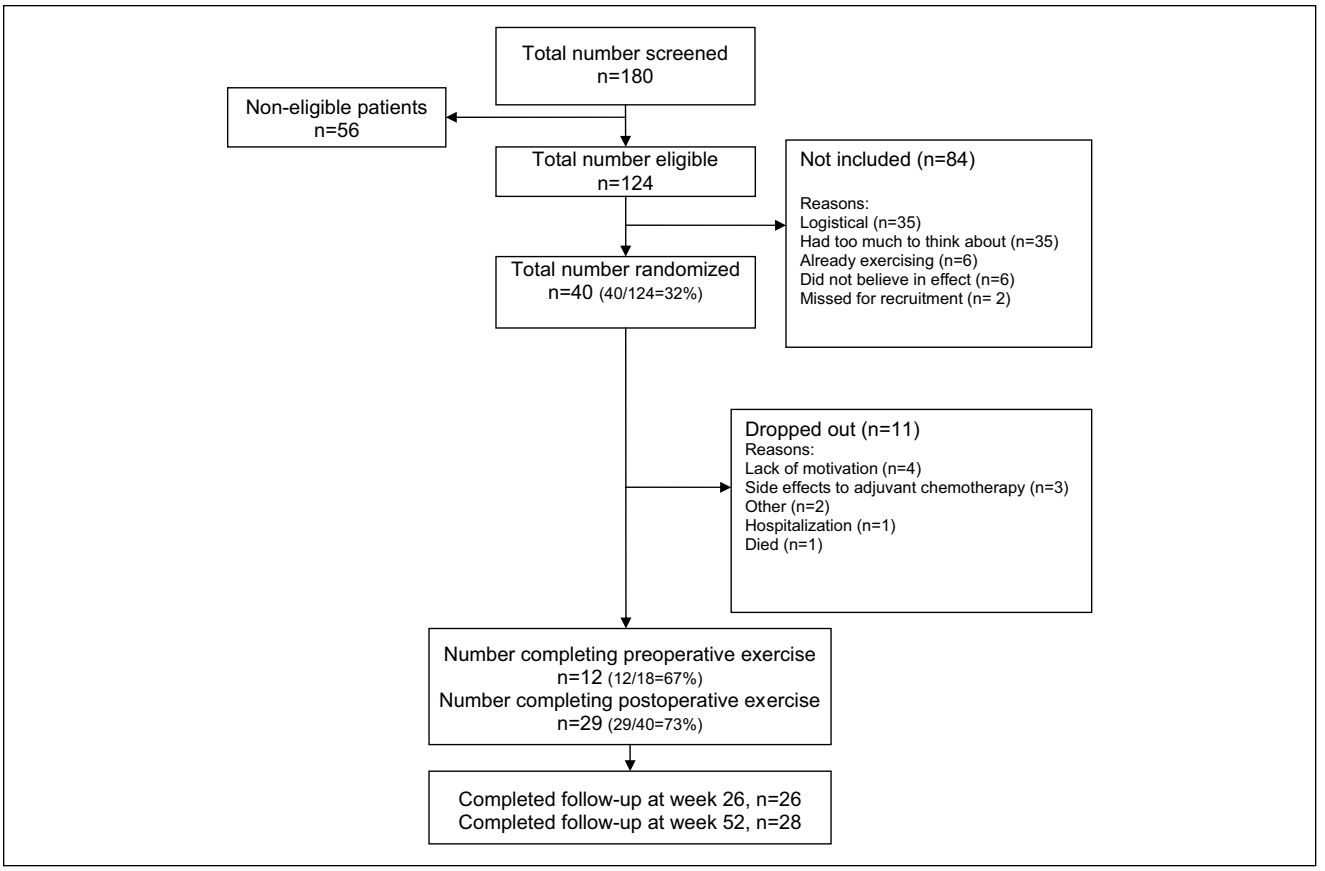

Figure 2. Patient flow chart for Perioperative Rehabilitation in Operation for LUng CAncer (PROLUCA) feasibility study.

$P = .0072$; Figure 5C, $P = .0110$; and Figure 5D, $P = .0001$, respectively). The SF-36 domain bodily pain showed no overall statistically significant difference between the 5 time points ($P = .1069$), but post hoc comparisons indicated that scores 6 months and 1 year after surgery were higher than the baseline scores (7.3 and 7.6 points, respectively).

Changes in Symptom Scales

Results for the 5 time points in EORTC symptom scales showed no differences across time points in any of the reported symptoms (results not shown).

Changes in Level of Anxiety, Depression, and Distress

Results from HADS and Distress Thermometer demonstrated a significant reduction in the level of anxiety, depression and distress, role of distress during the study period, and the greatest reduction was found 6 months after surgery (Figure 6A, $P = .0003$; Figure 6B, $P = .0062$; Figure 7A, $P = .0006$; and Figure 7B, $P = .0005$).

Changes in Perceived Social Support

The changes in perceived social support showed no overall statistically significant difference between the 5 time points in any of the subscales for support from significant others, family, friends, or in the total sum across the 12 items (results not shown). The baseline scores for all MSPSS subscales were high at baseline (Table 1) and during the study (results not shown). Changes in perceived support from other cancer patients were statistically significant during the study period (Figure 8; $P < .0001$).

Changes in Smoking, Alcohol, and Physical Activity Habits

The changes in smoking, alcohol and physical activity habits showed a reduction in the number of patients currently smoking from 25% at baseline to 5% after the intervention, followed by an increase to 12% one year after surgery. These percentages did not differ significantly (Wald test $\chi^2 = 8.47$, degrees of freedom (df) = 4, $P = .0759$, P for trend .0579). A similar pattern was seen in connection with alcohol consumption. At baseline, 28% consumed more alcohol than recommended by the Danish National Board

Table 1. Baseline Characteristics.

Variables	Total N = 40
Age, years, median (range)	68 (36-85)
Female, n (%)	24 (60%)
Body mass index, kg/m^2, mean (SD)	25 (5)
Academic professional degree <3 years, n (%)	17 (43%)
Smoking history	
Currently smoking, n (%)	10 (25%)
Never smoked, n (%)	2 (5%)
Ex-smoker, n (%)	28 (70%)
Years smoking, mean (SD)	41 (15)
Presence of comorbidity (5 patients had none)	
Hypertension, n (%)	15 (38%)
Dyslipidemia, n (%)	9 (23%)
Diabetes, n (%)	6 (15%)
Atrial fibrillation, n (%)	2 (5%)
COPD, n (%)	8 (20%)
Rheumatic diseases, n (%)	12 (30%)
Other type of cancer, n (%)	6 (15%)
Depression, n (%)	4 (10%)
Medication, number of drugs, median (range)	3 (1-6)
FACT-L health-related quality of life scores, mean (SD)[a]	
Physical well-being	24.6 (3.7)
Social/family well-being	22.6 (5.8)
Emotional well-being	17.0 (5.1)
Functional well-being	19.1 (7.3)
FACT-L lung cancer subscale	20.8 (5.0)
Trial outcome index	64.9 (14.0)
Total score	104.7 (19.9)
EORTC-QLQ functional scales, mean (SD)[b]	
Global quality of life (global health status)	65.6 (24.0)
Physical functioning	88.0 (17.4)
Role functioning	90.2 (17.8)
Emotional functioning	75.6 (20.3)
Cognitive functioning	88.9 (16.8)
Social functioning	92.7 (15.2)
SF-36 health-related quality of life scores, mean (SD)[b]	
Physical component score	50.3 (10.2)
Mental component score	43.7 (13.2)
Physical function	82.3 (21.1)
Role physical function	65.3 (42.3)
Bodily pain	75.9 (19.1)
General health perception	60.6 (17.2)
Vitality	61.0 (25.8)
Social functioning	85.5 (18.7)
Role emotional	62.2 (37.8)
Mental health	66.5 (21.9)
MSPSS, mean (SD)[c]	
Significant other	6.2 (1.4)
Family	6.2 (1.4)
Friends	6.0 (1.4)
Total MSPSS	6.2 (1.2)
Support from other patients with cancer	2.5 (1.6)
HADS, mean (SD)[d]	
Anxiety	5.8 (5.1)
Depression	6.2 (3.1)
NCCN Distress Thermometer, mean (SD)[e]	
Distress	4.4 (4.0)
Distress role	3.6 (3.5)

Abbreviations: COPD, chronic obstructive pulmonary disease; EORTC-QLQ, European Organization for Research and Treatment in Cancer–Quality of Life Questionnaire; FACT-L, Functional Assessment of Cancer Therapy–Lung; HADS, Hospital Anxiety and Depression Scale; MSPSS, Multidimensional Scale of Perceived Social Support; NCCN, National Comprehensive Cancer Network; SF-36, Short-Form Health Survey; SD, standard deviation.

[a]Score range 0 to 24, 0 to 28, 0 to 84, 0 to 136. High scores indicate good health-related quality of life or fewer symptoms.

[b]Score range 0 to 100. High scores indicate good health-related quality of life.

[c]Score range 0 to 7. High scores indicate high level of support.

[d]Score range 0 to 21. High scores indicate high levels of anxiety and depression.

[e]Score range 0 to 10. High scores indicate high levels of distress and role of distress.

of Health. This amount was reduced to 7% postintervention, followed by an increase to 14% one year after surgery. Comparing the number of drinks per week using Poisson regression did not indicate significant differences across the 5 time points (Wald test $\chi^2 = 4.33$, $df = 4$, $P = .3634$, P for trend .1371). Physical inactivity dropped from 15% at baseline to 4% one year after surgery. Comparing the distribution of the ordinal variable in multinomial logit regression models adjusted for the level 3 months before diagnosis did not indicate significant differences across the 5 time points (Wald test $\chi^2 = 8.10$, $df = 4$, $P = .0881$, P for trend .6985).

Discussion

This feasibility study demonstrated that global quality of life and domains representing emotional or mental well-being improved significantly during the study period, from prior to surgery until 1 year after resection, in patients with NSCLC participating in rehabilitation.

Results from the EORTC-QLQ-C30 showed that global quality of life improved significantly during the study and to a level higher than the level in an age-matched Danish cohort.[38] Braun et al found that, in patients with NSCLC, every 10-point increase in global quality of life was associated with a 9% increase in survival.[5] The present study found a 17-point increase in the domain global quality of life from baseline to 6 months after surgery and a 13-point

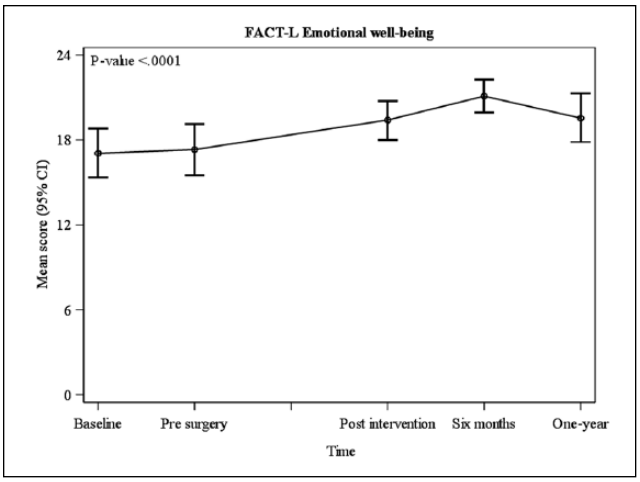

Figure 3A. Functional Assessment of Cancer Therapy–Lung (FACT-L) Emotional well-being.
Score range 0 to 24. High scores indicate good health-related quality of life. CI, confidence interval.

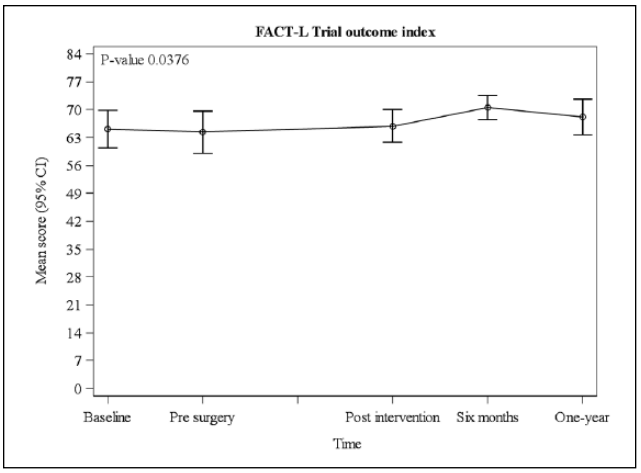

Figure 3C. Functional Assessment of Cancer Therapy–Lung (FACT-L) Trial Outcome Index.
Score range 0 to 84. High scores indicate good health-related quality of life. CI, confidence interval.

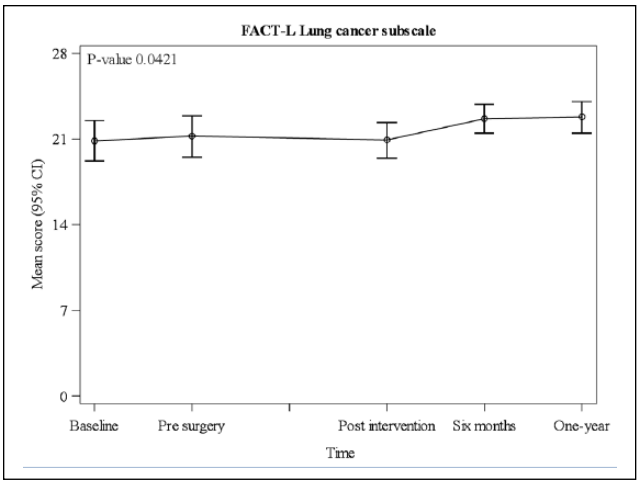

Figure 3B. Functional Assessment of Cancer Therapy–Lung (FACT-L) Lung cancer subscale.
Score range 0 to 28. High scores indicate low level of symptoms reported. CI, confidence interval.

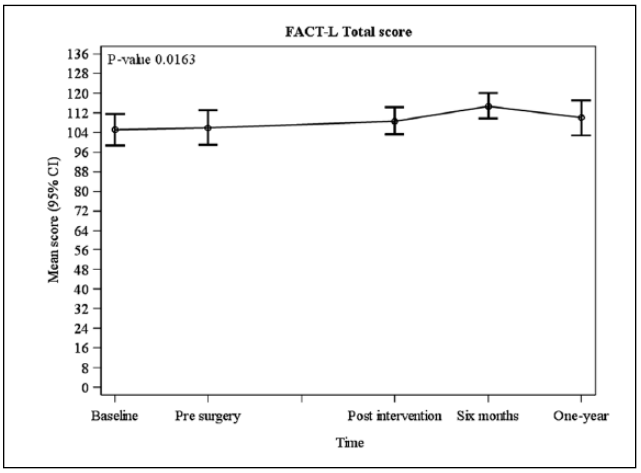

Figure 3D. Functional Assessment of Cancer Therapy–Lung (FACT-L) Total score.
Score range 0 to 136. High scores indicate good health-related quality of life. CI, confidence interval.

increase from baseline to 1 year after surgery. According to a study by Osoba, a difference of 5 to 10 points represents a small significant change, 10 to 20 points a moderate change, and greater than 20 points a larger clinically significant change from the patient's perspective.[27] Therefore, the improvement found in the present study is interpreted as a moderate change.

For 178 patients operated for NSCLC with no subsequent recurrence, Kenny et al found a substantial initial deterioration in the physical dimensions and global quality of life, with an improvement to baseline levels between hospital discharge and 2 years after diagnosis.[42] The study by Kenny et al was, in contrast to this study, not designed to evaluate participation in rehabilitation but examined the role of position emission tomography in preoperative assessment.[42] The findings in the present study showed an improvement from baseline to postintervention, with an additional increase 6 months after surgery, in global quality of life, which may be interpreted as an effect of the present rehabilitation program, although the lack of a control group weakens the conclusion.

In the present study, results from the SF-36 demonstrated that the mental health component score and the scores from the following domains: role physical function, vitality, and

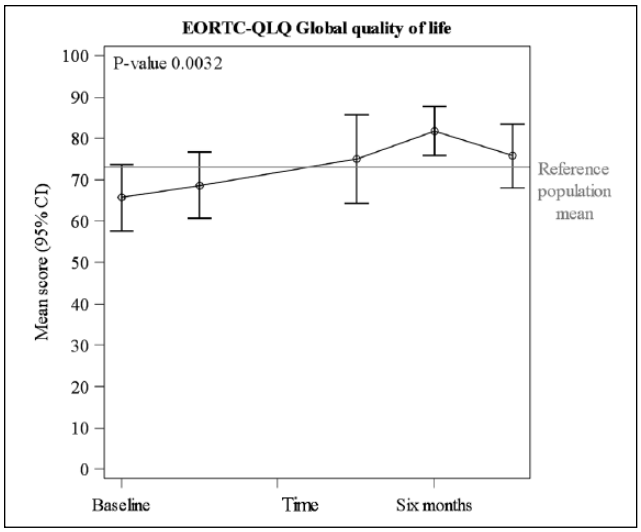

Figure 4A. European Organization for Research and Treatment in Cancer–Quality of Life Questionnaire (EORTC-QLQ) Global quality of life.
Score range 0 to 100. High scores indicate good health-related quality of life. CI, confidence interval.

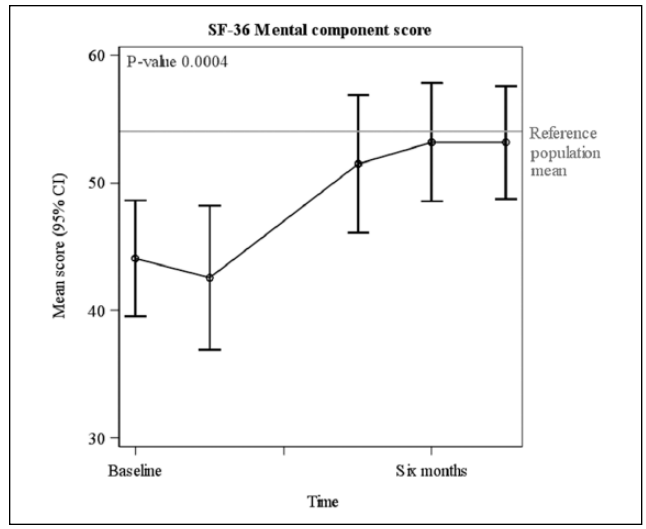

Figure 5A. Short Form Health Survey (SF-36) Mental component score.
Score range 0 to 60. High scores indicate good health-related quality of life. CI, confidence interval.

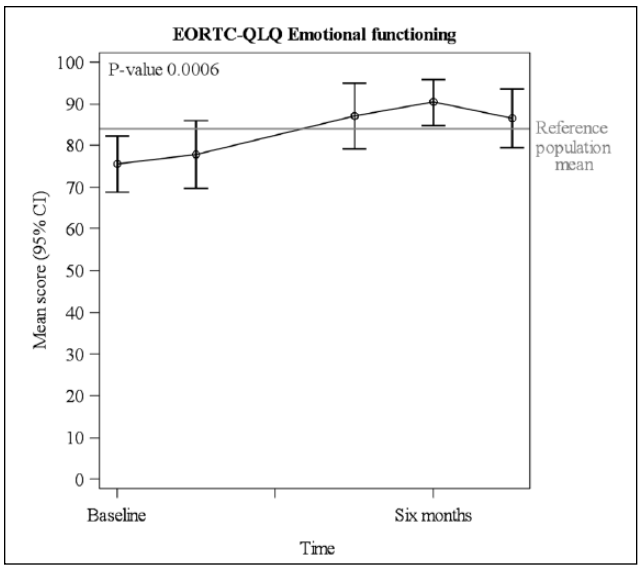

Figure 4B. European Organization for Research and Treatment in Cancer–Quality of Life Questionnaire (EORTC-QLQ) Emotional functioning.
Score range 0 to 100. High scores indicate good health-related quality of life. CI, confidence interval.

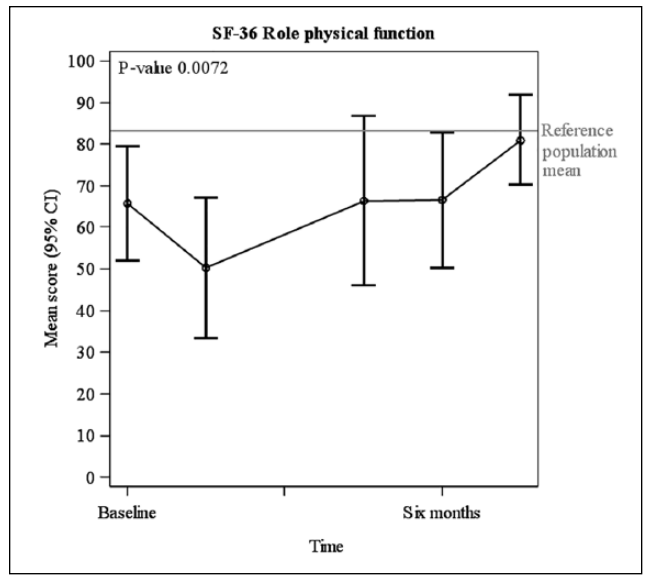

Figure 5B. Short Form Health Survey (SF-36) Role physical function.
Score range 0 to 100. High scores indicate good health-related quality of life. CI, confidence interval.

mental health improved significantly during the study period. The domain bodily pain showed that the patients experienced less pain over time during the study period and also less pain compared to an age-matched Danish cohort.[39] Brocki et al confirm this improvement postintervention and also found an effect in the bodily pain domain related to a supervised outpatient exercise program. They also found a trend in favor of the intervention for role physical function and the physical health component score.[43] In contrast to our findings, the tendency in the study of Brocki was reversed at 12 months after surgery, with the control group presenting overall slightly better measures.[43]

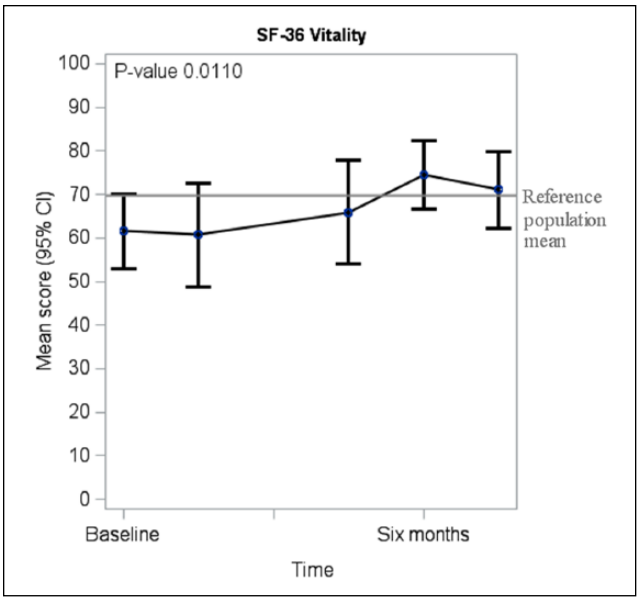

Figure 5C. Short Form Health Survey (SF-36) Vitality.
Score range 0 to 100. High scores indicate good health-related quality of life. CI, confidence interval.

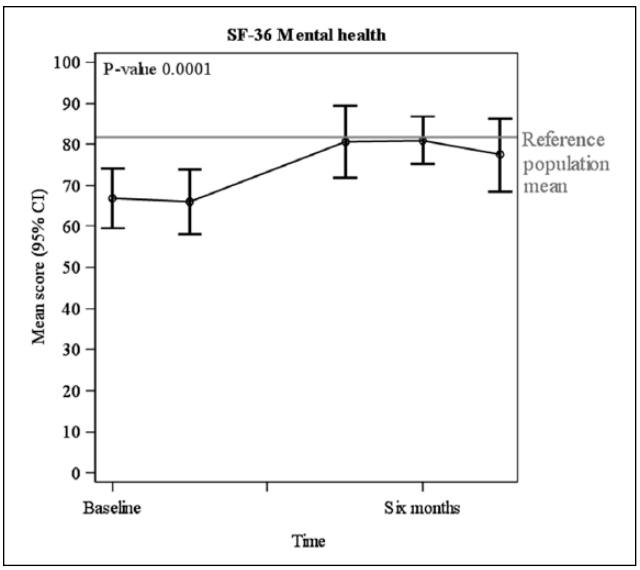

Figure 5D. Short Form Health Survey (SF-36) Mental health.
Score range 0 to 100. High scores indicate good health-related quality of life. CI, confidence interval.

Brunelli et al found that patients with NSCLC were below the norm population in the physical health component score. In addition, their study showed a decline in the same score 1 month after surgery returning to preoperative values 3 months after surgery.[44]

In contrast to the findings of Brunelli et al, the results from this study showed that the physical health component

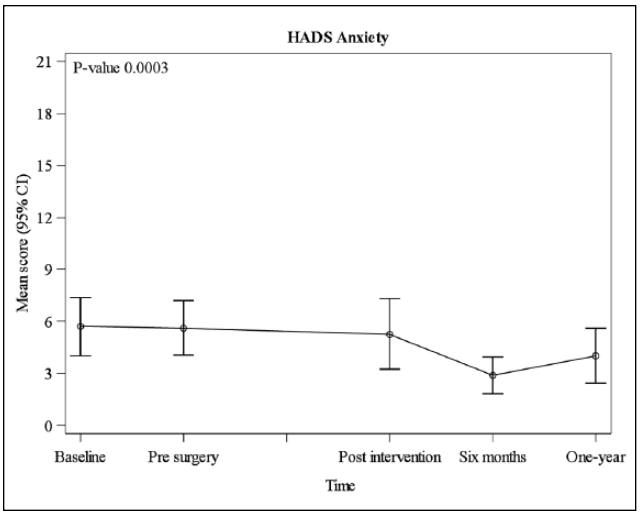

Figure 6A. Hospital Anxiety and Depression Scale (HADS) Anxiety.
Score range 0 to 21. Low scores indicate low level of anxiety. CI, confidence interval.

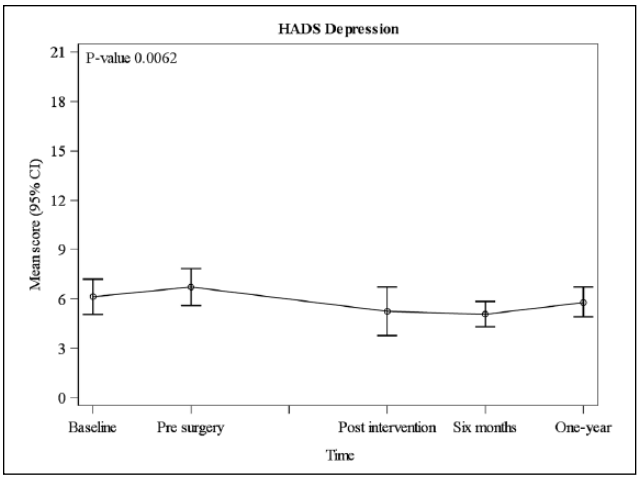

Figure 6B. Hospital Anxiety and Depression Scale (HADS) Depression.
Score range 0 to 21. Low scores indicate low level of depression. CI, confidence interval.

score was higher at baseline and 1 year after surgery compared to an age-matched Danish cohort.[39] A reasonable explanation could be selection bias, as we cannot rule out that patients participating in this study represent a group with better physical fitness than the group refusing to participate. The mental health component score improved form baseline level below the norm population to the same level as the norm population 6 months after surgery. Moller and Sartipy found in a cohort of patients with NSCLC that mental health component summary scores below the mean

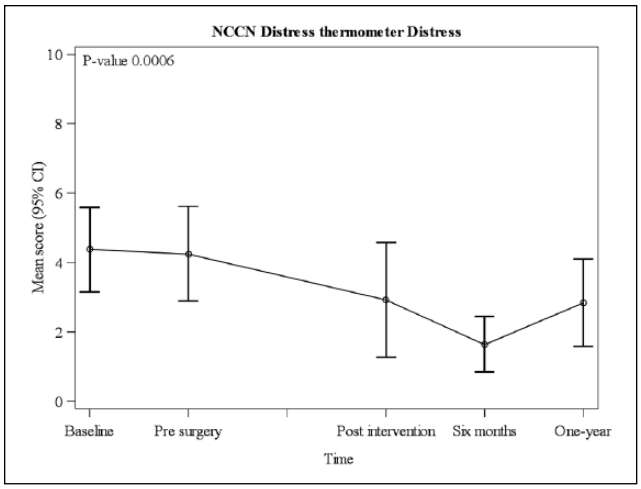

Figure 7A. National Comprehensive Cancer Network Distress Thermometer Distress.
Score range 0 to 10. Low scores indicate low level of distress. CI, confidence interval.

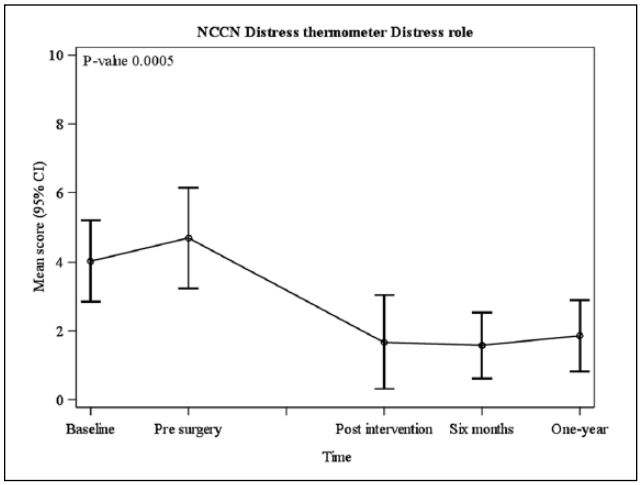

Figure 7B. National Comprehensive Cancer Network Distress Thermometer Distress role.
Score range 0 to 10. Low scores indicate that the distress plays a low role. CI, confidence interval.

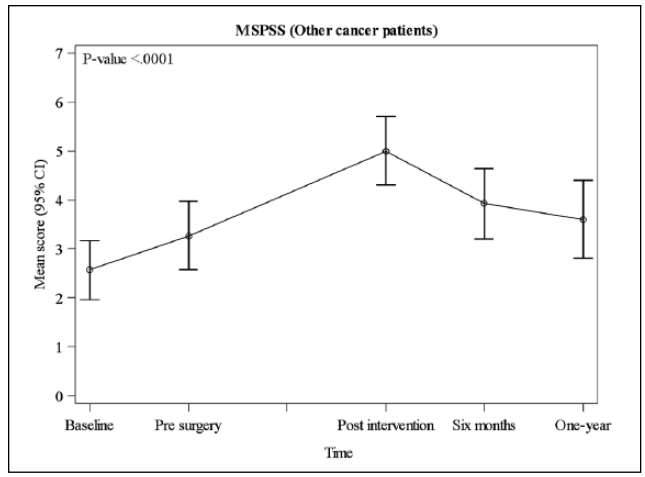

Figure 8. Multidimensional Scale of Perceived Social Support (MSPSS) Support from other cancer patients.
Score range 0 to 7. Low scores indicate low social support from other cancer patients. CI, confidence interval.

of the age- and gender-matched normal population were associated with a 3-fold increase in the risk of death.[6]

Results from FACT-L showed that emotional well-being improved significantly during the study. The improvement in emotional well-being postintervention is similar to the effect found in patients with advanced lung cancer participating in rehabilitation.[45]

The improvement in TOI (5 points) and lung cancer subscale (2 points) are according to Cella et al clinically meaningful for patients with NSCLC.[46] Cella and colleagues demonstrated that a 2- to 3-point change in LCS and a 5- to 6-point change in TOI was a clinically meaningful change in patients with NSCLC.[46] As this feasibility study is underpowered, no conclusions can be drawn.

As only 33% of the patients (n = 13) were treated with chemotherapy, it is not possible in this study to evaluate the influence of chemotherapy on HRQoL.

According to Zigmond and Snaith, HADS anxiety and depression subscale scores can be classified as normal (0-7), mild (8-10), moderate (11-14), or severe (15-21).[32] The levels of anxiety and depression in the present study are therefore judged to be normal, but the level of anxiety still showed a decrease in the anxiety score between baseline and 6 months after surgery, which reversed between 6 months and 1 year after surgery without reaching the baseline level. This tendency was not observed in levels of depression.

Results from distress (NCCN Distress Thermometer) showed the same pattern as HADS regarding anxiety, the scores showing parallel fluctuations. This indicates a correlation between anxiety and distress, which was also found in a study by Bidstrup et al.[33] The present study showed that the level of anxiety decreased 6 months after surgery, but reversed 1 year after surgery without reaching the baseline level. This pattern was not found in patients with COPD, where the level of anxiety increased with time.[47]

According to parameters from a study by Zimet et al, concerning social support, the results from the present study can be interpreted as high social support at baseline and during the study period.[48] Zimet et al found that a mean score ranging from 1 to 2.9 represents a low level of support, a score of 3 to 5 moderate support, and 5.1 to 7 high support.[48] This is in contrast to a Danish study by Quist et al that involved a similar intervention where social well-being decreased.[45] The patients participating in their study had advanced lung cancer, and their condition and disease stage differ from the

patients participating in the present study. The significant increase in support from other cancer patients during our study could hypothetically have a connection to the improvement in emotional well-being and reflects the value of establishing a social network. A qualitative study by Missel et al, in the present population, found that group training had social benefits, such as patients experiencing a sense of belonging and that exercising with others in a similar circumstance is meaningful due to the sense of community created.[49]

The level of patients reporting being sedentary dropped from 15% to 4% during our study. Granger et al found that 40% of patients with NSCLC did not meet physical activity recommendations at time of diagnosis and after 6 months; without a specific exercise intervention, these patients experienced a decline in physical activity, functional capacity, and strength compared to healthy individuals.[50] Cavalheri et al found that patients with NSCLC treated with lobectomy were more sedentary than healthy age-matched controls.[51] Results from the present study on smoking and alcohol habits showed a decrease in the number of smokers and patients with an intake above the recommended amount from baseline to postintervention, but this effect reversed 1 year after surgery without reaching the baseline. The present changes in smoking, alcohol, and physical activity habits were not statistically significant, but the results are of clinical importance and they underline the need for optimizing maintenance from rehabilitation.

Strengths and Limitations

The strengths of this study are the use of well-validated HRQoL questionnaires and the analysis of the consumption of alcohol and tobacco from the time of diagnosis to 1 year after surgery.

A methodological weakness is the low number of participants and the absence of a control group, since it leaves out the possibility of concluding on the effect of the intervention.

The fact that only 32% of the eligible patients participated in the present study limits the generalization of the results, as the patients might not be representative of the population operated for NSCLC in Denmark. The low recruitment rate could also affect the results, because participation in the study could be related to patients with better performance status and physical fitness compared with the group not participating. However, a comparison of the baseline characteristics of the patients in the present study with cohort studies in patients with NSCLC reveals similarities regarding age, sex, pulmonary function, and comorbidities.[52,53]

Conclusion

This feasibility study demonstrated that global quality of life, mental health, and emotional well-improved significantly during the study, from time of diagnosis until 1 year after resection, in patients with NSCLC participating in rehabilitation. There was a reduction in distress and anxiety and smoking and alcohol habits from baseline to after the intervention, followed by an increase 1 year after surgery, which underlines the need for continued rehabilitation initiatives. The clinical implication of these results is awareness from the health care professionals in supporting patients with operable lung cancer to maintain the achieved lifestyle changes throughout life.

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Declaration of Conflicting Interests

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