Quality of life after preoperative home-based exercise training in patients with lung cancer: a secondary analysis

Sara Pimenta[1,2], Pedro Machado[1,3,4], Cândida G. Silva[1,2], Ana Luís Garcia[5], Tiago Nogueira[5], Sónia Silva[6], Claúdia Lares dos Santos[7], Maria Vitória Martins[8], André Canha[9], Bárbara Oliveiros[10,11,12], Raul A. Martins[3], Joana Cruz[1,2]

[1]Center for Innovative Care and Health Technology (ciTechCare), Polytechnic University of Leiria, Leiria, Portugal; [2]School of Health Sciences (ESSLei), Polytechnic University of Leiria, Leiria, Portugal; [3]University of Coimbra, Research Unit for Sport and Physical Activity (CIDAF, UID/PTD/04213/2019), Faculty of Sport Sciences and Physical Education, Coimbra, Portugal; [4]Physioclem, Physical Therapy Clinics, Alcobaça, Portugal; [5]Thoracic Surgery Unit, Portuguese Oncology Institute of Coimbra, Coimbra, Portugal; [6]Pulmonology Department, Leiria Hospital Center, Leiria, Portugal; [7]Pulmonology Department, Hospital Distrital de Santarém, Santarém, Portugal; [8]Pulmonology Department, Hospital Distrital da Figueira da Foz, Figueira da Foz, Portugal; [9]Physical Medicine and Rehabilitation Department, Hospital Distrital de Santarém, Santarém, Portugal; [10]Laboratory of Biostatistics and Medical Informatics (LBIM), Faculty of Medicine, University of Coimbra, Coimbra, Portugal; [11]Faculty of Medicine, University of Coimbra, Coimbra Institute for Clinical and Biomedical Research (iCBR), Coimbra, Portugal; [12]Institute for Biomedical Imaging and Translational Research (CIBIT), University of Coimbra, Coimbra, Portugal

Contributions: (I) Conception and design: S Pimenta, P Machado, J Cruz; (II) Administrative support: S Pimenta, P Machado, J Cruz; (III) Provision of study materials or patients: AL Garcia, T Nogueira, S Silva, CL dos Santos, MV Martins; (IV) Collection and assembly of data: S Pimenta, P Machado, A Canha; (V) Data analysis and interpretation: S Pimenta, CG Silva, P Machado, J Cruz; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Joana Cruz, PT, PhD. Center for Innovative Care and Health Technology (ciTechCare), Polytechnic University of Leiria, Leiria, Portugal; School of Health Sciences (ESSLei), Polytechnic University of Leiria, Campus 2, Morro do Lena – Alto do Vieiro, Apartado 4163, 2411-901 Leiria, Portugal. Email: joana.cruz@ipleiria.pt.

Background: A preoperative home-based exercise training (PHET) program appeared to improve health-related quality of life (HRQoL) in patients undergoing lung cancer surgery. However, inter-individual variability in response was observed. This secondary analysis aimed to identify characteristics of responders/non-responders to PHET, determine predictors of response, and examine whether preoperative HRQoL response to PHET is associated with postoperative HRQoL maintenance.

Methods: This was a secondary analysis of pooled data from a feasibility study and a randomized controlled trial, including sociodemographic/clinical data, physical performance and HRQoL (EORTC-QLQ-C30). Responders/non-responders were classified based on a change of ≥5 points in Global QoL score (EORTC QLQ-C30) from baseline to pre-surgery time point. Between-group differences and predictors of PHET response (logistic regression) were analysed.

Results: 32 patients (63% male, 67.1±7.8 years) were included, from which 56% (n=18) were responders to PHET in Global QoL. Responders had lower baseline scores in Global QoL, Emotional Function and Summary Score compared to non-responders ($P<0.05$), and 50% of responders had chronic obstructive pulmonary disease (COPD) ($P=0.02$). No other between-group differences were found ($P>0.05$). In the regression model including the Summary Score (EORTC-QLQ-C30) and COPD (Nagelkerke R2=0.511), COPD was a significant predictor of response: COPD patients were 13.4 times more likely to be responders (odds ratio =13.4; 95% confidence interval: 1.4; 132.2). 65% of PHET-responders maintained/improved HRQoL 1-month post-surgery.

Conclusions: Most patients awaiting lung cancer surgery responded in HRQoL to a PHET, however, a considerable proportion did not. Further research is needed to identify characteristics of non-responders and optimize prehabilitation strategies accordingly.

Keywords: Prehabilitation; health-related quality of life (HRQoL); lung cancer

Submitted Jul 16, 2025. Accepted for publication Nov 12, 2025. Published online Mar 24, 2026.
doi: 10.21037/jtd-2025-1444
View this article at: https://dx.doi.org/10.21037/jtd-2025-1444

Introduction

Lung cancer is the nineth leading cause of death (1), and remains one of the leading causes of cancer-related morbidity and mortality worldwide (2-4). Surgical resection of the tumour is the cornerstone of curative treatment for patients with early-stage lung cancer (5). Although it offers the best survival outcomes for these patients, with five-year survival rates for people with localized disease being approximately 60% (6,7), surgery leads to short- and long-term impairments on health-related quality of life (HRQoL) (8).

Patients awaiting lung cancer resection typically have poorer HRQoL than the general population (9). Surgical resection further impairs HRQoL, with many patients experiencing pain, fatigue, dyspnoea and a decline in physical and role functioning during the first postoperative month (8,10,11). Moreover, lower preoperative HRQoL has been associated with a higher risk of postoperative cardiopulmonary complications and longer hospital stays (12,13). The long-term negative impact of surgery on HRQoL is also a concern for patients, particularly regarding postoperative physical function, fatigue, and pain (14). Optimizing preoperative care to improve HRQoL in patients with lung cancer is, therefore, of clinical importance.

Current clinical guidelines strongly recommend the inclusion of exercise training in cancer care, based on moderate- to high-quality evidence from multiple randomized trials across various cancer types (15). Such exercise programs have been shown to improve depressive symptoms, anxiety, fatigue, HRQoL, and self-reported physical function (16,17). Preoperative exercise training has emerged as a promising intervention to improve clinical outcomes of cancer patients undergoing major surgery, including those with lung cancer (17-21), although evidence is still limited (16). From the existing interventions, home-based exercise programs represent a more accessible intervention than center-based programs, as they can minimize adherence problems to prehabilitation such as transportation issues, which are one of the main barriers encountered by patients (22-24). In two previous studies (25,26), a preoperative home-based exercise training (PHET) program was implemented in patients awaiting lung cancer surgery. This intervention was considered safe, feasible, well accepted (26), and it was found to be clinically effective in improving preoperative HRQoL and preventing its deterioration after surgery (25). Despite these beneficial effects, inter-individual variability in response to PHET was observed (25,26), which may be related to patients' characteristics and/or clinical status before surgery. In previous clinical trials involving breast and prostate cancer patients, it was found that baseline demographic, clinical and psychosocial variables explained the heterogenous effects of exercise training on HRQoL (27,28). Though, this topic has not yet been explored among patients with lung cancer.

The main aim of this study was to investigate whether baseline characteristics of patients with lung cancer undergoing PHET can account for the variability of the response in preoperative HRQoL (i.e., "responders" and

Highlight box

Key findings

- A preoperative home-based exercise appeared to improve health-related quality of life (HRQoL) in patients awaiting lung cancer surgery, with chronic obstructive pulmonary disease (COPD) potentially influencing response. However, some patients did not responded, highlighting the need for individualized prehabilitation approaches.

What is known and what is new?

- In a previous randomized controlled trial, a preoperative home-based exercise training (PHET) improved HRQoL in patients undergoing lung cancer surgery. However, individual variability in response to such intervention remains poorly understood.
- This study suggested that most patients awaiting lung cancer surgery experience meaningful improvements in HRQoL, particularly those with lower baseline Emotional Function and Global QoL scores. While comorbidities such as COPD appeared to be associated to a greater likelihood of response, further research is needed to clarify its role. Additionally, the study suggested a tendency for most responders before surgery to sustain or further enhance their HRQoL one month postoperatively.

What is the implication, and what should change now?

- These findings highlight the importance of individualizing prehabilitation strategies for patients with lung cancer. Future research should focus on larger samples to better characterize responders and non-responders and refine multicomponent prehabilitation approaches tailored to patient profiles.

Table 1 PHET program description

PHET component	Description
Educational session (first day of the PHET program)	Themes
	Importance of exercise training before lung cancer surgery
	Demonstration of the home-based exercise program
	Instruction on training intensity monitoring using the Borg Category Ratio (Borg CR-10)
Home-based exercise program (5 days/week, 3.6±0.2 weeks)	Aerobic training:
	F: 3× week
	I: RPE of 3–5 (moderate to strong)
	T: walking
	T/V: 30 min/session
	P: 40 min/session (2nd week)
	Resistance training:
	F: 2× week
	I: RPE of 3–5 (moderate to strong)
	T: sit-to-stand; calf raise; step up; glute bridge; biceps curl; shoulder press
	T/V: 2 sets 15 repetitions
	P: 3 sets 15 repetitions (2nd week)
Telephone supervision (weekly basis)	Monitor exercise adherence
	Identify adverse events
	Overcome exercise barriers
	Adjust planned exercise program

Parameters of the training components: F, frequency; I, intensity; T, type; T/V, time/volume; P, progression. PHET, preoperative home-based exercise training; RPE, rating of perceived exertion.

"non-responders") and predict a clinically meaningful response to PHET. A secondary goal was to determine whether the response to PHET (i.e., 'responders' and 'non-responders') is associated with clinically relevant changes (i.e., 'deterioration' and 'non-deterioration') in HRQoL following lung cancer surgery. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-1444/rc).

Methods

Study design and setting

This study is an exploratory secondary analysis of pooled data from a single-arm feasibility study (Clinicaltrials.gov NCT05473052) (26) and from the experimental group of a randomized efficacy controlled trial (RCT, Clinicaltrials.gov NCT05469425) (25). Because this is a secondary analysis of these two original studies, no a priori sample size calculation was performed. These studies were part of a larger project (OncoEnergy) that aimed to explore the feasibility, safety and effectiveness of a PHET program on HRQoL in patients undergoing lung cancer resection.

The PHET program comprised three components, which are presented in *Table 1* and described in detail in the main studies (25,26). There were no modifications to the program from the feasibility trial to the RCT, thus patients in both studies received the same exercise program. It consisted of an initial educational session where patients were advised on the importance of exercise before surgery and where the exercise program was explained and exemplified. The exercise program consisted of 3 weekly sessions of aerobic training (walking) and 2 weekly sessions of resistance training, on alternate days. During the PHET, patients received support on a weekly basis by telephone calls. The duration of the PHET was adjusted based on the waiting times for surgery and patients were encouraged to complete the program until the date of the surgery. The PHET program was previously tested for feasibility, acceptability, and safety in a feasibility study (26) and for its effectiveness in a multicentre RCT (25).

Regarding adherence to the PHET, in the feasibility trial the median [Q1–Q3] adherence rate was 100% [89–100%] for the aerobic training and 100% [100–117%] for the resistance training (26); in the RCT, the mean (± standard deviation) adherence rate was 103%±19.8% for aerobic training and 92.1%±33.1% for resistance training (25).

This is a secondary analysis of data from two previous studies that were conducted in accordance with the Declaration of Helsinki and its subsequent amendments. Ethical approval was previously obtained from the Ethics Committees of the health units where patients were recruited—the Leiria Hospital Center (n.10-14/12/2021), District Hospital of Santarém (no ref; 22/04/2022), District Hospital of Figueira da Foz (Obs_CIC.12 / 2022) and Portuguese Oncology Institute of Coimbra (TI 36/2021, 18/11/2021). Data were collected between February 2022 and May 2023, at four health units in the center region of Portugal. These trials were reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines (29).

Participants

This secondary analysis used data from participants included in the feasibility study (ClinicalTrials.gov NCT05473052) (26) and the randomized controlled trial (experimental group) (ClinicalTrials.gov NCT05469425) (25), following the same eligibility criteria. Participant flow details are available in the primary study reports. Consecutive adult patients (≥18 years), candidates to surgery for confirmed or suspected lung malignancy (clinical stage IIIA or less), who had medical approval to exercise, and surgery scheduled for at least two weeks from study enrolment were considered for inclusion. Exclusion criteria were: (I) metastatic tumour (II) contraindications for exercise training or physical testing (III) inability to speak/understand Portuguese (IV) being already involved in regular exercise training (aerobic and resistance training over the past month for ≥2 days/week, ≥30 minutes/session). Participants were identified, screened for eligibility and subsequently invited to participate by their medical staff during routine appointments of Pulmonology or Thoracic Surgery. Patients who expressed interest in participating were contacted by the research team and provided with both oral and written information about the study. Those who agreed to take part gave written informed consent before any study-related assessments were conducted.

Data collection

In the feasibility study, the outcome assessor was the same physiotherapist who delivered the intervention. In the RCT, assessments were performed by a physiotherapist who was independent of the intervention delivery and blinded to group allocation at both baseline and post-intervention time points. There were 3 timepoints, at baseline (T0), after the PHET (1–5 days prior to surgery—T1), and 4–5 weeks after surgery (T2). Sociodemographic (age, sex, education) and anthropometric data (height, weight) were collected using a structured questionnaire. Clinical data (smoking status, lung function, cancer diagnosis, histological subtype, tumour stage) were collected from the electronic medical records. Comorbidities were assessed and scored according to the Charlson Comorbidity Index (CCI) which classifies comorbidities as mild (CCI scores of 1–2), moderate (CCI scores of 3–4) or severe (CCI scores ≥5) (30). Information on chronic obstructive pulmonary disease (COPD) as a comorbidity was obtained from medical records, with the diagnosis confirmed by spirometry. These data were only collected at T0 for sample characterization. HRQoL was assessed using the Portuguese version (31) of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC-QLQ-C30) version 3.0 (32), following the recommendations of the international consensus on patient-centred outcomes for lung cancer (33). The QLQ-C30 includes a global QoL scale, five functioning scales, three multi-item symptom scales, six single-item symptom scales, and a financial impact scale (34). Scores range from 0 to 100. For the global QoL and functioning scales, higher scores represent better QoL and higher levels of functioning, whereas higher scores on the symptom scales indicate greater symptom burden. In the present study, the Global QoL scale of the EORTC QLQ-C30 was selected as the primary outcome for HRQoL as previously recommended (34). In addition, in accordance with the recommendations of the EORTC Quality of Life Group, the QLQ-C30 Summary Score

(SumSc) was used to complement the 15-outcome profile provided by the QLQ-C30 (35). HRQOL was collected at the three time points (T0-T2). Physical performance tests were conducted to assess exercise capacity, strength and lower limb function. Exercise capacity was evaluated using the incremental shuttle walk test (ISWT) according to the protocol described by Singh *et al.* (36). Handgrip strength was measured with a Jamar Plus+ Dynamometer (Performance Health, Nottinghamshire, UK) following the standardized procedure recommended by the American Society of Hand Therapists (37). Lower limb functional performance was also assessed using the Five-Times Sit-to-Stand Test (5STS). For this test, participants were asked to stand up and sit down five times as quickly as possible from a standardized armless chair (0.41–0.45 m in height) without using their hands for assistance. The test was completed after the fifth repetition, and the time needed to perform the test was recorded using a stopwatch to the nearest 0.01 s (38).

Statistical analysis

Analyses were performed using SPSS Statistics (v29, IBM). Plots were created using GraphPad Prism (v7, GraphPad Software). Descriptive statistics were computed to characterize the sample. Data were presented as frequencies for categorical and ordinal variables; mean ± standard deviation (SD) or median [interquartile range (IQR)], for continuous variables, depending on data distribution.

Participants were classified as responders or non-responders based on within-subject change of ≥5 points on the Global QoL scale of the EORTC-QLQ-C30 from baseline to T1 (post-PHET, pre-surgery), corresponding to the minimal important difference (MID) (39). Baseline characteristics of the two independent groups (responders versus non-responders) were compared using independent samples *t*-tests, Mann-Whitney U tests, or Chi-squared/Fisher exact tests depending on data type and distribution. A statistical significance level of 0.05 was used.

To identify potential predictors of response in T1, univariate regression models between each independent variable from baseline assessment (sociodemographic and clinical variables, physical performance tests—ISWT, 5TSTS, handgrip strength; HRQoL EORTC QLQ-C30 subscales) and the dichotomized variable of the difference T1-T0 (i.e., 'responders' *vs.* 'non-responders') in Global QoL scale of the EORTC-QLQ-C30 (dependent variable) were computed. Predictor variables presenting a significant univariate association (P<0.10) (40) were examined in a binary logistic regression using the backward stepwise method to identify the main predictors. The logistic regression assumptions were verified (41,42).

Chi-square tests were performed to determine whether the response to PHET was associated with clinically relevant changes in HRQoL ('deterioration' *vs.* 'non-deterioration') following lung cancer surgery (T2). 'Deterioration' *vs.* 'non-deterioration' consists of the dichotomization of the difference between Global QoL in T2 and T0 using the MID for deterioration in Global QoL scale (−5 points) (39).

Results

Sample characteristics

Thirty-two participants were included in the analysis. Flowchart is presented in *Figure 1*. There were no missing data, all patients were assessed at all time points. Most participants were male (62.5%), had a mean age of 67.1±7.8 years, had a mean FEV_1 (%predicted) of 82.3±18.9 L/min, 46.9% were former smokers and 31.3% had COPD (from medical health records). Regarding diagnosis and surgery type, 75% had a diagnosis of adenocarcinoma and underwent lobectomy (84.4%) via video-assisted thoracoscopic surgery (65.6%). The median [Q1–Q3] length of hospital stay after surgery was 5 [2.25–9.5] days. Regarding HRQoL, the median [Q1–Q3] Global QoL score was 62.3 [50–83], while the Summary Score was 90.1 [82.3–93.0]. Among the functioning scales, Emotional Function scored the lowest {75 [60.2–83.3]}, followed by Physical Function {90 [80–93]}. On the symptom scales, Insomnia had the highest score {33.3 [0–33.3]}, followed by Fatigue {11 [0–30.3]}. Sociodemographic and clinical characteristics of participants are presented in *Table 2*.

Response to PHET

After PHET, 56.3% (n=18) of patients were responders to PHET in Global QoL. Baseline characteristics of responders and non-responders are presented in *Table 2*. The responders' group had a significantly higher proportion of patients with COPD compared to the non-responders' group (50% *vs.* 7.1%, respectively; P=0.02). The responders' group had a significantly longer hospital stay than non-responders {5 [4–11.25] *vs.* 3 [2–5.5] days, P=0.045}. There were no other significant differences regarding sociodemographic and clinical variables,

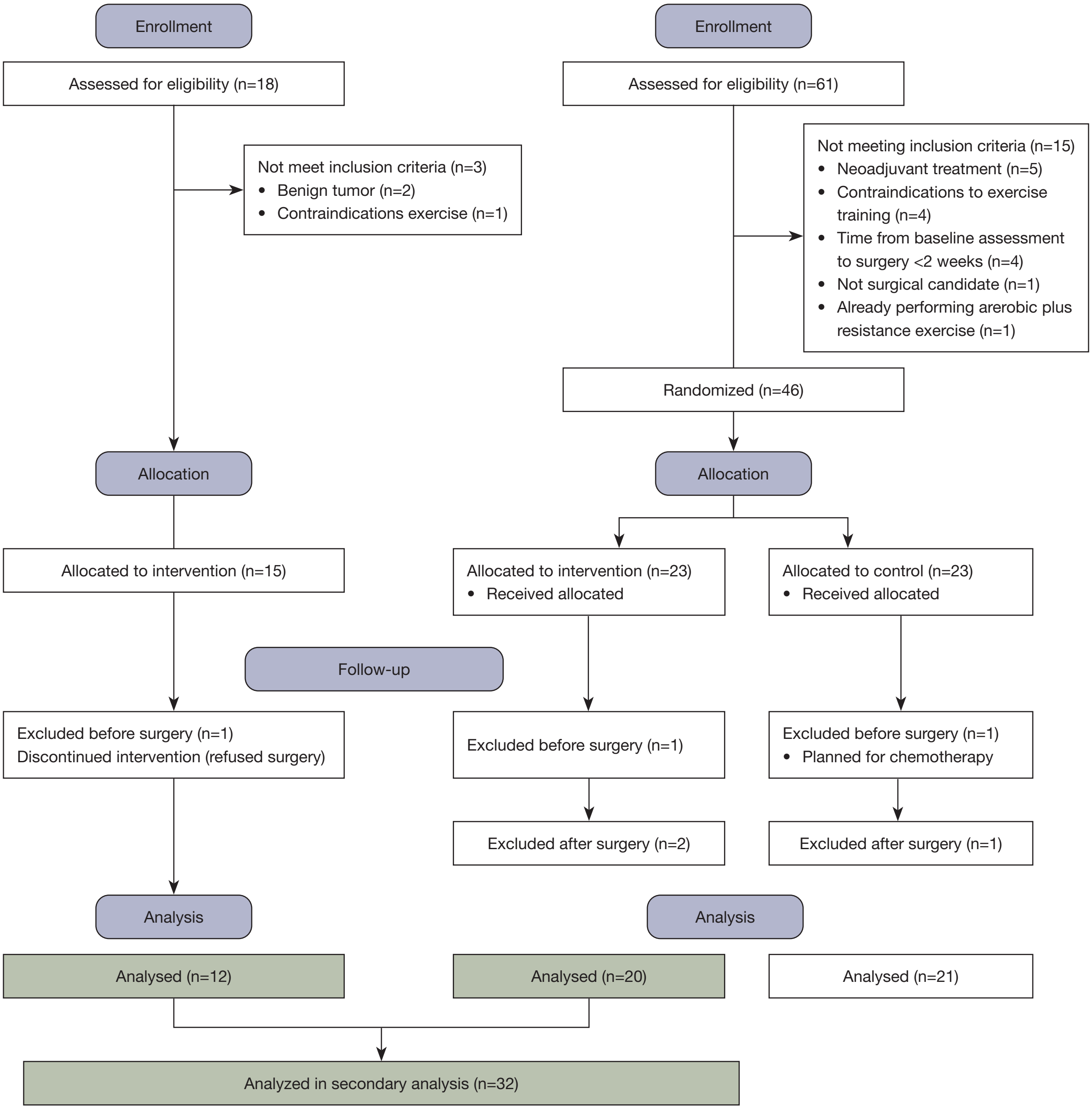

Figure 1 Adapted CONSORT flow diagram identifying the participants included in this secondary analysis of the feasibility study and the randomized controlled study. CONSORT, Consolidated Standards of Reporting Trials.

including pulmonary function, type of surgery, type of cancer and results from the physical performance tests (P>0.05, *Tables 2,3*).

Differences were found in EORTC-QLQ-C30 subscales (*Table 3*), with responders presenting significantly lower scores in Global QoL {50 [42–60.3] *vs.* 83 [72.9–83.1]}, Emotional Function {67 [48–83] *vs.* 83 [75–94]} and Summary Score {87.5 [79.8–91.3] *vs.* 92.5 [85.3–96.5]} when compared to non-responders. Mean differences between groups are provided in *Table 3*. There were no other significant differences in EORTC-QLQ-C30 subscales (P>0.05).

Table 2 Sociodemographic, clinical characteristics and differences between responders (n=18) and non-responders (n=14)

Variable	All participants (n=32)	Responders (n=18)	Non-Responders (n=14)	Between-group difference[†]	P value
Age (years)	67.1±7.8	65.2±8.1	69.5±6.9	4.33 [−1.19, 9.86]	0.12
BMI (kg/m^2)	25.8 [23.5–28.4]	25.7 [22.7–28.8]	26.3 [25–29.9]	−1.045	0.30
Sex (male)	20 (62.5)	10 (55.6)	10 (71.4)	–	0.16
Educational level				–	0.08
<10 years	21 (65.6)	11 (61.1)	10 (71.4)		
≥10 years	11 (34.4)	7 (38.9)	4 (28.6)		
Smoking status				–	0.15
Current	6 (18.8)	2 (11.1)	4 (28.6)		
Former	15 (46.9)	9 (50)	6 (42.9)		
Never	11 (34.4)	7 (38.9)	4 (28.6)		
Comorbidities				–	
Hypertension	16 (50.0)	9 (50.0)	7 (50.0)		>0.99
COPD	10 (31.3)	9 (50.0)	1 (7.1)		0.02*
Diabetes	4 (12.5)	2 (11.1)	2 (14.3)		>0.99
History of myocardial infarction	4 (12.5)	2 (11.1)	2 (14.3)		>0.99
Previous cancer	7 (21.9)	3 (16.7)	4 (28.6)		0.67
Other	7(21.9)	5 (27.8)	2 (14.3)		0.43
Mean CCI	4.5±1.5	4.6±1.4	4.3±1.7	–	–
CCI score				–	0.24
Mild comorbidities (CCI score 1 or 2)	4 (12.5)	1 (5.55)	3 (21.43)		
Moderate comorbidities (CCI score 3 or 4)	11 (34.34)	8 (44.44)	3 (21.43)		
Severe comorbidities (CCI score ≥5)	17 (53.13)	9 (50)	8 (57.14)		
Pulmonary function					
FVC (% predicted)	94±11.8	91.8±11.7	96.7±11.8	4.89 [−4.12, 13.91]	0.28
FEV_1 (% predicted)	82.3±18.9	76.8±20.9	89.4±13.7	12.55 [−1.14, 26.3]	0.07
DLCO (% predicted)	69.6±18.4	68.5±17.2	71.3±20.7	2.81 [−11.68, 17.30]	0.70
Type of lung cancer				–	0.14
NSCLC	27 (84.4)	17 (94.4)	10 (71.4)		
Neuroendocrine	5 (15.6)	1 (5.6)	4 (28.6)		
Histological subtype				–	0.06
Adenocarcinoma	24 (75)	15 (83.3)	9 (64.3)		
Squamous cell carcinoma	2 (6.3)	2 (11.1)	–		
Typical carcinoid	3 (9.4)	–	3 (21.4)		
Atypical carcinoid	3 (9.4)	1 (5.6)	2 (14.3)		

Table 2 *(continued)*

Table 2 *(continued)*

Variable	All participants (n=32)	Responders (n=18)	Non-Responders (n=14)	Between-group difference†	P value
Resection degree				–	0.20
Lobectomy	27 (84.4)	14 (77.8)	13 (92.9)		
Bi-lobectomy	1 (3.1)	1 (5.6)	–		
Segmentectomy	1 (3.1)	–	1 (7.1)		
Wedge resection	3 (9.4)	3 (16.7)	–		
Surgical approach				–	0.45
VATS	21 (65.6)	13 (72.2)	8 (57.1)		
Open thoracotomy	10 (31.3)	4 (22.2)	6 (42.9)		
RATS	1 (3.1)	1 (5.6)	–		
Length of hospital stay (days)	5 [2.25–9.5]	5 [4–11.25]	3 [2–5.5]	–1.962	0.045*

Data are presented as mean ± SD, n (%) or median [Q1–Q3]. *, significant at P<0.05. †, for normal distribution variables, between-group difference was presented as mean difference (95% CI); for non-normal distribution variables, Z value of Mann-Whitney test was listed in the column. BMI, body mass index; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; DLCO, diffusion lung capacity for carbon monoxide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; NSCLC, non-small cell lung cancer; RATS, robot-assisted thoracoscopic surgery; VATS, video-assisted thoracoscopic surgery.

Predictors of response

The presence of COPD (P=0.009) and the variables FEV1 (P=0.07), Emotional Function (P=0.04) and SumSc (P=0.03) were significantly associated with being a responder to PHET in Global QoL, in the univariate analysis. Since multicollinearity was found between COPD and FEV1 and between Emotional Function and SumSc, the independent variables included in the model were SumSc and COPD.

The logistic regression model containing SumSc and COPD as independent variables was statistically significant [$\chi^2(4)$ =12.1, P<0.05]. The model explained 42.1% (Nagelkerke R2) of the variability in patients' response to PHET in Global QoL and correctly classified 72% of the cases. In this model, COPD was the only significant predictor of being a responder to PHET (P=0.03. Patients with COPD were 13.4 times more likely to be a responder to PHET in preoperative Global QoL (OR =13.4; 95% CI: 1.4, 132.2).

Changes in global QoL after surgery

One month after surgery (T2), 62.5% (n=20) of patients maintained or improved Global QoL in relation to baseline (i.e., 'non-deterioration'), while 37.5% of patients (n=12) experienced a deterioration in this outcome. There was no significant association between the response to PHET (i.e., 'responders' and 'non-responders') in T1 and Global QoL change in T2 ('deterioration' *vs.* 'non-deterioration') (P=0.20). However, 65% (n=12) of patients who responded to the PHET program (i.e., T1-T0) maintained or improved their Global QoL scores 1-month after surgery, considering their baseline scores as the reference point (i.e., T2-T0) (*Figure 2*; green area). Similarly, 58.3% (n=7) of patients who experienced a deterioration in HRQoL after surgery (i.e., T2-T0) did not respond to PHET in T1 (*Figure 2*; red area).

Discussion

This study is the first to identify "responders", "non-responders", and predictors of response to a PHET program in HRQoL among patients with lung cancer awaiting surgery. Despite most patients responded to the PHET in Global QoL, a substantial proportion did not achieve clinically meaningful improvements. Responders had worse baseline scores in Emotional Function, Global QoL, and Summary Score, as well as a higher prevalence of COPD, although only having COPD significantly predicted response to PHET in Global QoL. This study

Table 3 Physical performance tests, EORTC-QLQ-C30 scale scores and differences between responders and non-responders

Variables	All participants (n=32)	Responders (n=18)	Non-responders (n=14)	Between-group difference†	P value
Physical performance tests					
ISWT (m)	459.7±184.9	480.8±229.4	432.5±106.2	−48.33 [−183.94, 87.27]	0.47
5TST (s)	8.9±3.1	8.5±3.3	9.4±3.0	0.94 [−1.36, 3.24]	0.41
Handgrip strength (kg)					
Left hand	31.6±9.6	30.7±9.4	32.7±10.2	2.02 [−5.06, 9.09]	0.57
Right hand	32.7±8.8	32.3±8.9	33.1±9.0	0.86 [−5.64, 7.37]	0.79
EORTC-QLQ-C30 scale					
Global QoL	62.3 [50–83]	50 [42–60.3]	83 [72.9–83.1]	−3.05	0.002*
Physical function	90 [80–93]	87 [78.3–100]	93 [80–93]	−0.193	0.87
Emotional function	75 [60.2–83.3]	67 [48–83]	83 [75–94]	−2.07	0.004*
Role function	100 [83–100]	91.67 [79–100]	100 [100–100]	−1.78	0.14
Cognitive function	100 [83–100]	100 [83–100]	91.67 [79–100]	−0.39	0.72
Social function	100 [83–100]	100 [67–100]	100 [95.8–100]		0.24
Dyspnoea	0 [0–24.8]	0 [0–33]	0 [0–0]	−1.23	0.36
Fatigue	11 [0–30.3]	16.50 [0–24.9]	5.50 [0–33]	−0.57	0.59
Pain	0 [0–17]	0 [0–17]	8.50 [0–17]	−0.189	0.87
Nausea and vomiting	0 [0–0]	0 [0–0]	0 [0–0]	−0.86	0.81
Insomnia	33.3 [0–33.3]	33.3 [0–75.3]	0 [0–33]	−1.98	0.06
Appetite loss	0 [0–0]	0 [0–0]	0 [0–0]	1.27	0.61
Constipation	0 [0–0]	0 [0–0]	0 [0–8.3]	−0.14	0.93
Diarrhoea	0 [0–0]	0 [0–0]	0 [0–0]	−0.18	0.96
Financial impact	0 [0–33]	0 [0–33]	0 [0–33]	−0.17	0.90
Summary score	90.1 [82.3–93.0]	87.5 [79.8–91.3]	92.5 [85.3–96.5]	−2.19	0.03*

Data are presented as mean ± SD or median [Q1–Q3]. *, significant at P<0.05. †, for normal distribution variables, between-group difference was presented as mean difference (95% CI); for non-normal distribution variables, Z value of Mann-Whitney test was listed in the column. 5TST, 5 times sit-to-stand test; ISWT, Incremental Shuttle Walking Test; QoL, quality of life; SD, standard deviation.

also suggested that most patients who had a clinically meaningful improvement in Global QoL before surgery at least maintained their baseline Global QoL scores 1-month after surgery.

The observed heterogeneity in response highlights the importance of analysing responders versus non-responders, rather than relying solely on mean differences. Patients with lower baseline HRQoL scores ("more room for improvement") exhibited greater gains, whereas those with higher baseline scores were limited by potential ceiling effects, which could also reflect regression to the mean. This distinction emphasises the need to move beyond average effects and to tailor interventions according to individual patient profiles defined based on clinical meaningful variables.

This variability in response to a pre-operative exercise training is consistent with previous literature. Huang *et al.* [2016] (43) reported that half of their study participants were responders in exercise capacity to an exercise prehabilitation program (home-, community-, or hospital-based) including aerobic and resistance training. Home-based delivery has been shown to improve accessibility

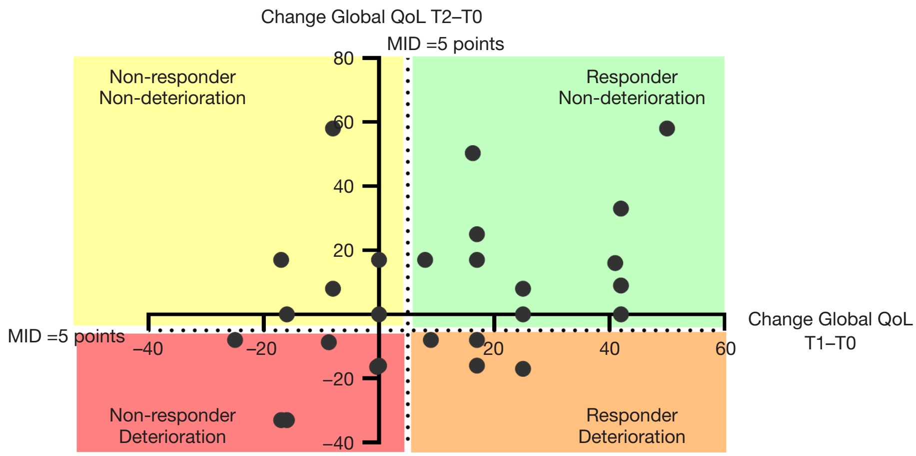

Figure 2 Scatter plot with the distribution of responders *vs.* non-responders in Global QoL scale to the PHET program (T1-T0), and patients who deteriorated *vs.* non-deteriorated in Global QoL scale score 1 month after surgery (T2-T0). X-axis: difference between T1 and T0 in the Global QoL scale scores; Y-axis: difference between T2 and T0 in the Global QoL scale scores. Dotted vertical line represents the minimal important difference for improvement (MID 5 points) of the Global QoL scale at T1. Dotted horizontal line represents MID for deterioration (-5 points) of the Global QoL scale at T2. Green shadow represents "responders" in T1 who maintained or improved Global QoL score in T2 compared to T0. Red shadow represents "non-responders" who deteriorated. Orange represents "responders" in T1 who deteriorated in T2. Yellow shadow represents "non-responders" who did not deteriorate at T2. MID, minimal important difference; PHET, preoperative home-based exercise training; QoL, quality of life.

(23,24), feasibility, and adherence (25,26), yet a considerable proportion of patients may still fail to achieve meaningful improvements in HRQoL.

No statistically significant differences were observed regarding surgical approach or extent of resection. However, a higher proportion of lobectomies and thoracotomies were performed in the non-responder group, while wedge resections and VATS procedures were more common among responders. These differences, although exploratory, could have influenced HRQoL outcomes. Less invasive surgical techniques have been associated with faster recovery and better postoperative quality of life in lung cancer patients (44). Future studies with larger samples are warranted to explore this potential interaction more thoroughly.

The between-group difference in ISWT distance did not reach statistical significance, but the mean change of approximately 50 m is close to the minimal clinically important difference (MCID) of 48 m reported by Parreira *et al.* [2014] (45) for patients with COPD. While this threshold has not been validated for individuals with lung cancer and, therefore, should be interpreted with caution, it provides a useful reference point suggesting that the magnitude of change observed may be clinically meaningful. This potential improvement in functional exercise capacity could partly explain the perceived gains in HRQoL among responders and underscores the relevance of exploring the interaction between physical function and QoL outcomes in future studies with larger samples.

COPD appeared to be a significant predictor of response in Global QoL. Among the 10 patients with COPD, 9 were classified as responders. Patients with COPD often experience ventilatory limitations, symptom burden, and functional impairment, factors that could potentially explain a positive response to moderate intensity exercise training (46) like the PHET. However, in our sample there were no significant between-group differences in baseline physical function (both self-reported and objectively measured) or symptom burden. A previous large-scale study (47) has shown that lung cancer patients with underlying COPD, particularly those with a prior diagnosis, exhibit a significantly greater overall symptom burden, including more frequent and severe physical and psychological symptoms, compared to those without COPD. These patients may therefore have a greater need of, and potentially greater responsiveness to, moderate intensity exercise interventions, even if baseline physical function appears comparable. However, the small sample size of our study, particularly the limited number of patients with COPD, warrants caution when interpreting these findings. The possibility of random variation influencing results cannot be excluded, and further research in larger, more diverse samples is needed to confirm whether COPD consistently predicts better response to a moderate intensity pre-operative exercise training.

An important consideration is the dose of the exercise intervention. Although the PHET followed standard exercise guidelines (15,16), some patients may require higher or more individualized training stimuli to achieve meaningful changes in QoL. This is a well-established research priority in prehabilitation, including the need to identify the optimal exercise modality, intensity, and volume, as current approaches are not yet effective for specific patient subgroups (48). Moreover, the 'standard' exercise guidelines applied in this study were derived from broader oncology and thoracic surgery populations rather than exclusively from preoperative lung cancer cohorts, which underscores the need to adapt and individualize exercise prescriptions to the specific characteristics and comorbidities of this group.

Patients who do not experience clinically meaningful improvements in Global QoL with the PHET may benefit from a more comprehensive, multimodal prehabilitation approach. Incorporating additional components such as symptom management, nutritional counselling, or social support may help address the potential unmet needs of non-responders (49). Further research is also needed to better characterize the non-responders' profile considering demographic factors such as age, weight, sex, preoperative fitness, and frailty in larger samples, and identify patterns of HRQoL impairment, including specific domains that contribute most to the overall QoL impairment (48). This will potentially enable a more effective tailoring of prehabilitation components to individual patient needs. Future research should move beyond standardised, fixed-dose exercise prescriptions and explore individualised or stratified prehabilitation models, incorporating decision algorithms or risk stratification tools. To evaluate personalised approaches, adaptive trial designs (e.g., response-adaptive randomisation, stratified RCTs) could be implemented, allowing exercise intensity, modality or volume to be adjusted based on baseline patient characteristics.

A limitation of this study is the absence of a sample size calculation. However, as this was an exploratory secondary analysis of pooled data from a feasibility study and the intervention arm of an RCT using the same intervention, a formal sample size calculation was not feasible. Future studies with larger samples are needed to confirm these findings and to explore the underlying factors associated with response to PHET. The evidence in the field of prehabilitation for lung cancer resection is still limited, although research on this topic is increasing. Most of the existing literature is from small, underpowered trials, implementing heterogenous protocols and interventions, and there is still a lack of studies exploring predictors of response to exercise-based prehabilitation interventions (48). However, there is limited and weak evidence on this association of (objectively measured) baseline physical activity levels and QoL scores in the perioperative period, in patients with lung cancer (50).

Participants included in our sample appeared to have a relatively preserved HRQoL at baseline which can be a limitation of this study. The baseline score in our sample was 83.2 points, that is higher than the values reported in similar preoperative lung cancer trials, for example in the study of Avery *et al.* [2020] (10) (71.9; 66.3–77.5), Nugent *et al.* [2020] (8) (79.9), and Lai *et al.* [2019] (51) (70.8; 58.3–83.3). Moreover, when compared to general European population normative values obtained from the EORTC Normative Data Initiative (median ~75 for adults aged 60–79 years) (52), our sample had higher scores. This may partly explain the limited magnitude of change observed due to potential ceiling effects.

A potential limitation of our analysis is that preoperative HRQL was included as a predictor of response to PHET, using the same instrument to assess postoperative HRQL. Although this creates some conceptual overlap between predictor and outcome, baseline HRQL still provides valuable insight into which dimensions of patient status may influence postoperative outcomes and can help guide personalized prehabilitation strategies. Lastly, the follow-up period was limited to the first month after surgery and long-term outcomes post-surgery were not assessed, which could provide a more comprehensive understanding of the exercise training benefits.

Conclusions

The current study suggested that most patients waiting for lung cancer surgery respond in HRQoL to a moderate intensity, home-based exercise program; however, there is still a considerable proportion of non-responders. Future studies with larger samples are needed to better understand non-responders' profile, including the potential role of comorbidities such as COPD as predictors of response, and identify unmet needs that can be potentially addressed through multicomponent prehabilitation programs.

Acknowledgments

This work was previously presented in abstract format at the European Respiratory Society International Congress 2024 (see: https://publications.ersnet.org/content/erj/64/suppl68/pa594).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-1444/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-1444/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-1444/prf

Funding: S.P. was supported by an MSc fellowship from the Centre for Innovative Care and Health Technology (ciTechCare), funded by the Portuguese Foundation for Science and Technology (FCT) (UIDB/05704/2020) during the study, and P.M. held a PhD fellowship supported by the FCT (UIDB/05704/2020) during the study. The study was supported by ciTechCare, funded by the FCT (UIDB/05704/2025, DOI: https://doi.org/10.54499/UID/05704/2025).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-1444/coif). S.P. reports the MSc fellowship supported by the Centre for Innovative Care and Health Technology (ciTechCare), funded by the Portuguese Foundation for Science and Technology (UIDB/05704/2020). P.M. reports a PhD fellowship supported by the Portuguese Foundation for Science and Technology (UIDB/05704/2020). The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This is a secondary analysis of data from two previous studies that were conducted in accordance with the Declaration of Helsinki and its subsequent amendments, and were approved by the Ethics Committee of the Leiria Hospital Center (n.10-14/12/2021), District Hospital of Santarém (no ref; 22/04/2022), District Hospital of Figueira da Foz (Obs_CIC.12 / 2022) and Portuguese Oncology Institute of Coimbra (TI 36/2021, 18/11/2021). Informed consent was obtained from all individual participants included in the study.

References

1. Institute for Health Metrics and Evaluation (IHME). Global Burden of Disease 2021: Findings from the GBD 2021 Study. Seattle, WA: IHME, 2024.
2. Leiter A, Veluswamy RR, Wisnivesky JP. The global burden of lung cancer: current status and future trends. Nat Rev Clin Oncol 2023;20:624-39.
3. Sharma R. Mapping of global, regional and national incidence, mortality and mortality-to-incidence ratio of lung cancer in 2020 and 2050. Int J Clin Oncol 2022;27:665-75.
4. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
5. Rosen JE, Keshava HB, Yao X, et al. The Natural History of Operable Non-Small Cell Lung Cancer in the National Cancer Database. Ann Thorac Surg 2016;101:1850-5.
6. Baltayiannis N, Chandrinos M, Anagnostopoulos D, et al. Lung cancer surgery: an up to date. J Thorac Dis 2013;5 Suppl 4:S425-39.
7. Kim D, Lee JW. Current Status of Lung Cancer and Surgery Based on Studies Using a Nationwide Database. J Chest Surg 2022;55:1-9.
8. Nugent SM, Golden SE, Hooker ER, et al. Longitudinal Health-related Quality of Life among Individuals Considering Treatment for Stage I Non-Small-Cell Lung Cancer. Ann Am Thorac Soc 2020;17:988-97.

9. Brunelli A, Socci L, Refai M, et al. Quality of life before and after major lung resection for lung cancer: a prospective follow-up analysis. Ann Thorac Surg 2007;84:410-6.
10. Avery KNL, Blazeby JM, Chalmers KA, et al. Impact on Health-Related Quality of Life of Video-Assisted Thoracoscopic Surgery for Lung Cancer. Ann Surg Oncol 2020;27:1259-71.
11. Kenny PM, King MT, Viney RC, et al. Quality of life and survival in the 2 years after surgery for non small-cell lung cancer. J Clin Oncol 2008;26:233-41.
12. Pompili C, McLennan Battleday F, Chia WL, et al. Poor preoperative quality of life predicts prolonged hospital stay after VATS lobectomy for lung cancer. Eur J Cardiothorac Surg 2021;59:116-21.
13. Pompili C, Velikova G, White J, et al. Poor preoperative patient-reported quality of life is associated with complications following pulmonary lobectomy for lung cancer. Eur J Cardiothorac Surg 2017;51:526-31.
14. Brown LM, Gosdin MM, Cooke DT, et al. Health-Related Quality of Life After Lobectomy for Lung Cancer: Conceptual Framework and Measurement. Ann Thorac Surg 2020;110:1840-6.
15. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, et al. Guidelines for enhanced recovery after lung surgery: recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). Eur J Cardiothorac Surg 2019;55:91-115.
16. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. Med Sci Sports Exerc 2019;51:2375-90.
17. Gerritsen JK, Vincent AJ. Exercise improves quality of life in patients with cancer: a systematic review and meta-analysis of randomised controlled trials. Br J Sports Med 2016;50:796-803.
18. Granger C, Cavalheri V. Preoperative exercise training for people with non-small cell lung cancer. Cochrane Database Syst Rev 2022;9:CD012020.
19. Machado P, Pimenta S, Oliveiros B, et al. Effect of Exercise Training on Quality of Life after Colorectal and Lung Cancer Surgery: A Meta-Analysis. Cancers (Basel) 2021;13:4975.
20. Rosero ID, Ramírez-Vélez R, Lucia A, et al. Systematic Review and Meta-Analysis of Randomized, Controlled Trials on Preoperative Physical Exercise Interventions in Patients with Non-Small-Cell Lung Cancer. Cancers (Basel) 2019;11:944.
21. Steffens D, Beckenkamp PR, Hancock M, et al. Preoperative exercise halves the postoperative complication rate in patients with lung cancer: a systematic review of the effect of exercise on complications, length of stay and quality of life in patients with cancer. Br J Sports Med 2018;52:344.
22. Coats V, Maltais F, Simard S, et al. Feasibility and effectiveness of a home-based exercise training program before lung resection surgery. Can Respir J 2013;20:e10-6.
23. Ferreira V, Agnihotram RV, Bergdahl A, et al. Maximizing patient adherence to prehabilitation: what do the patients say? Support Care Cancer 2018;26:2717-23.
24. Shukla A, Granger CL, Wright GM, et al. Attitudes and Perceptions to Prehabilitation in Lung Cancer. Integr Cancer Ther 2020;19:1534735420924466.
25. Machado P, Pimenta S, Garcia AL, et al. Effect of Preoperative Home-Based Exercise Training on Quality of Life After Lung Cancer Surgery: A Multicenter Randomized Controlled Trial. Ann Surg Oncol 2024;31:847-59.
26. Machado P, Pimenta S, Garcia AL, et al. Home-Based Preoperative Exercise Training for Lung Cancer Patients Undergoing Surgery: A Feasibility Trial. J Clin Med 2023;12:2971.
27. Buffart LM, Newton RU, Chinapaw MJ, et al. The effect, moderators, and mediators of resistance and aerobic exercise on health-related quality of life in older long-term survivors of prostate cancer. Cancer 2015;121:2821-30.
28. Courneya KS, McKenzie DC, Mackey JR, et al. Moderators of the effects of exercise training in breast cancer patients receiving chemotherapy: a randomized controlled trial. Cancer 2008;112:1845-53.
29. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c869.
30. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
31. Pais-Ribeiro J, Pinto C, Santos C. Validation study of the Portuguese version of the QLC-C30-V.3. Psicologia, Saúde & Doenças 2008;9:89-102.
32. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst

1993;85:365-76.
33. Mak KS, van Bommel AC, Stowell C, et al. Defining a standard set of patient-centred outcomes for lung cancer. Eur Respir J 2016;48:852-60.
34. Fayers PM, Aaronson NK, Bjordal K, et al. EORTC QLQ-C30 Scoring Manual. 3rd ed. European Organisation for Research and Treatment of Cancer, Brussels; 2001.
35. Giesinger JM, Kieffer JM, Fayers PM, et al. Replication and validation of higher order models demonstrated that a summary score for the EORTC QLQ-C30 is robust. J Clin Epidemiol 2016;69:79-88.
36. Singh SJ, Morgan MD, Scott S, et al. Development of a shuttle walking test of disability in patients with chronic airways obstruction. Thorax 1992;47:1019-24.
37. Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing 2011;40:423-9.
38. Alcazar J, Losa-Reyna J, Rodriguez-Lopez C, et al. The sit-to-stand muscle power test: An easy, inexpensive and portable procedure to assess muscle power in older people. Exp Gerontol 2018;112:38-43.
39. Koller M, Musoro JZ, Tomaszewski K, et al. Minimally important differences of EORTC QLQ-C30 scales in patients with lung cancer or malignant pleural mesothelioma - Interpretation guidance derived from two randomized EORTC trials. Lung Cancer 2022;167:65-72.
40. Ranganathan P, Pramesh CS, Aggarwal R. Common pitfalls in statistical analysis: Logistic regression. Perspect Clin Res 2017;8:148-51.
41. Harris JK. Primer on binary logistic regression. Fam Med Community Health 2021;9:e001290.
42. Stoltzfus JC. Logistic regression: a brief primer. Acad Emerg Med 2011;18:1099-104.
43. Huang GH, Ismail H, Murnane A, et al. Structured exercise program prior to major cancer surgery improves cardiopulmonary fitness: a retrospective cohort study. Support Care Cancer 2016;24:2277-85.
44. Asemota N, Maraschi A, Lampridis S, et al. Comparison of Quality of Life after Robotic, Video-Assisted, and Open Surgery for Lung Cancer. J Clin Med 2023;12:6230.
45. Parreira VF, Janaudis-Ferreira T, Evans RA, et al. Measurement properties of the incremental shuttle walk test. a systematic review. Chest 2014;145:1357-69.
46. Spruit MA, Singh SJ, Garvey C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med 2013;188:e13-64.
47. Butler SJ, Louie AV, Sutradhar R, et al. Impact of COPD on lung cancer symptom burden: A population-based study. Eur Respir J 2023;62:PA3887.
48. Raichurkar P, Denehy L, Solomon M, et al. Research Priorities in Prehabilitation for Patients Undergoing Cancer Surgery: An International Delphi Study. Ann Surg Oncol 2023;30:7226-35.
49. McIsaac DI, Kidd G, Gillis C, et al. Relative efficacy of prehabilitation interventions and their components: systematic review with network and component network meta-analyses of randomised controlled trials. BMJ 2025;388:e081164.
50. Zhou W, Webster KE, Smith EL, et al. Physical activity in surgical lung cancer patients: a systematic review. Support Care Cancer 2022;30:6473-82.
51. Lai Y, Wang X, Zhou K, et al. Impact of one-week preoperative physical training on clinical outcomes of surgical lung cancer patients with limited lung function: a randomized trial. Ann Transl Med 2019;7:544.
52. Nolte S, Liegl G, Petersen MA, et al. General population normative data for the EORTC QLQ-C30 health-related quality of life questionnaire based on 15,386 persons across 13 European countries, Canada and the Unites States. Eur J Cancer 2019;107:153-63.

Cite this article as: Pimenta S, Machado P, Silva CG, Garcia AL, Nogueira T, Silva S, dos Santos CL, Martins MV, Canha A, Oliveiros B, Martins RA, Cruz J. Quality of life after preoperative home-based exercise training in patients with lung cancer: a secondary analysis. J Thorac Dis 2026;18(3):209. doi: 10.21037/jtd-2025-1444

