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STRUCTURED AND TAILORED EXERCISE PREHABILITATION IN COMPLEX PATIENTS SCHEDULED FOR LUNG RESECTION

A RETROSPECTIVE–PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background

Lung resection represents the standard curative treatment for early-stage lung cancer and selected pulmonary metastases; however, postoperative morbidity remains frequent, particularly in elderly, frail, and comorbid patients with reduced cardiopulmonary reserve. Functional impairment, physical deconditioning, and multiple comorbidities significantly increase surgical risk and negatively influence postoperative recovery. Exercise-based prehabilitation has recently gained a role as a strategy aimed at improving physiological reserve before surgery, but clinical implementation in thoracic surgery remains limited and poorly standardized, especially in complex patients. Since 2018, a structured collaboration between the Thoracic Surgery Unit and the Sports Medicine Unit of the Policlinico Riuniti of Foggia has progressively developed a multidisciplinary prehabilitation pathway integrated within an Enhanced Recovery After Surgery (ERAS) program, culminating in the implementation of a formally approved prospective protocol.

Methods

This retrospective–prospective single-centre observational study evaluated the effects of a structured and individualized exercise-based prehabilitation program in patients scheduled for lung resection. Patients underwent comprehensive functional assessment before (T0) and after prehabilitation (T1), including spirometry, body composition analysis, handgrip strength, and performance evaluation through the six-minute walk test (6MWT). The training program consisted of supervised aerobic, mobility, and resistance exercises prescribed according to ACSM principles and the FITT-VP model. Postoperative outcomes were analysed in patients undergoing major lung resection and compared with a contemporaneous non-prehabilitated control group with comparable baseline characteristics. Outcomes included postoperative complications, prolonged air leak (PAL), chest drain duration, and length of hospital stay (LOS). Multivariable regression analyses were performed to adjust for relevant clinical confounders.

Results

Between December 2022 and November 2025, 76 patients were referred for prehabilitation; 48 completed the program and were evaluated at T0 and T1, and 30 subsequently underwent major lung resection. Prehabilitation resulted in significant improvements in functional performance, with marked increases in 6MWT distance and walking speed, together wit favourable trends in respiratory and muscular parameters. Multivariable analysis demonstrated that functional improvement was primarily associated with exercise intensity rather than the number of training sessions performed. Compared with matched controls, prehabilitated patients experienced a significantly lower incidence of postoperative complications and prolonged air leak, together with shorter air leak duration and trends toward reduced chest drain duration and hospital stay.

Conclusions

Exercise-based prehabilitation represents a feasible and effective strategy for perioperative optimization in complex thoracic surgical patients. The integration of a multidisciplinary, hospital-based prehabilitation pathway within ERAS programs may improve functional status before surgery and contribute to reducing postoperative morbidity, supporting its broader implementation in thoracic surgical practice.

1. INTRODUCTION

1.1 Physiopathology of lung resection and functional impairment

Lung resection remains the standard curative treatment for early-stage lung cancer and selected pulmonary metastases. Despite major advances in minimally invasive techniques and the widespread adoption of Enhanced Recovery After Surgery (ERAS) pathways, postoperative morbidity after lung resection remains clinically relevant, particularly in frail and comorbid patients. Postoperative pulmonary complications (PPCs), prolonged air leak (PAL), secretion retention, and delayed functional recovery are among the most frequent adverse events and are major determinants of prolonged chest drainage, extended length of hospital stay (LOS), readmissions, and increased healthcare costs.

In contemporary thoracic surgical practice, patient complexity is steadily increasing as a consequence of population ageing and the rising prevalence of multimorbidity. Frailty, sarcopenia, physical deconditioning, and malnutrition are highly prevalent in patients with lung cancer and significantly contribute to surgical vulnerability. As a result, a growing proportion of candidates for lung resection present with limited cardiopulmonary reserve, impaired functional capacity, and multiple comorbidities, often challenging traditional operability criteria. These features define the so-called complex patient, who is at particularly high risk of postoperative complications and delayed recovery. Importantly, functional capacity represents a potentially modifiable risk factor and therefore an attractive target for preoperative optimisation.

1.2 Exercise-based prehabilitation: evidence and current limitations

Prehabilitation in thoracic surgery has emerged as a multimodal strategy aimed at enhancing physiological reserve before surgery, mitigating the surgical stress response, and improving postoperative outcomes. Current evidence and expert consensus support structured exercise interventions—including aerobic training, resistance training, and inspiratory muscle training—combined with nutritional optimisation, smoking cessation, and patient education as key components of thoracic prehabilitation programs [1–4]. Among these elements, structured physical exercise represents the cornerstone intervention, with consistent evidence demonstrating improvements in aerobic capacity, peak oxygen uptake (VO_2peak), muscle strength, and exercise tolerance.

Systematic reviews and meta-analyses suggest that preoperative pulmonary rehabilitation may reduce PPCs and LOS while improving functional outcomes such as six-minute walk distance (6MWD) and VO_2peak [5–7]. However, the overall quality of evidence remains heterogeneous. In a recent systematic review and meta-analysis, Voorn et al. highlighted that although exercise-based prehabilitation is associated with favourable functional and clinical outcomes in patients undergoing surgery for non-small cell lung cancer (NSCLC), the therapeutic quality of available studies remains low and no clear recommendations can be drawn regarding the optimal content, intensity, or duration of exercise programs [8]. This lack of standardisation is particularly evident in high-risk and multimorbid populations, who are often underrepresented in prospective studies.

From a pathophysiological perspective, lung resection represents a major surgical insult characterised by loss of functional lung parenchyma, altered chest wall mechanics, ventilation–perfusion mismatch, and a systemic inflammatory response. These changes are further exacerbated in patients with pre-existing pulmonary disease, reduced respiratory muscle strength, or impaired exercise tolerance. Prehabilitation aims to improve ventilatory efficiency, respiratory muscle performance, peripheral oxygen utilisation, and overall physical resilience, thereby increasing the patient's ability to tolerate the physiological stress of thoracic surgery and the early postoperative period.

In this context, national and international recommendations increasingly recognise prehabilitation as part of optimal perioperative care. The Italian intersociety consensus on Perioperative Anesthesia Care in Thoracic Surgery (PACTS) identifies multimodal prehabilitation as a recommended component of good clinical practice in the preoperative management of patients undergoing elective lung resection, particularly when implemented for at least three weeks before surgery, with potential benefits in reducing postoperative complications and LOS [9]. Similarly, ERAS Society and European Society of Thoracic Surgeons (ESTS) guidelines auspicate the integration of prehabilitation within ERAS pathways to improve functional recovery and overall surgical outcomes [1,10]. Nonetheless, substantial heterogeneity persists regarding patient selection, intervention content, intensity, and timing, and real-world prospective evidence in complex thoracic surgical populations remains limited [6,7].

Beyond the clinical domain, there is growing interest in recognising structured physical exercise as a preventive and therapeutic intervention within healthcare systems. In Italy, this perspective is reflected in the proposal to include adapted physical exercise for high-risk patients among the Essential Levels of Care (LEA), as outlined in the legislative initiative (DDL 287), underscoring the potential role of prehabilitation as a public health strategy.

1.3 Rationale of the study

Within this evolving framework, the present study arises from a structured clinical pathway jointly developed by the Thoracic Surgery Unit and the Sports Medicine Unit of the Policlinico Riuniti of Foggia. Since 2018, both units have progressively integrated preoperative functional optimisation into the perioperative management of patients undergoing lung resection, with particular attention to frail and comorbid individuals. This collaboration enabled the accumulation of clinical experience aimed at refining indications for prehabilitation and tailoring exercise-based interventions to the specific needs of thoracic surgical patients. However, all previous experiences were retrospective in nature and not supported by a formally approved prospective study protocol.

1.4 Study objectives

To address these limitations, a structured and standardised exercise-based prehabilitation protocol was subsequently developed and implemented, allowing prospective patient enrolment and systematic functional and clinical assessment within an officially approved ethical framework. Therefore, the present retrospective–prospective observational study aimed to evaluate the impact of a structured and tailored exercise-based prehabilitation program in complex patients undergoing lung resection. The primary objective was to assess preoperative functional improvements by comparing baseline (T0) and post-training (T1) functional performance. Secondary objectives were to evaluate postoperative outcomes by comparing prehabilitated patients with a non-prehabilitated control group with similar baseline characteristics, focusing on overall postoperative complications, prolonged air leak, chest drain duration, and length of hospital stay. By combining prospective functional assessment with comparative postoperative outcome analysis, this study seeks to provide real-world evidence to support the integration of exercise-based prehabilitation into thoracic ERAS pathways.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This was a single-centre, retrospective–prospective observational case–control study conducted at the Thoracic Surgery Unit of the Policlinico Riuniti University Hospital of Foggia, in collaboration with the Sports Medicine Unit. It was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the local Ethics Committee of the Policlinico Riuniti of Foggia (protocol number 180/CE/2024, approved on 17 December 2024). All patients provided written informed consent before enrolment.

The study consisted of two phases: a prospective phase, including patients referred for and enrolled in a structured preoperative exercise-based prehabilitation program; a retrospective phase, including patients who underwent lung resection without prehabilitation (control group).

2.2 Patient Pathway and Referral to Prehabilitation

All patients listed for elective lung resection for primary or secondary lung cancer were evaluated during the preoperative surgical assessment. Patients deemed potentially eligible for prehabilitation were referred by the Thoracic Surgery Unit to the Sports Medicine Unit through an official institutional consultation request.

At baseline (T0), patients underwent a comprehensive clinical and functional evaluation in both units. Eligibility for the prehabilitation program was confirmed jointly by thoracic surgeons and sports medicine physicians. Patients fulfilling clinical and functional criteria were offered participation in the supervised exercise-based prehabilitation program. Written informed consent was obtained before enrolment.

2.3 Study Population

Inclusion Criteria

- Age between 18 and 85 years;
- Diagnosis of resectable primary or secondary lung cancer;
- Surgical indication for major lung resection (lobectomy, anatomical segmentectomy, or pneumonectomy);
- Multiple comorbidities (Charlson Comorbidity Index >5);
- Clinical stability;
- Modified Borg dyspnoea score <2.5;

- Reduced functional capacity;
- Stable oxygen saturation and blood pressure values according to American College of Sports Medicine (ACSM) guidelines.

Exclusion Criteria
- Inability to provide informed consent;
- Severe cardiac or respiratory instability;
- Contraindications to physical exercise;
- Severe locomotor limitations;
- Neurological or cognitive disorders preventing participation in structured exercise programs.

2.4 Baseline Assessments (T0)

Thoracic Surgery Evaluation

Baseline evaluation included:
- Detailed medical history and physical examination;
- Vital signs and body mass index (BMI);
- Blood tests, electrocardiogram, cardiology consultation with echocardiography, arterial blood gas analysis;
- Pulmonary function tests including spirometry and DLCO.

Sport Medicine Evaluation

The Sports Medicine Unit performed:
- Physical examination and vital signs assessment;
- Body composition analysis by bioelectrical impedance analysis (BIA);
- Spirometry and cardiopulmonary exercise testing when clinically indicated;
- Functional musculoskeletal evaluation;
- Handgrip strength assessment;
- Six-minute walk test (6MWT) on treadmill;
- Exercise-Based Prehabilitation Protocol (Planned Intervention).

The prehabilitation program was designed according to ACSM guidelines [11,12] and the FITT-VP model (Frequency, Intensity, Time, Type, Volume, Progression) [13]. The planned protocol consisted of a three-week supervised program, with three sessions per week, for a total of nine sessions. Each session included three sequential phases:

1)Warm-up:

- Five minutes of low-intensity cycling on a cycle ergometer.

2)Conditioning phase:

- Aerobic exercise on a treadmill (20–30 minutes), at moderate intensity (60–80% of predicted HRmax or Borg RPE 11–13);
- Shoulder mobility exercises using pulley systems;
- Resistance training for upper and lower limbs (2–3 sets, progressive overload);
- Respiratory exercises, including inspiratory muscle training with incremental resistance, breathing expansion exercises, and PEP techniques.

3)Cool-down

- Low-intensity cycling followed by static stretching exercises.

All sessions were supervised by a certified kinesiologist, with continuous availability of a consultant physician from the Sports Medicine Unit.

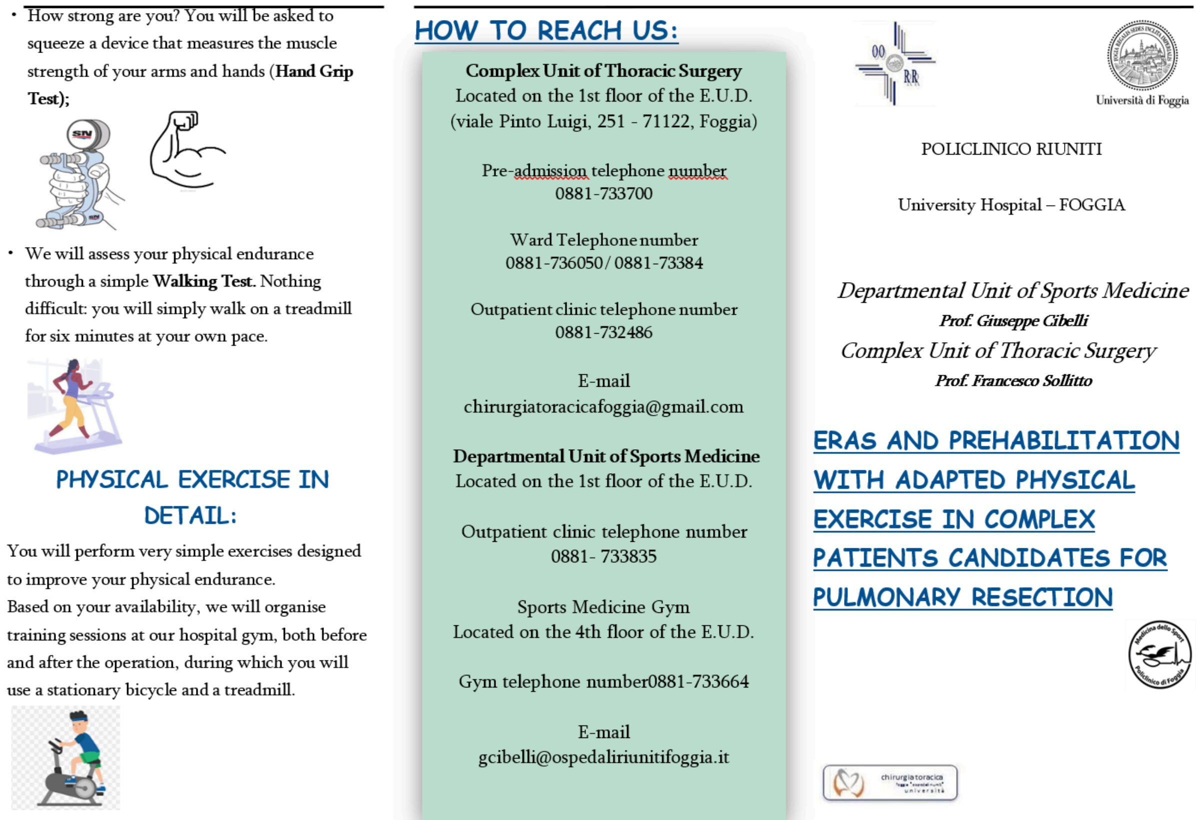
Before and after each training session, vital parameters were assessed, including blood pressure and heart rate. Capillary blood glucose was measured in participants with diabetes. Participants' overall clinical condition was reviewed at each session to ensure safety and adherence to the program.

2.5 Education and counselling

In addition to the supervised exercise training, the prehabilitation program included education and counselling interventions delivered throughout the training period. These focused on:

- Smoking cessation counselling, when applicable;
- Optimisation of ongoing medical therapy, in collaboration with the referring thoracic surgeon and anesthesiologist;
- Patient education on early postoperative mobilisation, breathing strategies, and adherence to ERAS principles.

Education and counselling were provided during training sessions by the sports medicine team and reinforced during multidisciplinary discussions. During the enrolment phase, all patients referred for prehabilitation received a dedicated informative brochure describing the ERAS pathway and the exercise-based prehabilitation program, including preoperative assessments, training sessions, and postoperative recommendations. The brochure was used as an educational tool to improve patient understanding, adherence, and active participation in the perioperative pathway. These interventions were integrated into routine clinical care and aimed at improving patient engagement and perioperative preparedness.



- How strong are you? You will be asked to squeeze a device that measures the muscle strength of your arms and hands (**Hand Grip Test**);
- We will assess your physical endurance through a simple **Walking Test**. Nothing difficult: you will simply walk on a treadmill for six minutes at your own pace.

PHYSICAL EXERCISE IN DETAIL:

You will perform very simple exercises designed to improve your physical endurance.
Based on your availability, we will organise training sessions at our hospital gym, both before and after the operation, during which you will use a stationary bicycle and a treadmill.

HOW TO REACH US:

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Located on the 1st floor of the E.U.D.
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Pre-admission telephone number
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University Hospital – FOGGIA

Departmental Unit of Sports Medicine
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Prof. Francesco Sollitto

ERAS AND PREHABILITATION WITH ADAPTED PHYSICAL EXERCISE IN COMPLEX PATIENTS CANDIDATES FOR PULMONARY RESECTION

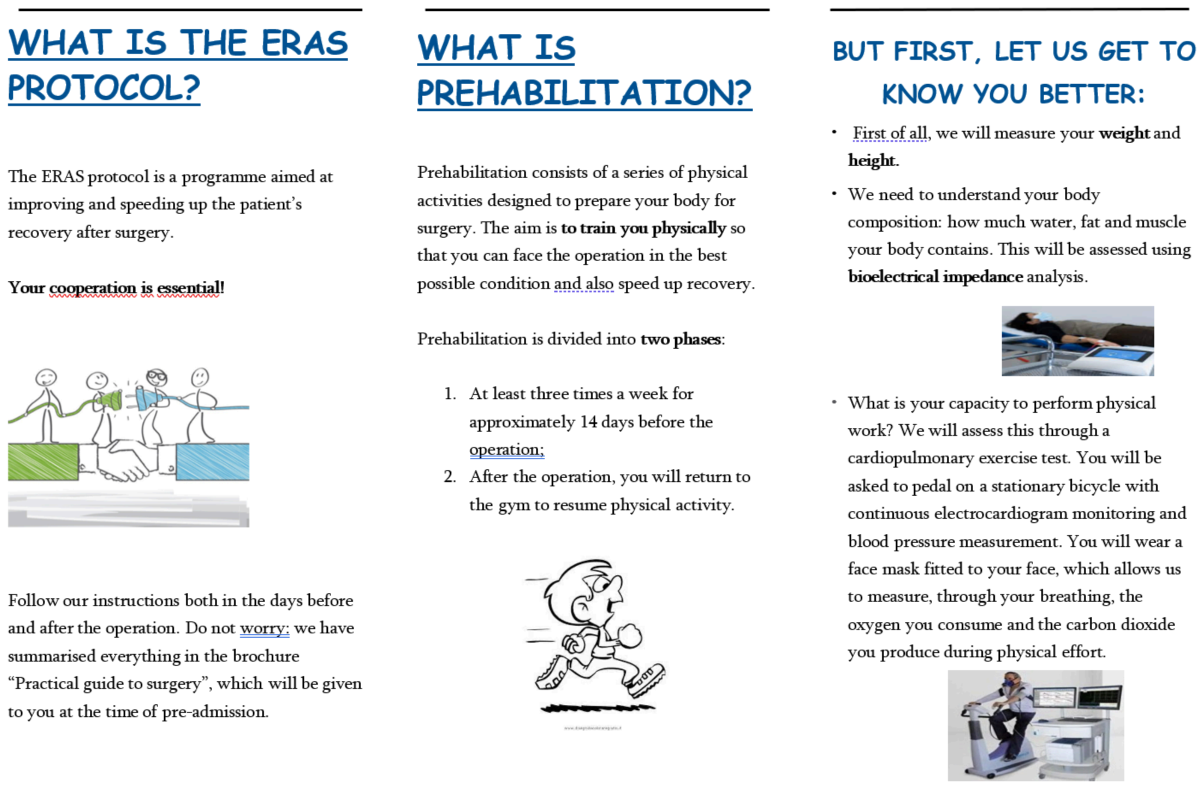

Figure 1. Informative brochure.

2.6 Implementation of the Prehabilitation Program (Real-World Adherence)

A dedicated multidisciplinary team was established to oversee patient enrolment, prehabilitation delivery, and perioperative management. The team included thoracic surgeons, sports medicine physicians, anaesthesiologists, specialised nurses, and certified kinesiologists, ensuring comprehensive clinical supervision throughout the preoperative period. Patient selection and surgical indication were defined by the thoracic surgery team, while functional assessment and exercise prescription were performed by the Sports Medicine Unit in collaboration with the anaesthesiology team as part of perioperative risk stratification. The hospital is equipped with a dedicated Sports Medicine facility, including an indoor gym specifically designed for supervised therapeutic exercise, which allowed the implementation of a structured and safe prehabilitation program within the hospital setting.

Although the planned protocol included nine sessions, the actual number of completed sessions ranged from five to twelve, depending on individual clinical status and logistical factors. The mean number of sessions performed was seven. Training sessions were primarily conducted individually; from the third week onward, selected phases were performed in small groups of two participants.

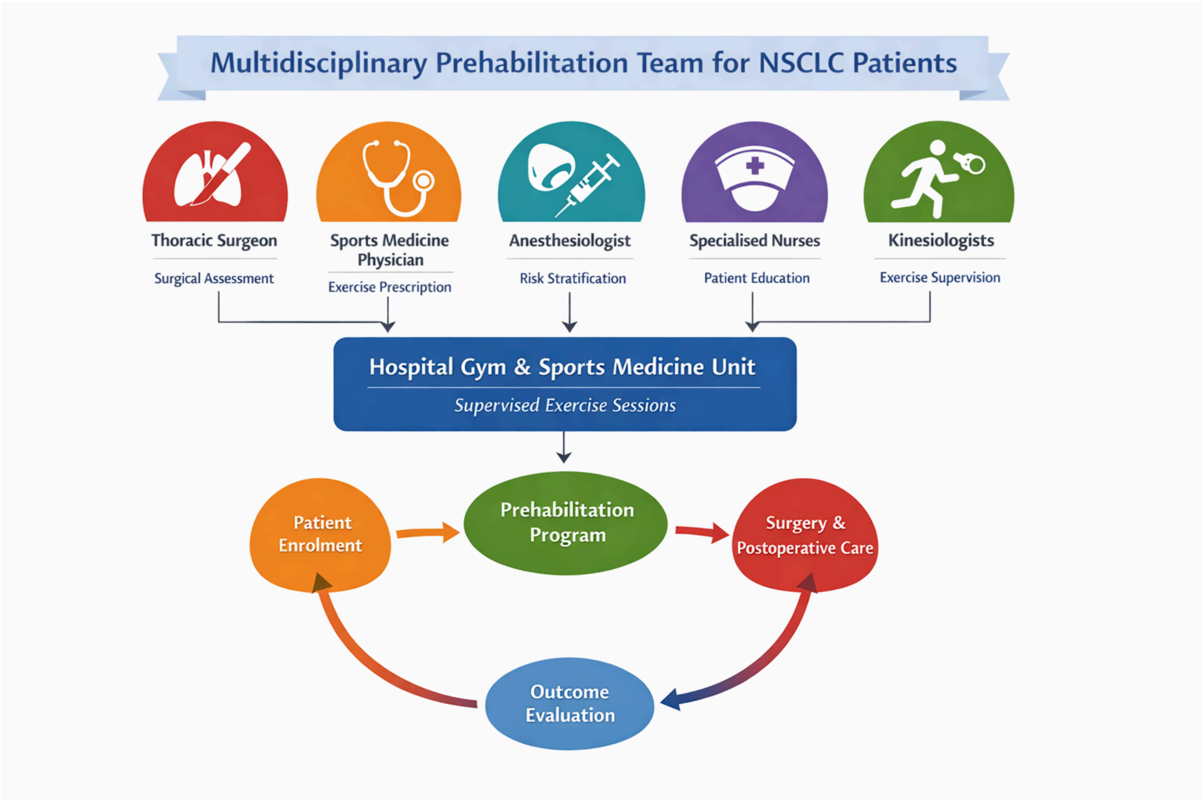

Figure 2. Multidisciplinary team and organisational framework.

2.7 Exercise prescription

Exercise prescription was individualised based on target heart rate, baseline functional capacity, medical history, comorbidities, and current pharmacological therapy. The program followed the FITT-VP model (Frequency, Intensity, Time, Type, Volume, and Progression) in accordance with the American College of Sports Medicine (ACSM) guidelines.

Training Session Structure

Warm-up

Each session began with five minutes of cycling on a cycle ergometer at low intensity.

Conditioning Phase

- Shoulder Joint Mobility Exercises

Shoulder mobility was performed using a pulley system to allow controlled and progressive joint movement.

- Assisted alternating upper limb elevation

Participants stood upright with support from wall bars, holding a rope attached to a pulley. Alternating elevation of the upper limbs in the sagittal plane was performed in three sets of 20 repetitions.

Figure 3. Alternating elevation of the upper limbs assisted by a pulley, performed in a standing position while holding onto the wall bars for support.

- Upper limb abduction with respiratory synchronization

Participants performed bilateral upper limb abduction in the frontal plane while coordinating movement with breathing (inspiration during abduction, expiration during adduction), for three sets of 10 repetitions.

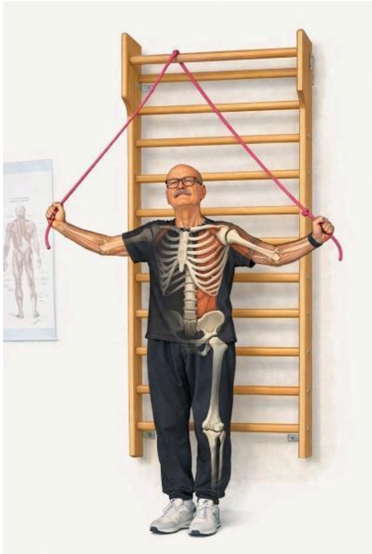

Figure 4. Bilateral abduction of the upper limbs assisted by a pulley, performed while maintaining controlled breathing

- Aerobic Exercise – Treadmill Walking

Participants performed 20 minutes of treadmill walking. Exercise intensity was set at 60–70% of predicted maximal heart rate (220 − age), corresponding to 11–13 on the Borg RPE scale (6–20). Heart rate was continuously monitored using a Polar H9 device. Treadmill speed was initially set at approximately 80% of the speed achieved during the six-minute walk test and adjusted as needed to remain within the target heart rate and RPE ranges. Intensity and duration were progressively increased until participants were able to complete 20 minutes of continuous walking at an RPE of 13.

Figure 5. Aerobic exercise performed on a treadmill under the supervision of healthcare staff.

- Hand Bike Resistance Training

Following the initial functional assessment, five minutes of hand bike resistance training were added at the end of each session. This consisted of three one-minute backward intervals and two one-minute forward intervals, performed continuously without rest. This component aimed to improve upper-limb muscular endurance, neuromuscular coordination, and overall exercise tolerance.

Cool-down

The cool-down phase included five minutes of low-intensity cycling, followed by static stretching exercises.

- Shoulder muscle stretching

Participants performed static elevation and abduction exercises, holding each position for 20 seconds. Elevation was done one limb at a time, while abduction was maintained at maximal separation. Each exercise was repeated three times.

- Hamstring stretching

Hamstrings were stretched while seated, with one leg extended forward, heel on the floor, knee straight, and ankle neutral (90°). The opposite leg was flexed at 90°, foot on the floor. A rope under the sole of the extended foot assisted the stretch. Each leg was stretched for two sets of 20 seconds, avoiding bouncing.

Figure 6. Stretching of the hamstring muscles in a seated position with the assistance of a rope.

- Iliopsoas stretchin

Participants stretched the iliopsoas while standing, supporting themselves with one hand on a wall bar. The leg to be stretched was positioned behind the body with knee extended, while body weight was on the contralateral leg. Each stretch was held for 20 seconds and repeated twice per leg.

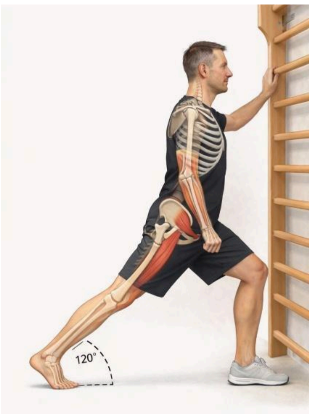

Figure 7. Stretching of the iliopsoas muscles in a standing position with support from the wall bars.

From the third week onward, the cool-down phase was conducted in pairs under kinesiologist supervision.

Post-Prehabilitation Assessment (T1)

At the end of the prehabilitation period and before surgery (T1), all prehabilitated patients underwent repeat functional evaluation at the Sports Medicine Unit, including:

- 6MWT;
- Handgrip strength;
- Spirometry;
- Body composition analysis.

Results were discussed in a multidisciplinary setting involving thoracic surgeons, anesthesiologists, and sports medicine specialists as part of the final preoperative risk assessment.

Surgery and Postoperative Management

Patients subsequently underwent the planned surgical procedure. Patients who received a different procedure than initially indicated (e.g. atypical wedge resection due to negative frozen section) were excluded from postoperative outcome analysis.

Postoperative Follow-up

After discharge, prehabilitated patients in stable clinical conditions were allowed to continue adapted exercise training voluntarily. Follow-up functional reassessment (T2) was offered 50–90 days after surgery; however, T2 data were not included in the present analysis.

2.8 Data Collection

All data were prospectively collected in a shared, anonymized Excel database in accordance with privacy regulations. Collected data included demographic, clinical, functional, body composition, exercise training, and postoperative outcome variables, as detailed in the approved study protocol.

Controls were selected from the institutional surgical database and were matched according to age, sex, Charlson Comorbidity Index, ECOG performance status and type of pulmonary resection.

2.9 Statistical Analysis

Continuous variables were assessed for distributional properties. Variables with an approximately normal distribution are reported as mean ± standard deviation (SD), whereas variables with a skewed distribution and/or ordinal nature (including Charlson Comorbidity Index and ECOG Performance Status) are reported as median and interquartile range (IQR, 25th–75th percentile). Categorical variables are presented as absolute frequencies and percentages. Between-group comparisons were performed using the Student's *t* test for normally distributed continuous variables and the Mann–Whitney *U* test for non-normally distributed variables. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. A two-sided *p* value <0.05 was considered statistically significant.

Multivariable analysis of functional improvement

To identify determinants of functional improvement following prehabilitation, a multivariable linear regression analysis was performed with the change in six-minute walk distance (Δ6MWT, expressed in meters) as the dependent variable. Δ6MWT was calculated as the difference between post-prehabilitation (T1) and baseline (T0) values. Clinically relevant baseline characteristics and training-related parameters were selected *a priori* based on physiological plausibility and previous literature. The model included age (years), sex, Charlson Comorbidity Index, ECOG performance status, baseline 6MWT distance (T0), total number of supervised training sessions completed, and exercise intensity expressed as metabolic equivalents (METs) achieved at T1 during the 6MWT. Only patients with complete data for all variables included in the model were analysed (complete-case analysis). Continuous variables were entered as linear terms. Regression coefficients (β) are reported as the expected change in Δ6MWT (in meters) associated with a one-unit increase in each predictor, with corresponding 95% confidence intervals (CI) and *p* values.

Analysis of postoperative clinical outcomes

Postoperative clinical outcomes were analysed in patients undergoing major lung resection. Overall postoperative complications were defined as the occurrence of at least one postoperative adverse event, including pulmonary, cardiovascular, or surgical complications, and/or any complication graded ≥ I according to the Clavien–Dindo classification. Specific outcomes included prolonged air leak (PAL >5 days), secretion retention, atrial fibrillation, hemothorax, pneumothorax, need for reintervention, blood transfusion, home oxygen prescription, air leak duration, chest drain duration, length of hospital stay (LOS), and complication severity according to the Clavien–Dindo classification. Any postoperative complication was defined as the occurrence of at least one postoperative adverse event or a Clavien–Dindo grade ≥ I. Categorical postoperative outcomes were compared using Fisher's exact test or the χ^2 test, as appropriate. Continuous postoperative variables are reported as median and IQR and were compared using the Mann–Whitney *U* test. Multivariable analyses were performed according to outcome type and event distribution. For dichotomous outcomes with sufficient event frequency, fully adjusted binary logistic regression models were constructed including age, sex, Charlson Comorbidity Index, ECOG performance status, and surgical approach (VATS). For overall postoperative complications, given the limited number of events and the marked imbalance between groups, a parsimonious logistic regression model was applied to avoid overfitting; this model included prehabilitation status and clinically relevant covariates selected *a priori* (age and surgical approach). For continuous postoperative outcomes (air leak duration, chest drain duration, and LOS), multivariable linear regression analyses were performed adjusting for age, sex, Charlson Comorbidity Index, ECOG performance status, and surgical approach. Results are reported as odds ratios (ORs) or regression coefficients (β), with 95% confidence intervals (CI).

Missing data

Missing data were handled using a complete-case approach. For each multivariable model, only patients with complete data for the outcome of interest, group allocation, and adjustment covariates were included. Consequently, the analysed sample size varied according to the specific outcome (n = 58 for overall postoperative complications, n = 57 for prolonged air leak >5 days, and n = 58 for secretion retention). No imputation of missing data was performed.

3. RESULTS

3.1 Study population and flow of patients

A total of 76 patients meeting the inclusion criteria were referred for the prehabilitation program between December 2022 and November 2025 and underwent baseline evaluation (T0). Following baseline assessment, 28 patients were excluded from the prehabilitation pathway for the following reasons: refusal to participate in the protocol (n = 8), logistical problems (n = 10), change in surgical indication (n = 3), and clinical unsuitability for prehabilitation (n = 7).

As a result, 48 patients were included in the prehabilitation program and completed the intervention, undergoing post-intervention assessment (T1).

Paired analyses were performed between T0 and T1 in this cohort to evaluate changes in functional performance following prehabilitation.

After completion of the prehabilitation program, 18 patients underwent atypical lung resections and were excluded from the surgical outcomes analysis.

The remaining 30 patients underwent anatomical lung resection and constituted the prehabilitation surgical group.

The clinical outcomes of 30 prehabilitated patients undergoing anatomical lung resection were compared with those of 30 control patients who underwent similar surgical procedures without prehabilitation and with comparable baseline characteristics.

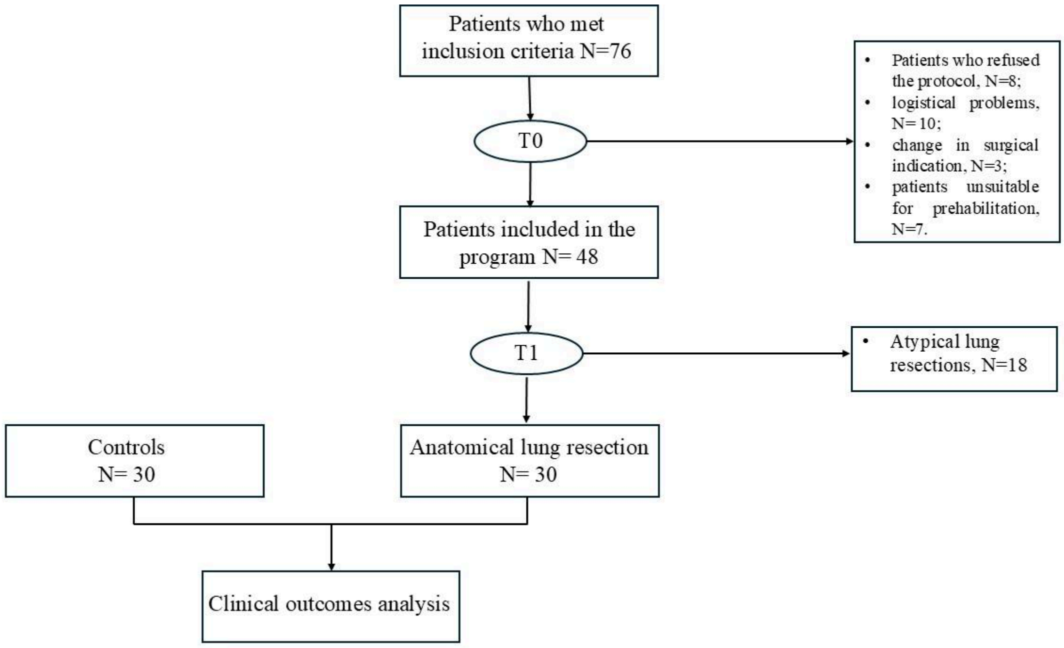

Figure 8. Flowchart of patient enrollment, exclusions, prehabilitation completion, and inclusion in functional and clinical outcomes analyses.

3.2 Patients' baseline characteristics

Baseline characteristics of the prehabilitation cohort are reported in Table 1. Patients were characterised by advanced age and a high burden of comorbidities. Although the mean preoperative FEV1 was relatively preserved, gas exchange was moderately impaired, with a mean DLCO of 66.8%. Predicted postoperative pulmonary function further declined, with mean ppoFEV1 and ppoDLCO values of 66.7% and 53.4%, respectively, indicating an intermediate-to-high operative risk profile according to current guidelines.

Table 1. Patients' baseline characteristics

Variable	Value
Age (years), mean ± SD	69.6 ± 9.1
Male sex, n (%)	30 (62.5)

ECOG performance status, median [IQR]	1 [1–2]
Charlson Comorbidity Index, median [IQR]	6 [5–7]
Body mass index (kg/m^2), mean ± SD	26.4 ± 4.3
FEV1% , mean ± SD	83.9 ± 23.6
FVC%, mean ± SD	92.1 ± 18.7
DLCO%, mean ± SD	66.8 ± 19.1
ppoFEV1%,mean ± SD	66.7 ± 19.5
ppoDLCO%, mean ± SD	53.4 ± 15.9
Fat mass (%), mean ± SD	30.2 ± 8.1
Fat-free mass (kg), mean ± SD	52.6 ± 9.4
Phase angle (°), mean ± SD	4.7 ± 0.9
6-minute walk distance at T0 (m), mean ± SD	336.8 ± 82.4

Table 1. Patients' baseline characteristics

3.3 Functional outcomes

The number of training sessions before intervention showed a median of 7 sessions interquartile range(IQR 4.0–11.25). The duration of training before T1 was 3 weeks IQR: 2.0–4.0. The time elapsed between T1 and intervention was 3 days IQR:**1.0–5.0**. Most patients (67.9%) underwent surgery within 1–3 days after T1, whereas 32.1% waited more than 3 days. Functional outcomes before and after completion of the prehabilitation program are summarised in Table 2. A significant improvement in exercise capacity was observed following training. Mean 6-minute walk distance increased by 80.8 meters, corresponding to a relative improvement of approximately 24%, while mean walking speed increased by 0.80 km/h (both $p<0.001$). The estimated VO_2 peak showed a non-significant increase. These findings indicate a clinically meaningful enhancement of functional performance before surgery. Cardiopulmonary exercise testing was available in a subgroup of 16 patients. No significant changes were observed in maximal aerobic capacity following prehabilitation. Mean VO_2peak and MET at peak exercise did not differ significantly between T0 and T1, suggesting that short-term prehabilitation mainly affected submaximal functional performance rather than maximal cardiopulmonary capacity.

Table 2. Functional outcomes before and after prehabilitation (T0 vs T1)

Variable	T0	T1	Δ (T1–T0)	p value
6-minute walk distance (m), mean ± SD	336.8 ± 82.4	417.6 ± 86.9	+80,8	<0.001
Walking speed (km/h), mean ± SD	3.38 ± 0.82	4.18 ± 0.87	+0,8	<0.001

Table 2. Functional outcomes before and after prehabilitation (T0 vs T1).

Figures 9 and 10 include the Boxplots showing the distribution of changes in 6-minute walk distance (Δ6MWT) and walking speed (Δspeed) following completion of the prehabilitation program. Boxes represent the interquartile range, the horizontal line indicates the median, and whiskers represent the range excluding outliers. Most patients experienced a clinically meaningful improvement in both functional parameters, with median values well above zero.

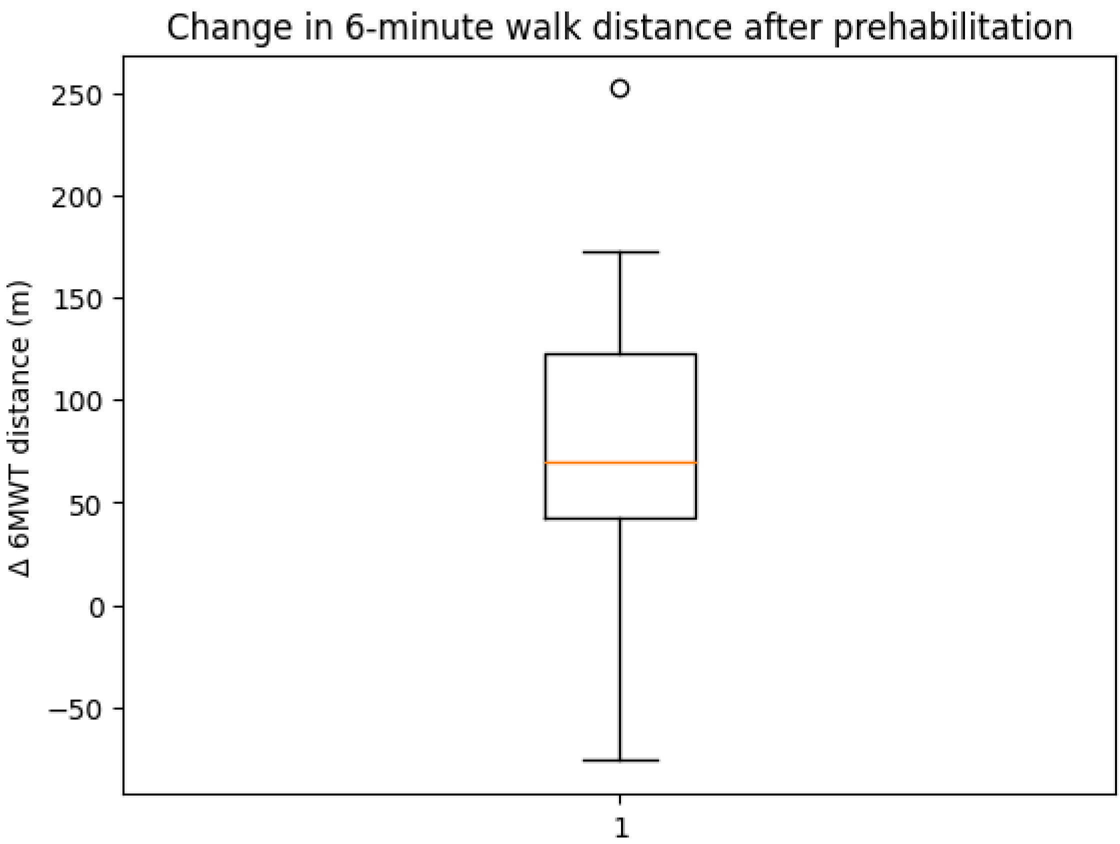

Figure 9. Change in 6-minute walk distance after prehabilitation

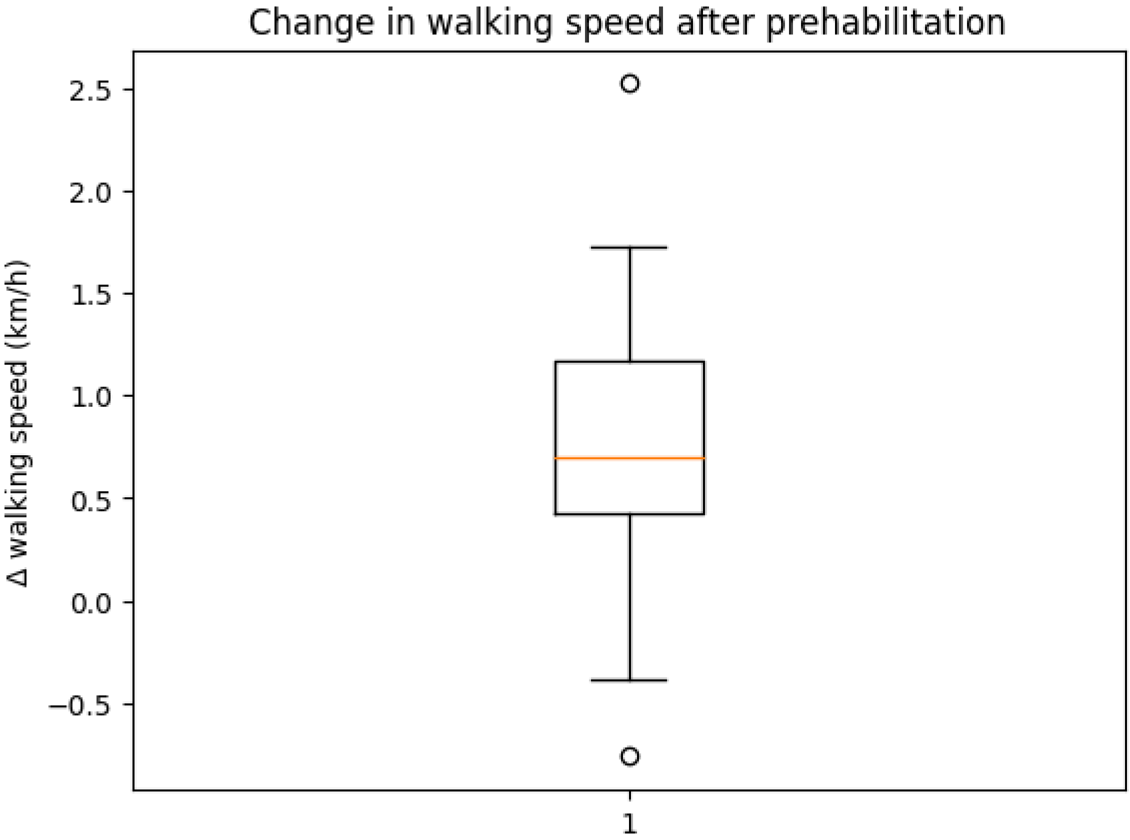

Figure 10. Change in walking speed after prehabilitation

3.4 Exploratory analyses: determinants of functional improvement

To explore the determinants of functional improvement after prehabilitation, a multivariable linear regression model was built with change in 6-minute walk distance (Δ6MWT) as the dependent variable (Table 3). The model included both clinical and training-related variables: age, sex, Charlson Comorbidity Index, ECOG performance status, baseline 6-minute walk distance, total number of training sessions, and exercise intensity expressed as METs achieved at T1 during the 6MWT. The analysis was performed in 32 patients with complete data for all included variables. Age, sex, Charlson index and ECOG were included in the model but were not independently associated with functional improvement. Regression coefficients (β) represent the expected change in 6-minute walk distance (meters) associated with a one-unit increase in each predictor. Higher exercise intensity, expressed as METs achieved at T1, was independently associated with greater functional improvement, whereas the total number of training sessions was not. Baseline functional capacity showed an inverse association with Δ6MWT, indicating larger gains in patients with lower initial performance.

Table 3. Multivariable linear regression analysis for Δ6MWT

Predictor	β (meters)	95% CI	p-value
MET at T1 (6MWT)	113.41.00	88.54 to 138.27	<0.001
Number of training sessions	−0.52	−2.57 to +1.54	1.00
Baseline 6MWT (T0)	−0.92	−1.08 to −0.77	<0.001

Table 3. Multivariable linear regression

3.4.1 Changes in body composition and muscle strength

Changes in body composition and muscle strength before and after completion of the prehabilitation program were also evaluated. No significant differences were observed in bioelectrical impedance analysis parameters, including fat mass, fat-free mass, and phase angle, between baseline (T0) and post-prehabilitation (T1) assessments. Similarly, upper limb muscle strength, assessed by handgrip dynamometry, did not show significant changes following the training period.

3.5 Clinical postoperative outcomes

To evaluate the impact of prehabilitation on postoperative outcomes, patients who underwent major lung resection after completing the prehabilitation program were compared with a control group of patients undergoing major lung resection without prehabilitation. Only patients undergoing anatomical resections were included in this analysis. Baseline characteristics of the two groups are reported in Table 4.

Table 4. Patients' baseline characteristics

Variable	ERAS (n=30)	Control (n=30)	p-value
Age (years), mean ± SD	71.2 ± 8.3	72.3 ± 8.9	0.6
Sex (male), n (%)	21 (72.4)	21 (70.0)	0.8
Smoking status, n (%)			
Yes	7 (24.1)	12 (40.0)	0.3
No	7 (24.1)	8 (26.7)	
Ex	15 (51.7)	10 (33.3)	
Charlson comorbidity index, median [IQR]	6.0 [6.0–7.0]	6.0 [6.0–7.0]	0.8
ECOG score, median [IQR]	0.0 [0.0–1.0]	1.0 [0.0–1.0]	0.09
FEV1% (T0), mean ± SD	85.0 ± 25.4	82.4 ± 19.1	0.6
DLCO% (T0), mean ± SD	69.6 ± 22.6	60.4 ± 10.5	0.1
ppoFEV1%,mean ± SD	66.7 ± 19.5	69.5±15.4	0.3
ppoDLCO%, mean ± SD	53.4 ± 15.9	55±12.3	0.4

Table 4. Patients' baseline characteristics

Baseline characteristics

Baseline demographic, clinical, and functional characteristics of patients undergoing lobectomy in the prehabilitation group (n = 30) and in the control group (n = 30) are summarised in Table 4. The two groups were well balanced with respect to age (71.2 ± 8.3 vs 72.3 ± 8.9 years, p = 0.6) and sex distribution, with a similar proportion of male patients (72.4% vs 70.0%, p = 0.8). Smoking status did not significantly differ between groups (p = 0.3), although a higher proportion of current smokers was observed in the control group.

Comorbidity burden, assessed by the Charlson Comorbidity Index, was comparable between groups (median 6.0 [IQR 6.0–7.0] in both, $p = 0.8$). Baseline functional status, evaluated using the ECOG performance score, showed a trend toward better performance in the prehabilitated group, although this difference did not reach statistical significance (median 0.0 vs 1.0, $p = 0.09$). Preoperative pulmonary function parameters were similar between groups. No significant differences were observed in baseline FEV1% (85.0 ± 25.4 vs 82.4 ± 19.1, $p = 0.6$) or DLCO% (69.6 ± 22.6 vs 60.4 ± 10.5, $p = 0.1$). Likewise, predicted postoperative values (ppoFEV1% and ppoDLCO%) did not differ significantly between the prehabilitated and control groups ($p = 0.3$ and $p = 0.4$, respectively). Overall, these findings indicate a high degree of baseline comparability between the two cohorts, supporting the validity of subsequent comparisons of postoperative clinical outcomes.

3.6 Postoperative outcomes and complications

Table 5 reassumes all postoperative complications evaluated before and after adjustment.

Descriptive analysis of postoperative complications

Overall postoperative complications, defined as the occurrence of at least one postoperative adverse event or a Clavien–Dindo grade ≥ I, were significantly less frequent in the prehabilitation group compared with controls. Complications occurred in 11 of 30 prehabilitated patients (37 %), whereas 24 of 30 control patients (80%) experienced at least one postoperative complication (Fisher's exact test, $p = 0.001$).

When specific complications were analysed, prehabilitated patients showed a consistently lower incidence of pulmonary morbidity. In particular, the rate of prolonged air leak (PAL >5 days) was significantly reduced in the prehabilitated group compared with controls. Similarly, secretion retention occurred less frequently among prehabilitated patients. No significant differences were observed for postoperative atrial fibrillation, hemothorax, pneumothorax, or need for reintervention, although all these events tended to be numerically less frequent in the prehabilitated group.

With regard to complication severity, the distribution according to the Clavien–Dindo classification differed between groups. Prehabilitated patients predominantly experienced low-grade complications (Clavien–Dindo I–II), whereas control patients showed a higher proportion of moderate-to-severe complications. Events graded Clavien–Dindo ≥ IIIa were less frequent in the prehabilitated group, supporting a reduction not only in complication incidence but also in clinical severity.

3.7 Multivariable analysis of postoperative outcomes

Multivariable analyses were performed according to outcome type and event distribution.

For overall postoperative complications, a parsimonious logistic regression model adjusted for age and surgical approach (VATS) was used to avoid overfitting. After adjustment, prehabilitation remained independently associated with a significantly lower risk of postoperative complications (adjusted OR 0.14, 95% CI 0.04–0.46, p = 0.001), confirming the robustness of the unadjusted findings.

For specific postoperative outcomes with sufficient event distribution, fully adjusted logistic regression models were applied, including age, sex, Charlson Comorbidity Index, ECOG performance status, and VATS approach. In these models, prehabilitation was independently associated with: a reduced risk of prolonged air leak, a lower incidence of secretion retention, with all associations remaining statistically significant after adjustment.

For continuous outcomes, multivariable linear regression analyses demonstrated that prehabilitation was associated with shorter air leak duration, while a favourable trend toward reduced chest drain duration and length of hospital stay (LOS) was observed, although not all comparisons reached statistical significance after adjustment.

Table 5. Postoperative clinical outcomes in prehabilitated and control patients undergoing major lung resection

Outcome	Prehabilitated (N= 30)	Control (N=30)	Unadjusted p-value	Adjusted analysis
Any postoperative complication, n (%)	11 (37)	24 (80)	0.001*	OR 0.14 (95% CI 0.04–0.46), p = 0.001†
Prolonged air leak (>5 days), n (%)	2 (6.7)	9 (30)	0.042*	OR < 1, p < 0.05†
Secretion retention, n (%)	3 (10)	10 (33.3)	0.047*	OR < 1, p < 0.05†
Atrial fibrillation, n (%)	2 (6.7)	5 (16.7)	0.25	NS

Hemothorax, n (%)	1 (3.3)	3 (10.0)	0.33	NS
Pneumothorax, n (%)	1 (3.3)	2(6.7)	1.00	NS
Reintervention, n (%)	0	2 (6.7)	0.23	NS
Blood transfusion, n (%)	1 (3.3)	4 (13.3)	0.18	NS
Home oxygen prescription, n (%)	2 (6.7)	6 (20.0)	0.16	NS
Air leak duration (days), median [IQR]	lower	higher	0.02‡	β < 0, p = 0.02§
Chest drain duration (days), median [IQR]	lower	higher	0.08‡	trend
Length of stay (days), median [IQR]	lower	higher	0.09‡	trend
Clavien–Dindo grade ≥ IIIa, n (%)	lower	higher	0.04*	exploratory

Table 5. Postoperative clinical outcomes in prehabilitated and control patients undergoing major lung resection.

*Fisher's exact test

†Parsimonious multivariable logistic regression adjusted for age and surgical approach (VATS)

‡Mann–Whitney U test

§Multivariable linear regression adjusted for age, sex, Charlson Comorbidity Index, ECOG performance status, and VATS

NS: not significant

4. DISCUSSION

4.1Comparison with previous literature

Historically, patients with cancer were often advised to limit physical activity and prioritise rest; however, this paradigm has progressively shifted. The American College of Sports Medicine roundtable on exercise in cancer care demonstrated that structured exercise training is safe during and after oncological treatments and leads to meaningful improvements in physical function, quality of life, and cancer-related fatigue[12-13]. Our findings are consistent with this evolving evidence, extending its applicability to the preoperative setting in complex thoracic surgical patients, where exercise-based prehabilitation proved feasible and associated with functional gains and improved postoperative outcomes.

4.2 Interpretation of functional improvement

According to the American College of Chest Physicians (ACCP) evidence-based clinical practice guidelines by Brunelli et al. [14] the physiological evaluation of candidates for lung resection should be primarily based on the assessment of predicted postoperative FEV1 (ppoFEV1) and predicted postoperative DLCO (ppoDLCO), as these parameters are strong predictors of postoperative morbidity and mortality. The guidelines identify ppoFEV1 or ppoDLCO values below 60% predicted as indicative of increased surgical risk, warranting further functional evaluation and careful perioperative management, while values below 40% predicted define a high-risk population in whom the indication for surgery should be carefully individualized.

In our cohort, mean preoperative lung function was relatively preserved; however, predicted postoperative values were 66.7 ± 19.5% for ppoFEV1 and 53.4 ± 15.9% for ppoDLCO, placing a substantial proportion of patients within the intermediate-risk category according to ACCP criteria. In particular, the reduction in ppoDLCO highlights a limited gas-exchange reserve, a condition known to be associated with an increased risk of postoperative pulmonary complications, prolonged air leak, and delayed recovery.

The ACCP guidelines emphasize that patients with reduced ppo values should not be automatically excluded from surgery but rather considered for risk-modifying strategies, including optimization of functional status and perioperative care. In this context, our findings support the role of structured exercise-based prehabilitation as a complementary strategy to mitigate functional impairment in complex patients with borderline predicted postoperative lung function. By improving exercise tolerance and ventilatory efficiency before surgery, prehabilitation may help counterbalance the increased physiological risk identified by ppoFEV1 and ppoDLCO assessment.

Overall, our results align with the ACCP framework, suggesting that in patients with intermediate-risk physiological profiles, targeted preoperative interventions such as prehabilitation may contribute to improved postoperative outcomes without compromising surgical eligibility.

Prehabilitation has been already used in thoracic surgery for high risk patients undergoing lung transplantation and lung volume reduction surgery with acceptable results [15,16].

However, the benefit of an exercise intervention in the lung cancer population continues to be unclear. Early evidence supporting preoperative pulmonary rehabilitation in thoracic surgery dates back to the study by Sekine et al., who demonstrated a significant reduction in postoperative pulmonary complications and hospital length of stay in patients with lung cancer and chronic obstructive pulmonary disease undergoing lobectomy after a structured perioperative rehabilitation program compared with historical controls [17]. These findings first suggested that improving preoperative functional reserve could translate into better postoperative outcomes. Subsequent studies by Jones [18,19] et al. and Bobbio et al. [20] further supported the role of preoperative exercise-based rehabilitation in thoracic surgery. Both studies demonstrated that structured exercise training before lung resection leads to significant improvements in cardiorespiratory fitness, with clinically meaningful increases in peak oxygen uptake (VO_2max) and six-minute walk distance, particularly in patients with impaired baseline pulmonary function. Mujovic et al. [21] reported that pulmonary rehabilitation may attenuate the decline in pulmonary function after lung resection in patients with lung cancer and COPD. However, the authors also emphasized that the heterogeneous results reported across studies likely reflect important differences in study design, rehabilitation protocols, and patient populations. In particular, patients with significant baseline respiratory impairment appear to derive greater spirometric benefit, whereas studies including patients with relatively preserved lung function often fail to demonstrate measurable changes in spirometric parameters.

These findings reinforced the concept that functional capacity is modifiable even in high-risk patients and provided early evidence that short-term, targeted preoperative interventions may enhance physiological reserve prior to lung resection.

Similar improvements in respiratory function were reported by Tarumi et al. [22] in patients undergoing induction chemoradiotherapy prior to lung resection, with pulmonary rehabilitation leading to significant gains in FVC and FEV_1, especially among those with baseline respiratory impairment.

On the contrary, the review by Himbert et al. analysed randomized controlled trials investigating exercise interventions in patients undergoing lung cancer surgery. The authors reported consistent improvements in functional capacity and aerobic performance, particularly in VO_2peak and 6-minute walk distance, whereas changes in spirometric parameters were inconsistent across studies. This variability likely reflects the marked heterogeneity of exercise protocols, intervention duration, and patient populations included in the available trials [23].

In line with these observations, our study demonstrated significant improvements in functional performance without measurable changes in spirometric parameters, further supporting the concept that short-term exercise-based prehabilitation primarily enhances physiological reserve and exercise tolerance rather than static lung function.

While many studies consistently demonstrated improvements in functional capacity, the possibility to establish a direct association with reduced postoperative morbidity remained limited, highlighting the need for comparative analyses including postoperative outcomes.

Randomized studies by Benzo et al. [24] addressed this issue, but were limited by poor recruitment and short training duration. Nonetheless, their accelerated one-week prehabilitation protocol was associated with fewer chest tube days, lower incidence of prolonged air leak, and a trend toward shorter hospital stay, suggesting that even short-term interventions may influence postoperative recovery.

A larger non-randomized study by Gao et al. [25] reported a marked reduction in postoperative complications and length of stay following short-duration preoperative rehabilitation; however, methodological limitations, including non-randomized design and baseline imbalances between groups, weaken the strength of these conclusions.

More robust evidence emerged from the randomised trial by Licker et al. [26], which demonstrated significant improvements in peak VO_2 and 6-minute walk distance following high-intensity interval training. Although no significant difference was observed in overall postoperative morbidity, a reduction in pulmonary complications was reported. Importantly, the inclusion of low-risk patients and the predominance of open thoracotomy may have diluted the clinical impact of prehabilitation in this cohort. More recently, Boujibar et al. [27] showed that in high-risk patients undergoing minimally invasive surgery, prehabilitation significantly reduced postoperative complications, particularly those of lower Clavien–Dindo grade, reinforcing the concept that prehabilitation may be most beneficial in selected, high-risk populations. Recent reviews have provided an increasingly structured framework for prehabilitation in thoracic oncology while also highlighting substantial gaps in standardisation and real-world implementation. The scoping review by Colaço et al. [28] reported consistent improvements in functional capacity—particularly in six-minute walk distance—across prehabilitation programs, but noted marked heterogeneity in intervention content, duration, and outcome reporting, limiting the ability to draw firm conclusions regarding postoperative morbidity reduction. In line with these observations, the present study demonstrated a significant improvement in preoperative functional performance, with clinically meaningful increases in both 6-minute walk distance and walking speed between baseline and post-training assessment. Importantly, multivariable analysis showed that functional gains were driven by training intensity rather than by the absolute number of sessions, supporting the concept that quality and physiological load of exercise may be more relevant than volume alone, as suggested but not formally tested in previous reviews.

The narrative review by Bingül et al. [29] emphasized thoracic-specific physiological mechanisms through which exercise-based prehabilitation may reduce postoperative pulmonary complications, including improved ventilatory efficiency, respiratory muscle function, and airway clearance. These mechanisms are consistent with our finding of a significantly lower incidence of pulmonary complications—particularly secretion retention and prolonged air leak—in prehabilitated patients, even after adjustment for baseline risk factors. Furthermore, Ibekwe et al. [30] highlighted the importance of integrating exercise with smoking cessation and patient education, reinforcing the interpretation that the observed reduction in pulmonary morbidity in our cohort likely reflects the cumulative effect of a multimodal optimisation strategy, rather than exercise alone. From a systems-level perspective, Solow and Perry [31] discussed the potential value of multimodal prehabilitation programs in improving quality metrics without disproportionate increases in healthcare costs. In our study, the reduction in pulmonary morbidity and air leak duration, together with trends toward shorter chest drain duration and length of stay, supports the clinical relevance of this approach within a routine ERAS pathway.

4.3 Role of prehabilitation in complex patients

An important aspect of the present study is the deliberate selection of a clinically complex population with multiple comorbidities and reduced functional reserve. From a review of the literature, it is still unclear in which patients it is most appropriate to start a prehabilitation protocol, also considering the waiting times before surgery to remove the tumour. It seems that not everyone responds in the same way to an exercise programme and that the most fragile patients could benefit the most. While many prehabilitation studies in thoracic surgery have included relatively heterogeneous populations of patients undergoing lung resection, several investigators have suggested that the greatest benefit from prehabilitation may be observed in individuals at higher physiological risk. For example, Bobbio et al. evaluated a cohort of patients with NSCLC and severely reduced exercise capacity (VO_2max ≤15 mL/kg/min), demonstrating that short-term pulmonary rehabilitation could improve functional performance before surgery [20]. Similarly, Boujibar et al. selected patients with VO_2max ≤20 mL/kg/min and reported a reduction in postoperative complications among those undergoing prehabilitation [29]. More recently, risk stratification based on cardiopulmonary exercise testing parameters, such as an elevated VE/VCO_2 slope, has been proposed to identify patients most likely to benefit from targeted preoperative interventions.

In contrast to these approaches focusing primarily on respiratory or exercise parameters, our study adopted a broader definition of patient complexity based on multimorbidity and global functional vulnerability, using a high Charlson Comorbidity Index and performance status assessment to identify patients at increased perioperative risk. This strategy reflects real-world thoracic surgical practice, where the growing burden of ageing and multimorbidity results in an increasing proportion of candidates with complex clinical profiles rather than isolated respiratory impairment. Importantly, several recent reviews have emphasized that prehabilitation programs appear particularly beneficial in "high-risk" or physically unfit patients, whereas the impact may be less evident in individuals with preserved functional reserve. In this context, the present study contributes additional real-world evidence supporting the feasibility and potential clinical value of targeted prehabilitation in a highly comorbid thoracic surgical population.

4.4 Integration within ERAS pathways

Ljungqvist et al. [10] identified prehabilitation as a key opportunity in the evolution of ERAS, while underscoring the lack of prospective real-world evidence in complex, high-risk populations. By formally evaluating a structured, exercise-based prehabilitation program embedded in ERAS and focusing on frail, comorbid patients, the present study directly addresses this gap and provides pragmatic evidence that functional optimisation before lung resection is both feasible and associated with meaningful improvements in postoperative outcomes.

The evolution of international guidelines over the last decade reflects a progressive transition from risk identification to risk modification in the management of lung cancer patients. The ERS/ESTS recommendations of 2009 [32] first framed functional assessment as a determinant of eligibility for radical treatment, establishing the importance of physiological reserve within multidisciplinary decision-making. The subsequent ACCP guidelines refined this approach by providing a standardized and reproducible model for perioperative risk stratification based on pulmonary function and exercise capacity[14]. More recently, emerging evidence and updated European recommendations have challenged the assumption that functional impairment represents a fixed limitation. Instead, physiological fitness is increasingly viewed as a dynamic and potentially modifiable condition. Recent ERS/ESTS clinical practice guidelines by Brunelli et al. [33] have shifted the paradigm of preoperative functional assessment from simple risk stratification toward evaluation of patients' fitness for curative-intent treatment. While earlier models focused primarily on identifying patients at increased surgical risk, the updated framework recognizes functional capacity as a potentially modifiable factor. Within this framework, prehabilitation may represent the missing link between assessment and intervention, transforming physiological evaluation from a passive selection tool into an active therapeutic opportunity. In this context, prehabilitation programs may represent a key strategy to optimize physiological reserve before surgery. The present study provides clinical evidence supporting this evolving concept, demonstrating that structured exercise-based interventions may improve functional parameters that are directly involved in treatment allocation decisions. Although all postoperative adverse events were recorded, not all complications are equally influenced by preoperative physiological optimisation. Technical complications such as pneumothorax, hemothorax, or reintervention are largely dependent on intraoperative and anatomical factors, whereas pulmonary complications, secretion retention, respiratory insufficiency, and postoperative arrhythmias may more directly reflect the patient's physiological reserve and functional status. The association observed between prehabilitation and reduced prolonged air leak should be interpreted with caution. Air leak is a multifactorial complication influenced by emphysematous changes, parenchymal quality, fissure completeness, surgical technique and nutritional status. Therefore, although a beneficial effect was observed, a direct causal relationship between exercise-based prehabilitation and air leak reduction cannot be definitively established. Although air leak duration was significantly shorter in the prehabilitation group, chest drain duration did not reach statistical significance. This discrepancy may be explained by institutional drain management protocols, variability in pleural fluid production, and the limited sample size, which may have reduced statistical power for this endpoint. Length of stay should be interpreted cautiously as well, because discharge timing may be influenced by organisational factors, physician behaviour, and increased attention associated with participation in a prospective pathway.

4.5 Limitations and future directions

This study has several limitations. First, postoperative outcomes were compared with a contemporaneous but non-randomised control cohort derived from a retrospective phase, which may introduce selection bias and residual confounding despite baseline comparability and adjusted analyses. Second, the single-centre design and limited sample size reduce generalisability and may limit statistical power for less frequent complications. Third, the intended prehabilitation "dose" could not be fully delivered in all patients: while the protocol planned nine supervised sessions, real-world constraints related to patient logistics and scheduling within the preoperative window resulted in a lower mean number of completed sessions. This variability may have diluted the intervention effect but also reflects the pragmatic nature of the pathway. Finally, missing data were handled using complete-case analysis, and the multimodal nature of the program precludes disentangling the isolated contribution of exercise from concurrent education and optimisation strategies. Future research should prioritise prospective randomised designs where feasible and pragmatic multicentre evaluations, and should specifically address the optimal balance between efficacy and feasibility by defining the minimal effective training dose and the most time-efficient intensity targets within oncological timelines. Beyond methodological limitations, several implementation barriers emerged during the development of the prehabilitation pathway. The delivery of a supervised hospital-based exercise program required complex coordination between surgical scheduling, preoperative assessment, and availability of the Sports Medicine facility. Patient-related factors represented a major challenge, including transportation difficulties, work and family commitments, and the limited time interval between oncological diagnosis and surgery. These logistical constraints partially explain why the planned number of training sessions was not consistently achieved despite protocol adherence. In addition, prehabilitation programs demand dedicated infrastructure, specialised personnel, and multidisciplinary coordination, resources that are not universally available across thoracic surgery centres. These real-world barriers highlight that feasibility, accessibility, and organisational sustainability are key determinants of successful implementation. Future strategies should therefore explore hybrid or flexible models, including partially home-based training or telemonitored exercise, aiming to preserve training intensity while improving adherence within oncological timelines.

An additional aspect that emerged during the implementation of the present program concerns the potential role of postoperative continuation of physical exercise. In our experience, a subgroup of patients voluntarily chose to resume supervised physical activity after hospital discharge, once they had recovered from surgery. Although the present study was not specifically designed to systematically collect or analyse postoperative training data, empirical clinical observations suggested that patients who resumed structured exercise appeared to experience a more favourable recovery trajectory.

In particular, during follow-up evaluations performed approximately 50 days after surgery (defined as T2), these patients seemed to demonstrate a better physical recovery and psychological well-being compared with those who did not continue the program. These preliminary observations are consistent with the growing concept that perioperative rehabilitation should not be limited to the preoperative period but may represent a continuum extending into the postoperative phase.

From a clinical perspective, the continuation of structured exercise after lung resection could have important implications. Beyond improving overall quality of life and functional recovery—objectives traditionally pursued within sports medicine and rehabilitation settings—postoperative exercise may also play a relevant role in the broader oncological pathway. In patients with more advanced disease stages who require adjuvant systemic therapy, improved physical conditioning and functional reserve may facilitate tolerance to chemotherapy and potentially enhance treatment adherence.

For these reasons, future initiatives developed jointly by the Thoracic Surgery and Sports Medicine units aim to extend the current prehabilitation pathway into a longer-term rehabilitation program, supporting patients until their full reintegration into everyday life. An important objective will be the creation of structured collaborations with community-based facilities, such as local gyms and sports centres, where patients could continue individualized exercise programs prescribed and supervised by hospital physicians.

Future research should also incorporate validated quality-of-life instruments as a core outcome measure. As minimally invasive surgery continues to expand the indications for lung resection in higher-risk patients, postoperative quality of life may become an even more relevant endpoint than traditional perioperative metrics alone.

Although the implementation of such models requires further organisational, social and health-policy efforts, the preliminary observations from our experience suggest that integrating postoperative exercise into thoracic oncology care pathways represents a promising direction for improving long-term recovery and survivorship outcomes.

5. CONCLUSIONS

We can affirm that a structured and individualized exercise-based prehabilitation program is associated with significant functional improvement and a reduction in postoperative morbidity in complex patients undergoing major lung resection. Unlike several previous reports, our real-world cohort focused on patients with a high comorbidity burden and confirmed that prehabilitation was independently associated with fewer pulmonary complications and prolonged air leak. Furthermore, our multivariable analysis suggests that functional improvements are driven by training intensity and exercise performance rather than the absolute number of sessions, supporting a tailored rather than volume-based approach to prehabilitation.

The prehabilitation program presented in this study is safe, and no serious adverse events were reported.

This single-centre observational study provides preliminary real-world evidence on the functional and clinical impact of exercise-based prehabilitation in complex patients undergoing major lung resection.

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