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Contents

Contents

Contents

ABOUT COVER

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AIMS AND SCOPE

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INDEXING/ABSTRACTING

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ORIGINAL ARTICLE

Observational Study

Reduced exercise capacity and self-perceived health status in high-risk patients undergoing lung resection

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Abstract

BACKGROUND

Lung resection represents the main curative treatment modality of non-small cell lung cancer. Patients with high-risk to develop postoperative pulmonary complications have been classified as "high-risk patients." Characterizing this population could be important to improve their approach and rehabilitation.

AIM

To identify the differences between high and low-risk patients in exercise capacity and self-perceived health status after hospitalization.

METHODS

A longitudinal observational prospective cohort study was carried out. Patients undergoing lung resection were recruited from the "Hospital Virgen de las Nieves" (Granada) and divided into two groups according to the risk profile criteria (age ≥ 70 years, forced expiratory volume in 1 s ≤ 70% predicted, carbon monoxide diffusion capacity ≤ 70% predicted or scheduled pneumonectomy). Outcomes included were exercise capacity (Fatigue Severity Scale, Unsupported Upper-Limb Exercise, handgrip dynamometry, Five Sit-to-stand test, and quadriceps hand-held dynamometry) and patient-reported outcome (Euroqol-5 dimensions 5 Levels Visual Analogue Scale).

RESULTS

In total, 115 participants were included in the study and divided into three groups: high-risk, low-risk and control group. At discharge high-risk patients

presented a poorer exercise capacity and a worse self-perceived health status ($P <$ 0.05). One month after discharge patients in the high-risk group maintained these differences compared to the other groups.

CONCLUSION

Our results show a poorer recovery in high-risk patients at discharge and 1 mo after surgery, with lower self-perceived health status and a poorer upper and lower limb exercise capacity. These results are important in the rehabilitation field.

Key Words: Non-small cell lung cancer; Exercise tolerance; health status; Patient-reported outcomes; Postoperative quality of life; Exercise test

Core Tip: Lung cancer is the leading cause of cancer death among men and the second among women worldwide. A revolutionary change in this approach is being witnessed with less invasive techniques. However, it is still associated with a high incidence of postoperative pulmonary complications, which could lead to a reduced exercise capacity. Patients with higher risk to develop postoperative pulmonary complications have been classified as "high-risk patients," and they could present a lower exercise capacity and self-perceived health status.

INTRODUCTION

Lung cancer is the leading cause of cancer death among men and the second among women worldwide. Non-small cell lung cancer represents 80% of all lung cancer cases, and lung resection still represents the main curative treatment modality[1].

In the last years, a revolutionary change in this approach is being witnessed[2] with less invasive techniques. However, it is still associated with a high incidence of postoperative pulmonary complications (PPCs), particularly common in patients with comorbid conditions and elderly individuals[2,3]. PPCs include (1) respiratory failure, (2) pneumonia, (3) atelectasis requiring bronchoscopy, (4) myocardial infarction, and (5) arrhythmias requiring intravenous treatment. Patients with a higher risk to develop PPCs have been classified as "high-risk patients," and many authors have focused specifically on the approach for these patients. Besides being a clinical marker for decreased survival[3], PPCs have been associated with a longer length of hospital stay and a negative influence on the patient's ability to resume usual daily physical activity [3].

Lung cancer patients are known to frequently exhibit poor exercise capacity, low physical activity levels and an impaired health-related quality of life that can be further aggravated after lung resection surgery[4]. Pulmonary resection causes a decrease in the lung volume, which is linked to the pain related to the chest wall, the respiratory muscle injury and the loss of muscle strength caused by bed rest, resulting in a disturbance of cardiopulmonary function and can lead to this postoperative exercise limitation. Exercise capacity has been associated with PPCs, showing a lower VO_2max or a major extent of lung tissue resection in patients with PPC after curative lung resection[5]. However, other factors could affect exercise capacity like quadriceps weakness[6], illness perception[7], depressive symptoms or quality of life[8]. Moreover, we have not found specific studies based on the upper and lower limb evaluation. Functional exercise testing offers an opportunity to objectively measure patients' exercise capacities, to identify exercise limitations that would otherwise remain undetected and to identify self-perceived capacity[9]. Moreover, the survivor's

perception of functional capacity and health status provides important information beyond objective pulmonary function testing. Despite this, we have not found studies about functional exercise limitation in these patients depending on their risk profile.

To stratify patients undergoing lung resection could be important to improve the specific rehabilitation programs and targeting these patients. Therefore, the aim of this study was to identify the differences between high and low-risk patients in exercise capacity and self-perceived health status at discharge and in the following month.

MATERIALS AND METHODS

Study population and data collection

A longitudinal observational prospective cohort study has been carried out. Patients undergoing lung resection were recruited from the Thoracic Surgery Service of the "Hospital XXX" (XXX) between April 2017 and July 2018. They had to be between 18 and 80-years-old, and they were informed about the study purpose. Patients were excluded if they presented with cognitive impairment, mental instability, orthopedic pathologies that limited the test performance or neurologic pathologies. Informed consent was obtained from all individual participants included in the study. The study protocol was reviewed and approved by the XXX Ethics Committee (XXX). The STROBE guideline was followed during the course of the research[10].

Group assignment

Lung resection patients were divided into two groups according to the risk profile criteria[11]. High risk was defined as one or more of the following: age ≥ 70 years, forced expiratory volume in 1 s ≤ 70% predicted, carbon monoxide diffusion capacity ≤ 70% predicted or scheduled pneumonectomy. The maximum and minimal age of both lung resection groups were used to calculate the age range where control group should be included.

Outcome measures

Data collecting was performed before lung resection, at discharge and 1 mo after surgery, always by the same investigators previously trained and blinded to the patient's allocation. All patients followed a similar recovery pathway: after lung surgery, patients remained in the resuscitation unit 24 h and followed a similar analgesic treatment during their hospital stay, with non-steroidal anti-inflammatories. A normalized interview and an initial assessment were carried out when inclusion criteria were confirmed. Some data were collected from the medical history: anthropometric data, comorbidities (Charlson comorbidities index)[12] and operative duration. Respiratory capacity was assessed by spirometry[13] and anxiety and depression through the Hospital Anxiety and Depression Scale[14].

Main outcomes included were exercise capacity and self-perceived health status.

Exercise capacity

Exercise capacity included the self-perceived fatigue and a lower and upper limb evaluation.

To evaluate the fatigue severity, the Fatigue Severity Scale was used. The Fatigue Severity Scale[15] was developed to measure the impact of disabling fatigue on daily functioning. The instrument consists of nine items, and the total score ranges between 9 and 63. A higher score indicates more self-perceived fatigue. Minimal clinically important difference (MCID) for Fatigue Severity Scale has been reported to be 20.2.

Lower limb assessment: A hand-held dynamometer (Lafayette Manual Muscle Testing System, model 01163, Lafayette, IN, United States) was used to assess the lower limbs[16]. The test was performed with the patient seated with his/her knees and hips flexed at 90°. Resistance was applied to the anterior tibia during 5 s of maximal muscle contraction. Three trials were done in the dominant leg, and the highest value in Newton was selected for the analysis. An MCID of 46 Newton has been established.

The Five Sit-to-Stand Test (5STS) has been previously used to evaluate exercise tolerance in respiratory patients[17]. It was performed with standard height (46 cm) chair without armrests. Participants were asked to stand up all the way and sit down landing firmly, as fast as possible, five times without using the arms, and the time taken was recorded as the participant's score. The self-perceived dyspnea and lower limb fatigue were recorded, previously and after the test, using the modified version

Table 1 Baseline characteristics of the groups

		Low-risk group, *n* = 39	High-risk group, *n* = 44	Control group, *n* = 32	*F*
Age in yr		52.18 (13.91)	69.91 (7.97)	48.44 (13.57)	37.171[a,c]
Sex, % males		31.88	42.03	26.09	0.704
BMI		27.08 (5.02)	26.50 (4.56)	26.08 (4.42)	0.405
Length of hospital stay		6.56 (1.82)	6.95 (2.03)	-	0.362
Charlson index		4.10 (2.38)	4.93 (2.43)	1.38 (1.60)	22.861[b,c]
Operation duration in min		208.79 (86.34)	208.81 (52.29)	-	0.999
Surgical procedure, %VATS		74.5	72.4	-	0.722
Spirometric parameters	FEV_1	2.71 (0.83)	1.60 (0.50)	2.88 (0.86)	18.301[a,c]
	FVC	3.57 (1.02)	2.5 (1.05)	3.59 (0.92)	8.605[a,c]
HADS	Anxiety	3.95 (2.71)	4.64 (2.95)	2.38 (2.94)	5.866[b,c]
	Depression	0.92 (1.49)	4.36 (3.84)	0.31 (0.78)	28.964[a,b,c]
	Total	4.87 (3.34)	9 (5.65)	2.69 (3.59)	20.253[a,b,c]

Variables are expressed as mean (SD) or percentage.

[a]Significant differences between low-risk and high-risk groups.

[b]Significant differences between low-risk group and control group.

[c]Significant differences between high-risk group and control group. BMI: Body mass index; FEV_1: Forced expiratory volume in 1 s; FVC: Forced vital capacity; HADS: Hospital Anxiety and Depression Scale; VATS: Video-assisted thoracic surgery.

of the Borg Scale[18]. The MCID for the 5STS has been reported to be 5 s.

Upper limb assessment: Handgrip strength is a reliable marker of peripheral muscle strength[19]. A handgrip dynamometer (TEC-60; Productos Técnicos, EE.UU.) was used to do three in the dominant hand, and the peak force in Newton was recorded. A difference of 49 Newtons has been established as the MCID.

The unsupported upper-limb exercise (UULEX) test is an incremental test developed by Takahashi *et al*[20] to measure peak unsupported arm exercise capacity. The subjects need to move a bar from their lap to the highest level they can reach until exhaustion. The total score was the total duration of the test in seconds. The self-perceived dyspnea and lower limb fatigue were recorded using the modified version of the Borg Scale[18]. The MCID for Borg scores was set at 1 score.

Patient-reported outcome

The Euroqol-5dimensions 5 Levels (EQ-5D-5L) was used to evaluate the general health status. The questionnaire comprises two parts. The first section includes five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each with five levels (no problem, slight problems, moderate problems, severe problems and extreme problems), and the result is an index. A value of 1 indicates full health and a value of less than zero indicates a quality of life worse than death. The second part includes a Visual Analogue Scale [EQ-5D-5L visual analogue scale (VAS)], which records the responder's self-evaluated health between 0 (the worst imaginable health) and 100 (the best imaginable health)[21]. The MCID for the EQ-5D-5L index ranges from 0.05 and for the EQ-5D-5L VAS has been reported to be 8 points.

Statistical analysis

Statistical power calculation (GPower version 3.1.9.2 for Windows) was performed at the conception stage utilizing expected differences in the primary endpoint (EQ-5D-5L VAS) based on our previous pilot study in related subjects that employed similar methodology (unpublished). This suggested that a sample size of 30 in each group will have 80% power to detect a probability of 0.5. To allow for a generous safety margin, we decided to aim for approximately 35 patients in each study group.

Statistical Package SPSS version 20.0 (International Business Machines, Armonk, NY: http://www-01.ibm.com/support/docview.wss?uid=swg21476197) was used to analyze the data obtained. Descriptive statistics (mean ± SD) or percentages (%) were used to describe sample baseline characteristics. The Kolmogorov–Smirnov test was

Table 2 Exercise capacity and self-perceived health status before lung resection				
	Low-risk group, *n* = 35	**High-risk group, *n* = 40**	**Control group, *n* = 32**	***F***
Exercise capacity				
FSS	19.72 (12.99)	28 (19.49)	9.00	16.469 1[a,b,c,1]
Lower limb assessment				
Hand-held dynamometry	107.24 (51.59)	112.31 (47.99)	213.01 (60.58)	43.669 1[b,c,1]
5STS Dyspnea baseline	0.41 (1.33)	0.32 (1.12)	0	1.478
LL fatigue baseline	0.36 (1.20)	1.23 (2.38)	0	5.829 1[a,c,1]
Time	12.43 (4.49)	18.23 (14.27)	9.87 (2.66)	8.202 1[a,b,c,1]
Dyspnea post-test	1.03 (1.98)	0.86 (1.79)	0	4.098[b,c]
LL fatigue post-test	0.72 (1.57)	1.77 (2.94)	0	7.297 1[a,b,c,1]
Upper limb assessment				
Handgrip dynamometry	329.46 (93.08)	291.57 (117.29)	380 (79.31)	7.178 1[b,c,1]
UULEX test Dyspnea baseline	0.44 (1.50)	0.38 (1.03)	0	1.64[c]
UL Fatigue baseline	1.00 (1.59)	1.13 (1.82)	0	6.322 1[b,c,1]
Time	442.50 (230.69)	187.50 (201.80)	555.00 (124.75)	23.245 1[a,b,c,1]
Dyspnea post-test	2.19 (2.54)	0.88 (1.59)	0.25 (0.98)	7.439 1[b,1]
UL Fatigue post-test	6.56 (2.19)	6.38 (2.19)	5.50 (2.66)	1.283
Self-perceived health status				
EQ-5D-5L VAS	86.81 (16.99)	66.23 (22.94)	94.69 (4.91)	23.147 1[a,c,1]
EQ-5D-5L index	1.00	0.76 (0.43)	1.00	11.238[a,b,c]

Variables are expressed as mean (SD).

[a]Significant differences between low-risk and high-risk groups.

[b]Significant differences between low-risk group and control group.

[c]Significant differences between high-risk group and control group.

[1]Global *P* value adjusted by multiplicity. 5STS: Five sit-to-stand test; EQ-5D-5L: Euroqol 5 dimensions 5 levels; FSS: Fatigue severity scale; LL: Lower limb; UL: Upper limb; UULEX: Unsupported upper-limb exercise; VAS: Visual analogue scale.

performed to assess continuous data normality, prior to statistical analysis. Normally distributed baseline demographic variables were compared by analysis of variance (ANOVA). The one-way ANOVA was used for baseline data. For each outcome measure, a three (high-risk, low-risk, control) × two (admission and discharge or discharge and follow-up) mixed ANOVA was performed. If the three × two ANOVA showed a significant interaction for each variable, then Bonferroni's post hoc test was used to identify the specific mean differences. A 95% confidence interval was used for statistical analysis. A *P* value of less than 0.05 was considered statistically significant. Global *P* values were adjusted for multiplicity with the Bonferroni method.

RESULTS

A total of 115 participants were deemed eligible and accepted to participate in this study. The distribution of participants is shown in Figure 1. Baseline characteristics of the sample are described in Table 1.

Significant differences were found in age between high-risk and the other groups. The low-risk and high-risk groups presented a similar length of hospital stay (*P* = 0.320) and Charlson index. Surgical procedures were similar in both groups, with most of them undergoing video-assisted thoracic surgery (74.5% *vs* 72.4%). As expected, forced expiratory volume in 1 s and forced vital capacity presented significant differences between low and high-risk groups (*P* < 0.05). Hospital Anxiety and Depression Scale presented poorer scores in the high-risk group.

Table 3 Exercise capacity and self-perceived health status differences at discharge among and between groups

		Low-risk group, *n* = 29			High-risk group, *n* = 36			Control group, *n* = 32			*F*
		Mean change	95%CI	*P* value among groups	Mean change	95%CI	*P* value among groups	Mean change	95%CI	*P* value among groups	
Exercise capacity											
FSS		-4.17 (16.76)	(-10.02, 1.67)	0.156	-8.00 (18.56)	(-14.10, -1.90)	0.012	0	-	1	21.735 1[a,b,c,1]
Lower limb assessment											
Hand-held dynamometry		7.20 (24.49)	(2.11, 16.52)	< 0.001	22.94 (31.12)	(12.41, 33.47)	< 0.001	-0.05 (0.85)	(-0.35, 0.25)	0.729	15.8 1[b,c,1]
5STS test	Dyspnea baseline	-0.64 (1.45)	(-1.15, -0.12)	0.017	-1.05 (2.14)	(-1.75, -0.35)	0.004	0	-	1	4.122 1[b,c,1]
	LL fatigue baseline	-0.30 (1.28)	(-0.76, 0.15)	0.186	-0.42 (1.81)	(-1.02, 0.17)	0.160	0	-	1	8.735 1[a,b,c]
	Time	-3.30 (7.28)	(-5.88, -0.72)	0.014	-7.84 (11.39)	(-11.58, -4.09)	< 0.001	-0.06 (0.50)	(-0.24, 0.13)	0.531	14.818 1[a,b,c,1]
	Dyspnea post-test	-0.91 (2.02)	(-1.63, -0.19)	0.015[1]	-2.74 (2.92)	(-3.69, -1.78)	< 0.001	0	-	1	20.128 1[a,b,c,1]
	LL fatigue post-test	-0.42 (2.00)	(-1.13, -0.28)	0.008[1]	-1.74 (2.77)	(-2.65, -0.83)	< 0.001	0	-	1	23.570 1[a,b,c,1]
Upper limb assessment											
Handgrip dynamometry		34.14 (46.47)	(16.46, 51.81)	0.124	28.05 (40.84)	(14.24, 41.87)	< 0.001	15.28 (64.29)	(-7.89, 38.46)	0.188	7.663 1[b,c,1]
UULEX test	Dyspnea baseline	-1.62 (2.78)	(-3.10, -0.14)	0.034[1]	-2.00 (2.15)	(-3.24, -0.76)	0.004	0	-	1	11.262 1[b,c,1]
	UL fatigue baseline	-0.75 (2.74)	(-2.21, 0.71)	0.292	-4.29 (3.27)	(-6.17, -2.39)	< 0.001	0	-	1	37.713 1[a,b,c,1]
	Time	202.50 (204.20)	(93.68, 311.31)	0.002	145.70 (232.63)	(11.39, 280.03)	0.036	-3.75 (40.14)	(-18.22, 10.72)	0.601	86.717 1[a,b,c,1]
	Dyspnea post-test	-1.87 (3.44)	(-3.71, -0.04)	0.046	-2.29 (2.05)	(-3.47, -1.10)	0.001	0	-	1	17.854 1[b,c,1]
	UL fatigue post-test	0 (3.40)	(-1.81, 1.81)	1	-1.71 (2.05)	(-2.90, -0.53)	0.008	0	-	1	9.688 1[a,c,1]
Self-perceived health status											
EQ-5D-5L VAS		14.35 (20.48)	(3.82, 24.88)	0.011	11.10 (22.07)	(0.77, 21.43)	0.037	-0.50 (2.64)	(-1.45, 0.45)	0.292	38.091 1[a,b,c,1]
EQ-5D-5L index		0.14 (0.35)	(0.07, 0.21)	< 0.001	0.28 (0.46)	(0.11, 0.46)	0.003	0	-	1	9.686 1[a,c,1]

Variables are expressed as mean (SD).

[a]Significant differences between low-risk and high-risk groups.

[b]Significant differences between low-risk group and control group.

[c]Significant differences between high-risk group and control group.

[1]Global *P* value adjusted by multiplicity. 5STS: Five sit to stand test; CI: Confidence interval; EQ-5D-5L: Euroqol 5 dimensions 5 levels; FSS: Fatigue severity scale; LL: Lower limb; UL: Upper limb; UULEX: Unsupported upper-limb exercise; VAS: Visual analogue scale.

Exercise capacity and self-perceived health status scores before lung resection are presented in Table 2.

Significant differences were found in fatigue severity and lower limb and upper limb strength between groups. The 5STS and UULEX also presented significant differences between groups, with poorer results in the high-risk group. A significant poorer self-perceived health status was shown in the high-risk group.

Exercise capacity and self-perceived health status differences at discharge among and between groups are presented in Table 3.

The high-risk group presented a significant increase in the fatigue severity at discharge ($P = 0.012$) and a poorer strength ($P < 0.001$). In the 5STS test, the high-risk group obtained significantly poorer results than the other groups, with a significant clinical difference in dyspnea and time. In the UULEX, both resection groups presented a significant statistical and clinical increase in the dyspnea levels ($P < 0.05$). However, only the high-risk group presented a significant increase in upper limb fatigue pretest ($P < 0.001$). The time reached in the UULEX was lower in both groups at discharge ($P < 0.05$), and a significant increase in upper limb fatigue and dyspnea post-test were found in the high-risk group ($P < 0.05$). The EQ-5D-5L VAS and index decreased in both groups after the intervention ($P < 0.05$), and it was clinically relevant in the high-risk group, which also presented significant differences in the between groups analysis.

Exercise capacity and self-perceived health status differences 1 mo after discharge, among and between groups are presented in Table 4.

Fatigue improved in the high and low-risk groups. However, the increase was not statistically or clinically significant ($P > 0.05$). The high-risk group presented poorer results in the 5STS and in the UULEX. The high-risk group increased, statistically and clinically significant, ($P = 0.004$), and the low-risk groups reduced ($P = 0.024$) the dyspnea. The EQ-5D-5L VAS and index improved significantly in the low-risk group ($P = 0.015$), with an improvement that clinically relevant. Significant differences were found between groups in the EQ-5D-5L VAS.

DISCUSSION

The aim of this study was to identify the differences between high and low-risk patients in exercise capacity and self-perceived health status at discharge and in the following month. Moreover, to compare the results with a control group is important to know if this population will reach the normative values of a similar population. Our findings show a poorer recovery in high-risk patients, with more self-perceived fatigue, a lower self-perceived health status and a poorer upper and lower limb exercise capacity. These results represent an advance in the field of rehabilitation because it allows the design of specific rehabilitation programs for each risk group.

The sample of subjects included in this study was representative of the general population undergoing lung resection, with similar sociodemographic characteristics [22].

Our results have shown significant differences in self-perceived fatigue between both surgery groups, with a higher score in the high-risk group. The occurrence of fatigue has been described following elective surgery as a negative predictor for the functional recovery[23]. Patients with persistent deficits in muscle performance will be more rapidly fatigued following motor tasks and will probably report higher levels of self-perceived fatigue. There are several possible mechanisms involved in fatigue, one of which is the release of proinflammatory cytokines by the tumor and its microenvironment. Our lung resection patients improved their fatigue level 1 mo after surgery. However, the results do not reach the control group scores. A vicious cycle may thereby be created in which these individuals avoid engaging in physical activity, further reducing their cardiorespiratory fitness and increasing their fatigability.

Our study shows poorer results in lower limb exercise capacity in the high-risk group. Similar studies[24] have shown that after lung resection surgery patients experience a decrease in maximal exercise tolerance during the first month after the intervention. This observed impairment in exercise tolerance has been reported to be induced by the cancer treatment or associated immobility; however, previous studies have suggested that deficits in exercise tolerance are likely to be apparent before surgery[24]. This aspect goes in line with our study, which suggests that exercise capacity could be determined prior to the intervention by the risk profile patient. This is important because some patients may regard immediate postoperative complications as an acceptable risk but are not prepared to accept significant postoperative

Table 4 Exercise capacity and self-perceived health status differences, 1 mo after discharge, among and between groups

		Low-risk group, *n* = 29			High-risk group, *n* = 36			Control group, *n* = 32			*F*
		Mean change	95%CI	*P* value, among groups	Mean change	95%CI	*P* value among groups	Mean change	95%CI	*P* value among groups	
Exercise capacity											
FSS		2.84 (16.33)	(-3.90, 9.58)	0.393	2.50 (14.78)	(-3.74, 8.74)	0.416	0	-	1	18.606 1[b,c,1]
Lower limb assessment											
Hand-held dynamometry		-15.56 (31.54)	(-32.37, 1.24)	0.067	-18.57 (27.73)	(-34.58, -2.56)	0.026	0.01 (9.61)	(-2.29, 4.64)	0.494	23.129 1[b,c,1]
5STS test	Dyspnea baseline	0.69 (1.98)	(-0.00, 1.39)	0.051	0.37 (2.26)	(-0.37, 1.11)	0.321	0	-	1	4.152[c]
	LL fatigue baseline	0 (2.15)	(-0.76, 0.76)	1	0.21 (1.49)	(-0.28, 0.70)	0.390	0	-	1	7.650 1[b,c,1]
	Time	1.75 (8.08)	(-1.10, 4.62)	0.221	3.95 (14.58)	(-0.84, 8.74)	0.104	-0.01 (0.57)	(-0.21, 0.20)	0.931	18.333 1[a,b,c,1]
	Dyspnea post-test	1.12 (1.87)	(0.46, 1.78)	0.002	0.68 (1.47)	(0.20, 1.17)	0.007[1]	0	-	1	26.453 1[a,b,c,1]
	LL fatigue post-test	0.39 (1.54)	(-0.15, 0.94)	0.151	0.11 (2.27)	(-0.64, 0.85)	0.777	0	-	1	47.483 1[a,b,c,1]
Upper limb assessment											
Handgrip dynamometry		3.80 (58.47)	(-28.58, 36.18)	0.805	3.21 (69.72)	(-37.04, 43.47)	0.866	-16.24 (64.27)	(-39.42, 6.93)	0.163	15.494 1[b,c,1]
UULEX[a] test	Dyspnea baseline	1.06 (3.29)	(-0.69, 2.82)	0.217	-0.60 (2.87)	(-2.66, 1.46)	0.526	0	-	1	54.082 1[a,b,c,1]
	UL fatigue baseline	0.94 (3.02)	(-0.67, 2.55)	0.234	0 (3.27)	(-2.34, 2.34)	1	0	-	1	194.932 1[a,b,c,1]
	Time	-225.00 (191.62)	(-327.11, -122.89)	< 0.001	-240.00 (187.62)	(-374.00, -105.00)	0.003	7.50 (80.28)	(-21.44, 36.44)	0.601	19.744 1[a,b,c,1]
	Dyspnea post-test	2.18 (2.61)	(0.79, 3.58)	0.004	-2.40 (2.79)	(-4.40, -0.39)	0.024	0.13 (0.49)	(-0.05, 0.30)	0.161	133.723 1[a,b,c,1]
	UL fatigue post-test	0.94 (2.32)	-0.30 (2.17)	0.127	0 (1.76)	(-1.26, 1.26)	1	-0.19 (0.90)	(-0.51, 0.14)	0.245	8.777 1[a,c,1]
Self-perceived health status											
EQ-5D-5L VAS		-19.58 (23.59)	(-34.57, -4.59)	0.015	-3.33 (14.03)	(-12.25, 5.58)	0.428	-2.81 (13.68)	(-7.74, 2.12)	0.254	42.089 1[a,c,1]
EQ-5D-5L index		-0.07 (0.35)	(-0.15, 0.01)	0.057	-0.22 (0.65)	(-0.54, 0.99)	0.163	0	-	1	0.789

Variables are expressed as mean (SD).

[a]Significant differences between low-risk and high-risk groups.

[b]Significant differences between low-risk group and control group.

[c]Significant differences between high-risk group and control group.

[1]Global *P* value adjusted by multiplicity. 5STS: Five sit to stand test; CI: Confidence interval; EQ-5D-5L: Euroqol 5 dimensions 5 levels; FSS: Fatigue severity scale; LL: Lower limb; UL: Upper limb; UULEX: Unsupported upper-limb exercise; VAS: Visual analogue scale.

functional disability[25].

Similar to our study, Cavalheri *et al*[26] assessed exercise capacity using the 6 min walking test in a cross-sectional study of lung cancer survivors and found that compared to age and gender-matched healthy controls there were statistically significant differences in exercise capacity. These results are similar to ours. However, they did not include a self-perceived report of dyspnea and fatigue levels, which gives us valuable information about how the patient feels their capacity or a risk profile differentiation. Benzo *et al*[27], in a meta-analysis, found a lower exercise capacity in patients who develop clinically relevant complications after curative lung resection. However, they only used the levels of VO_2max without taking into account self-perceived exercise limitations. In the same line, Snowden *et al*[28] analyzed a sample of 116 major elective surgery patients and showed that patients with a higher frequency of PPCs had a much reduced level of preoperative cardiorespiratory reserve when compared with those with fewer complications.

Concerning upper limbs, our study has shown that high-risk patients present a poorer exercise capacity after lung resection. Upper limb exercise capacity plays an important role in many basic and instrumental activities of daily living and may provide unique information about upper extremity endurance not reflected in the field-based walking tests. Previous studies in similar populations have found an upper limb impairment in patients after breast cancer or cardiac surgery[29], showing decreased functionality and exercise capacity after surgery, similar to our results. However, and despite its importance, we have not found studies about UL exercise capacity after lung resection.

Finally, our results have displayed poorer self-perceived health status in the high-risk group, even 1 mo after discharge. Self-perceived health status is an important variable that rarely has been measured, but it is of tremendous significance, particularly when treating high-risk operable patients[30]. What patients fear most is to be left physically and mentally handicapped and not be able to resume an acceptable daily lifestyle[25]. In line with our study, previous research has shown that more complex resections, such as pneumonectomy, are associated with worse postoperative quality of life[25]. Brunelli *et al*[31] also stated that lung resection patients presented reduced quality of life values compared with the general population. However, they considered that high-risk patients had a postoperative quality of life scores similar to those observed in younger and fitter patients, which contrasts with our results. Nevertheless, the authors explained that the patients who dropped-out could have changed the results, and it should be taken into account when interpreting the results.

Our study has some limitations that have to be reported. First, the 1 mo follow-up is not enough to verify if symptom burden and exercise limitation are maintained over time. However, we have based our study design on previous studies that use the same follow-up, and in the consideration that early recovery of patients is essential to improve their quality of life. Secondly, a specific assessment of respiratory function could be included to get an objective measure of lung tissue. However, we have considered that self-perceived exercise capacity could be more important to carry out daily activities. Third, the inclusion of some comorbidities such as chronic obstructive pulmonary disease, which could affect the assessment, were not included. However, we have based our study design on previous studies, which also did not include them [22].

CONCLUSION

Our results show a poorer recovery in high-risk patients at discharge and 1 mo after surgery, with more self-perceived fatigue, lower self-perceived health status and a poorer upper and lower limb exercise capacity. Moreover, none of the groups undergoing surgery reached the results of the control group. These results represent an advance in the field of rehabilitation because it allows the design of specific rehabilitation programs for each group of patients.
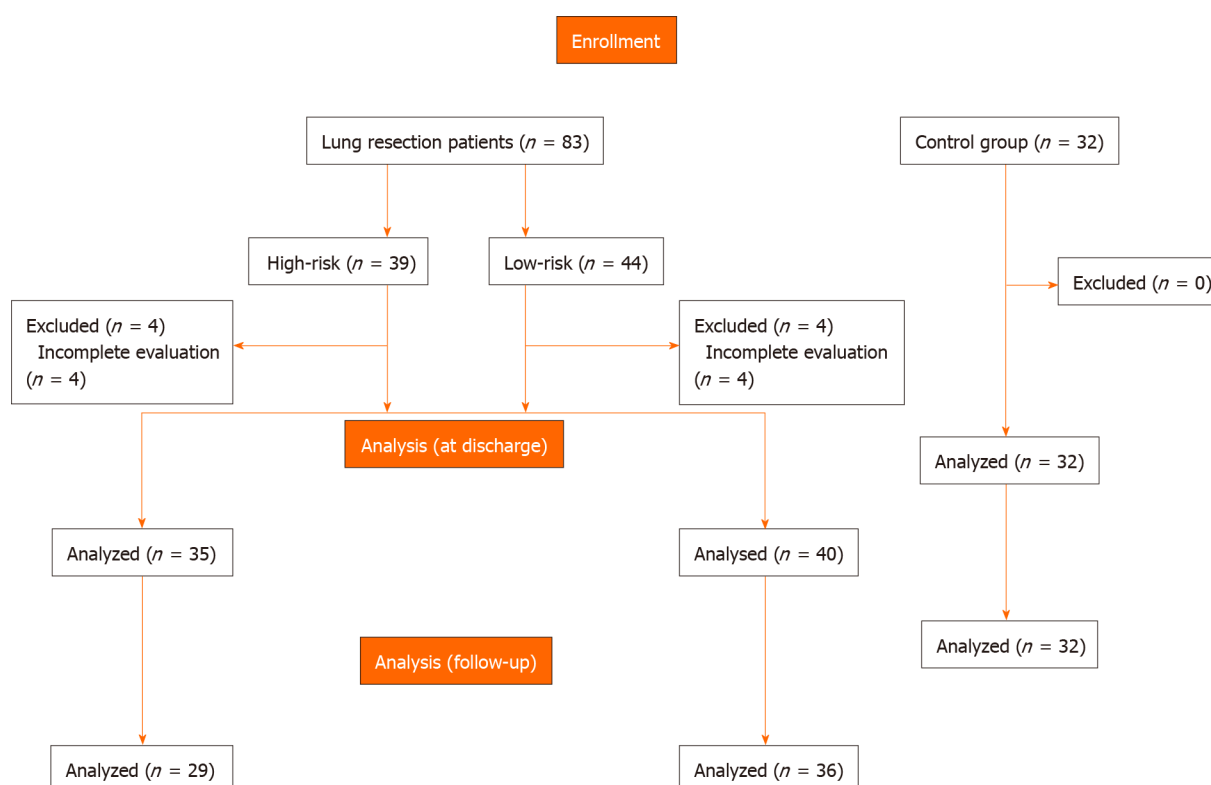
Figure 1 Consort flow diagram of participants.

ARTICLE HIGHLIGHTS

Research background

Lung cancer resection still produces a high incidence of postoperative pulmonary complications. High-risk lung cancer patients are more likely to have postoperative pulmonary complications. Exercise capacity and functionality is affected in lung cancer patients after hospitalization.

Research motivation

High-risk patients present more complications after hospitalization. Upper and lower limb exercise capacity could be affected in these patients.

Research objectives

To determine if there are differences between high and low-risk patients in exercise capacity. To identify differences in self-perceived health status depending on the risk of developing postoperative pulmonary complications at discharge and 1 mo after hospitalization.

Research methods

This was an observational prospective cohort study conducted between April 2017 and July 2018. Inclusion criteria included: to be between 18-years-old and 80-years-old and to be informed about the study purpose. Patients were divided into two groups according to the risk profile criteria. Outcome measures included: Fatigue Severity Scale, dynamometry, 5 Sit-to-Stand Test, unsupported upper-limb exercise, Euroqol-5 dimensions 5 levels.

Research results

Fatigue severity was higher in the high-risk group at discharge. Upper and lower limb exercise capacity presented poorer results in the high-risk group at discharge. Self-perceived health status also presented significant differences between groups. One month after hospitalization, all differences remained.

Research conclusions

High-risk patients present a poor recovery at discharge and 1 mo after hospitalization. More fatigue and a poorer exercise capacity were found in this group. Both groups undergoing lung resection did not reach control group levels even 1 mo after hospitalization.

Research perspectives

The approach of lung cancer patients should be different depending on the risk profile. Future studies are needed to research the differences between high and low-risk patients in a longer term. Future studies should include objective measures to identify these differences.

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