Original Article / Özgün Makale

Outcomes of pulmonary rehabilitation after lung resection in patients with lung cancer

Akciğer kanserli hastalarda akciğer rezeksiyonu sonrası pulmoner rehabilitasyon sonuçları

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ABSTRACT

Background: In this study, we aimed to examine the effectiveness of pulmonary rehabilitation applied after resection in patients with lung cancer.

Methods: Between October 2017 and December 2019, a total of 66 patients (53 males, 13 females; median age: 65 years; range, 58 to 70 years) who underwent lung resection for non-small cell lung cancer and who were not administered any chemotherapy or radiotherapy regimen were included in the study. An eight-week comprehensive outpatient pulmonary rehabilitation program was applied to half of the patients, while the other half received respiratory exercise training. After the intervention, the results of both groups were compared.

Results: In the pulmonary rehabilitation group, forced vital capacity value (p=0.011), six-minute walking distance (p<0.001), and Short Form-36 physical function, mental health, vitality scores increased significantly, while all scores of St. George's Respiratory Questionnaire, dyspnea (p<0.001) and anxiety score (p=0.041) significantly decreased. In the group given breathing exercise training, only dyspnea (p=0.046) and St. George's Respiratory Questionnaire symptom scores (p=0.038) were decreased. When the changes in the groups after pulmonary rehabilitation were compared, the decrease in dyspnea perception was significantly higher in the pulmonary rehabilitation group (p<0.001).

Conclusion: Pulmonary rehabilitation program applied after lung resection in patients with non-small cell lung cancer reduces dyspnea and psychological symptoms, increases exercise capacity, and improves quality of life. It should be ensured that patients with lung cancer who have undergone lung resection are directed to the pulmonary rehabilitation program and benefit from this program.

Keywords: Dyspnea, lung resection, non-small cell lung cancer, postoperative pulmonary rehabilitation, psychological symptoms, quality of life.

ÖΖ

Amaç: Bu çalışmada akciğer kanserli hastalara rezeksiyon sonrası uygulanan pulmoner rehabilitasyonun etkinliği incelendi.

Çalışma planı: Ekim 2017 - Aralık 2019 tarihleri arasında küçük hücreli dışı akciğer kanseri nedeniyle akciğer rezeksiyonu yapılan ve herhangi bir kemoterapi veya radyoterapi rejimi verilmeyen toplam 66 hasta (53 erkek, 13 kadın; median yaş: 65 yıl; dağılım, 58 to 70 yıl) çalışmaya alındı. Hastaların yarısına sekiz haftalık kapsamlı bir ayaktan pulmoner rehabilitasyon verilirken, diğer yarısına solunum egzersiz eğitimi verildi. Müdahaleden sonra, her iki grubun sonuçları karşılaştırıldı.

Bulgular: Pulmoner rehabilitasyon grubunda, zorlu vital kapasite değeri (p=0.011), altı dakikalık yürüme mesafesi (p<0.001) ve Kısa Form-36 fiziksel fonksiyon, mental sağlık ve vitalite skorları anlamlı olarak artarken, tüm St. George Solunum Anketi skorları, dispne (p<0.001) ve anksiyete skoru (p=0.041) anlamlı olarak azaldı. Nefes egzersizi eğitimi verilen grupta sadece nefes darlığı (p=0.046) ve St. George Solunum Anketi semptom skoru (p=0.038) azaldı. Pulmoner rehabilitasyon sonrası gruplardaki değişimler karşılaştırıldığında, dispne algısındaki azalma pulmoner rehabilitasyon grubunda anlamlı olarak daha yüksekti (p<0.001).

Sonuç: Küçük hücreli dışı akciğer kanseri olan hastalarda akciğer rezeksiyonu sonrası uygulanan pulmoner rehabilitasyon programı nefes darlığını ve psikolojik semptomları azaltır, egzersiz kapasitesini artırır ve yaşam kalitesini iyileştirir. Akciğer rezeksiyonu geçirmiş akciğer kanserli hastaların pulmoner rehabilitasyon programına yönlendirilmesi ve bu programdan yararlanmaları sağlanmalıdır.

Anahtar sözcükler: Dispne, akciğer rezeksiyonu, küçük hücreli dışı akciğer kanseri, ameliyat sonrası pulmoner rehabilitasyon, psikolojik semptomlar, yaşam kalitesi.

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Lung cancer ranks second among the most common cancers worldwide and first among cancer-related deaths.^[1] Despite all the developments in cancer management, the most effective method in early-stage non-small cell lung cancer is anatomical resection.^[2,3] Both thoracotomy and parenchymal resection cause impairment in pulmonary functions and a decrease in exercise tolerance.^[4,5] The decreased exercise tolerance negatively affects daily living activities and the quality of life (QoL).^[6] Patients who undergo surgery for lung cancer can only achieve a poor QoL six months after surgery, and a poor physical and mental QoL two years later.^[7]

Pulmonary rehabilitation (PR) is an evidencebased, interdisciplinary, comprehensive exercise program aimed at patients with symptomatic chronic respiratory disease. It integrates exercise and training interventions into a personalized treatment program.^[8] It has become an important component of the general treatment strategy in patients with high-risk surgical diseases such as lung resection.^[5] It helps patients to restore their physical health, as well as their emotional and mental well-being.^[4] In patients with lung cancer, preoperative PR increases exercise capacity and reduces postoperative morbidity and mortality.^[9] Although it is reported that the PR program implemented in the postoperative period increases physical performance and improves the QoL, the referral of patients in need of the PR unit is less than 25%. It is necessary to raise awareness among the pulmonologists and thoracic surgeons regarding the benefits of the PR program, which is a non-pharmacological and effective intervention.^[10]

In the present study, we aimed to examine the effectiveness of PR after lung resection in patients with lung cancer and to investigate the efficacy of the breathing exercises prescribed for patients who could not participate in the PR program.

PATIENTS AND METHODS

This single center, prospective study was conducted at Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital, Department of Chest Diseases between October 2017 and December 2019. A total of 66 patients (53 males, 13 females; median age: 65 years; range, 58 to 70 years) who underwent thoracotomy for non-small cell lung cancer during the last two years and who were not administered or scheduled to have any chemotherapy or radiotherapy were included in the study. Three months after surgery, patients with dyspnea, decreased daily living activities, and increased hospital admissions were pre-evaluated in the PR unit. As physical restraint was greater during the first three months postoperative due to pain,^[7] patients in this period were not included in the study. The patients who did not have an obstacle to participate in the program constituted the PR group and were included in the PR program for eight weeks. The patients who refused to participate in the program and/or had transportation problems were assigned to the control group. The patients who discontinued the program voluntarily; who had to quit due to newly diagnosed diseases; and who interrupted the program due to financial or transportation difficulties were excluded from the study.

Physical and demographic data, smoking histories, and procedure types of the patients were recorded. Respiratory and cardiac system examinations and pulmonary function tests (PFTs) were conducted for all patients. Lung radiograms were evaluated. Demographic and clinical characteristics of the patients were recorded.

Respiratory functions: They were evaluated by measuring the body plethysmograph (Zan 500; ZAN-Messgeraete GmbH, Oberthulba, Germany).

Evaluation of dyspnea: The Modified Medical Research Council (mMRC) dyspnea scale,^[11] consisting of five grades, was used to evaluate the severity of dyspnea. Grade 0 indicates the best level and Grade 4 indicates the worst level. The Modified Borg Scale (MBS),^[12] which is a 0 to 10 scoring system, was used to evaluate the dyspnea that occurred during effort. Zero indicates that there is no shortness of breath at all, and 10 indicates that shortness of breath is very severe.

Exercise capacity: It was determined by the six-minute walk test (6MWT). The 6MWT is a self-paced test of walking capacity. The patients were asked to walk as fast as possible for 6 min along a 30-meter flat corridor. The distance was recorded in meters. The patients were commonly provided with standardized instructions and encouraged. The test was applied two or more times due to the learning effect.^[13]

Quality of life: St. George's Respiratory Questionnaire (SGRQ) was used to determine the disease-specific QoL.^[14] High scores indicate a worsening of the disease and an increase in symptoms. To measure the overall QoL, the Short Form-36 (SF-36) Quality of Life Questionnaire,^[15] which evaluates eight primary health concepts, was used. An increase in the scores was considered as an increase in the QoL.

		All p	All patients (n=66)	(9)		PR	PR group (n=33)			Contro	Control group (n=33)	33)	
Variables	u	%	Median	IQR	u	%	Median	IQR	ц	%	Median	IQR	d
Age (year)			65	58-70			66	55-72			64	62-69	0.847
Sex													0.353
Male	53	80.3			25	75.8			28	84.8			
Body mass index (kg-m ²)			27	23-31			25	23-30			28	24-33	0.167
Smoking (pack-year)			50	40-80			60	40-85			50	33-80	0.600
Number of patients with COPD	42	63.6			23	69.7			19	57.6			0.222
Operation													0.559
Lobectomy	54	81.8			28	84.8			26	78.8			
Bilobectomy	1	1.5			I	I			1	3.0			
Pneumonectomy	11	16.7			2	15.2			9	18.2			
Respiratory function test													
FEV1 (%)			63	45-70			63	45-70			61	45-72	0.837
FVC (%)			65	51-77			65	53-76			65	49-79	0.908
FEV1/FVC			72	63-79			68	61-76			75	68-81	0.029
6-Minute-Walk Distance (m)			390	345-423			390	320-433			390	355-420	0.563
mMRC			3	2-3			З	2-4			2	2-3	0.066
SGRQ													
Symptom			54	42-68			45	29-61			28	18-45	0.007*
Activity			54	42-68			99	49-81			51	36-60	0.002*
Impact			35	24-50			36	29-59			31	18-49	0.130
Total			43	30-55			50	38-63			39	25-52	0.032*
SF-36													
Physical function			55	35-70			55	34-63			55	43-76	0.372
Social functioning			75	50-88			63	47-88			75	50-100	0.208
Role physical			50	0-100			0	0-100			75	13-100	0.097
Role emotional			33	0-100			33	0-100			67	0-100	0.466
General health			60	35-70			40	29-66			65	45-83	0.018*
Mental health			64	45-76			58	43-72			68	47-80	0.409
Bodily pain			72	45-100			65	42-86			90	68-100	0.007*
Vitality			60	35-80			53	34-65			75	38-85	0.034^{*}
HAD subscales													
Anxiety			11	5-13			12	5-15			11	5-13	0.238
Depression			6	6-11			11	5-13			10	6-12	0.452

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		PR group (n=33)	p (n=33)				Control group (n=33)	oup (n=33)		
Variables	Median	IQR	Median	IQR	p^*	Median	IQR	Median	IQR	d
Respiratory function test										
FEV1 (%)	63	45-70	63	51-75	0.054	61	45-72	64	49-72	0.508
FVC (%)	65	53-76	69	56-80	0.011^{*}	65	49-79	68	58-82	0.088
FEV1/FVC	68	61-76	99	60-79	0.458	75	68-81	74	67-80	0.424
6-MWD (meter)	390	320-433	430	365-480	<0.001*	390	355-420	400	370-450	0.232
mMRC	σ	2-4	2	1-3	<0.001*	ю	2-3	2	2-4	0.046
SGRQ										
Symptom	45	29-61	41	19-55	0.004^{*}	28	18-45	23	14-45	0.038
Activity	99	49-81	60	35-79	0.001^{*}	51	36-60	48	36-60	0.748
Impact	36	29-59	32	13-56	0.003*	31	18-49	29	21-48	0.808
Total	50	38-63	42	23.60	0.001*	39	25-52	35	26.48	0.955
SF-36										
Physical function	55	34-63	68	58-86	0.001^{*}	55	43-76	65	45-95	0.196
Social functioning	63	47-88	69	50-88	0.219	75	50-100	75	50-100	0.798
Role physical	0	0-100	63	0-100	0.090	75	13-100	75	0-100	0.959
Role emotional	33	0-100	67	0-100	0.182	67	0-100	67	33-100	0.996
General health	40	29-66	49	30-72	0.085	65	45-83	65	35-85	0.676
Mental health	58	43-72	68	59-81	0.05	68	47-80	68	48-84	0.475
Bodily pain	65	42-86	73	50-100	0.058	90	68-100	90	68-100	0.483
Vitality	53	34-65	60	44-80	0.001^{*}	75	38-85	65	40-85	0.532
HAD subscales										
Anxiety	12	5-15	7	2-10	0.041	11	5-13	6	4-11	0.793
Depression	11	5-13	10	4-12	0.199	10	6-12	8	5-11	0.278

Table 2. Results of the groups before and after PR

Turk Gogus Kalp Dama 2022;30(2):227-234 *Psychological symptoms:* The Hospital Anxiety and Depression (HAD) scale,^[16] consisting of 14 questions, was used to determine the psychological status of the patients. Anxiety and depression scores indicate the following; normal if between 0-7, borderline if between 8-11, anxiety or depression if >11.

Pulmonary rehabilitation program: All patients in the program were administered 2-h sessions two days a week for eight weeks. The exercise program included breathing exercises, relaxation and stretching exercises, exercises to strengthen the peripheral muscles, and aerobic exercises. The strengthening exercises began without weight, then evaluated according to the MBS every four sessions, and half kg weight was added. Aerobic exercises were performed for 30 min in total, of which 15 min was on the treadmill and 15 min was static cycling. Patients with joint discomfort or lower extremity anatomical disabilities were taken to the arm ergometer. The exercise workload of the patients was gradually increased to 60 to 90% of the maximum heart rate or 4 to 6 according to the MBS.^[4] All patients were instructed to exercise at home. Illustrated forms were provided to the patients to ensure they continued exercising on the days they did not come.

Respiratory exercises were instructed to the control group and they were asked to repeat them 10 times twice a day.

Breathing exercises: These consisted of pursed-lip breathing, diaphragmatic breathing, and thoracic expansion exercises. In addition, bronchial hygiene techniques and dyspnea reduction positions were taught.^[17]

At the end of eight weeks, both the PR group and the control group were re-evaluated for each parameter.

Statistical analysis

A sample size of at least 33 participants per group was chosen to provide a power of 0.90 to detect a 30-unit increase in mean 6MWD score assuming a standard deviation of 37.5 units with a two-sided test at 0.05 level. Statistical analysis was performed using the IBM SPSS for Windows version 20.0 software (IBM Corp., Armonk, NY, USA). The distribution of data normality was assessed using Shapiro-Wilk test. Since the distribution of the data is not normal, continuous variables were expressed in median (interquartile range [IQR]) and categorical variables in number and frequency. The Wilcoxon signed-rank test was used to compare the pre- and post-treatment values of the same group, and Mann-Whitney U test was used to compare the changes of the outcomes between the groups. Analysis of countable variables was performed

using the Fisher exact test. A p value of <0.05 was considered statistically significant.

RESULTS

The median time after surgery was 11 (range, 7 to 16) months. When the characteristics of the patients before PR were compared, age, sex distribution, body mass index (BMI), smoking, surgery types, respiratory functions, 6MWD, perception of dyspnea, anxiety, and depression scores of both groups were found to be similar (p>0.05). Besides, the distribution of the number of patients with coexisting chronic obstructive pulmonary disease (COPD) was similar in both groups (p=0.222). In terms of the SGRQ scores in the PR group, symptom (p=0.007), activity (p=0.002) and total (p=0.032) scores were higher than the control group at baseline. Also, SF-36 scores, general health (p=0.018), pain (p=0.007), and vitality (p=0.034), were higher in the PR group compared to the control group before the PR program (Table 1).

When the measurements before and after PR were compared for each group, a significant decrease was determined in the perception of dyspnea (p=0.046) and SGRQ symptom score (p=0.038) in the control group. In the PR group, the forced vital capacity (FVC) value (p=0.011) and 6MWD (p<0.001) significantly increased, and the mMRC score (p<0.001) significantly decreased. All SGRQ subcategories decreased significantly (p<0.05), while physical function (p=0.001), mental health (p=0.005), and vitality (p=0.001) were significantly increased among SF-36 QoL subscores. The hospital anxiety score was significantly decreased (p=0.041). No significant change was observed in the depression score (p>0.05).

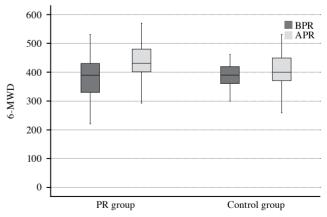


Figure 1. Six-Minute Walk Distance before and after pulmonary rehabilitation in two groups.

6-MWD: 6 Minutes Walk Distance; PR: Pulmonary rehabilitation; BPR: Before pulmonary rehabilitation; APR: After pulmonary rehabilitation.

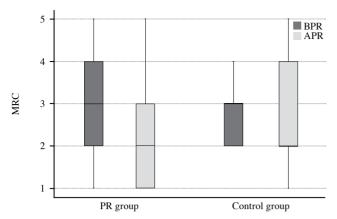


Figure 2. MRC scores before and after pulmonary rehabilitation in two groups.

PR: Pulmonary rehabilitation; MRC: Medical Research Council Dyspnea Scale; BPR: Before pulmonary rehabilitation; APR: After pulmonary rehabilitation.

In the control group, significant decreases were found in the perception of dyspnea (p=0.046) and the SGRQ symptom score (p=0.038) (Table 2). When the changes in the groups after PR were compared, the increase in 6MWD (p<0.001) (Figure 1) and the decrease in dyspnea perception were significantly higher (p<0.001) in the PR group (Figure 2). The anxiety score was significantly lower in the PR group (p=0.032). Besides, in the QoL questionnaires, the SGRQ activity (p=0.006) and impact score (p=0.028) decreased more, while SF-36 physical function (p=0.008) and vitality scores (p=0.006) increased more in the PR group compared to the control group (Table 3).

DISCUSSION

In this study, patients who underwent resection for lung cancer after PR had a significantly increased FVC% value and walking distance, while they had a significantly decreased perception of dyspnea and anxiety score. A significant improvement was seen in all SGRQ scores and some of the SF-36 scores. In the breathing exercise group, the perception of dyspnea decreased significantly, but this decrease was lower

	PR grou	p (n=33)	Control gr	oup (n=33)	
Variables	Median	IQR	Median	IQR	р
ΔRespiratory function test					
FEV1 (%)	0	-3-9	0	-2-5	0.430
FVC (%)	3	-1-10	2	-4-10	0.667
FEV1/FVC	-1	-5-3	0	-5-3	0.979
Δ6-MWD (m)	60	30-85	0	-15-40	<0.001*
ΔMRC	-1	-1-0	0	0-1	<0.001*
ΔSGRQ					
Symptom	-7	-17-2	0	-3-4	0.067
Activity	-7	-25-0	0	-6-1	0.006*
Impact	-8	-17-1	0	-2-3	0.028*
Total	-7	-17-0	0	-20-18	0.074
ΔSF-36					
Physical function	15	0-30	0	0-8	0.008*
Social functioning	0	-13-25	0	0-0	0.699
Role physical	0	0-50	0	-13-13	0.190
Role emotional	0	0-40	0	0-17	0.412
General health	4	-1-13	0	-5-0	0.062
Mental health	8	0-21	0	0-6	0.067
Bodily pain	0	0-21	0	0-0	0.106
Vitality	8	0-20	0	-5-0	0.006*
∆HAD subscales					
Anxiety	0	-2-1	0	-2-1	0.032
Depression	-1	-2-2	0	-2-0	0.550

Table 3. The comparison of changes of the outcomes between groups

PR: Pulmonary rehabilitation; IQR: Interquartile range; FEV1: Forced expiratory volume in the first second; FVC: Forced vital capacity; 6-MWD: 6 Minutes Walk Distance; mMRC: Modified Medical Research Council Dyspnea Scale; SGRQ: St. George's Respiratory Questionnaire; SF-36: Short-Form Health Survey; HAD: Hospital Anxiety and Depression Scale; Results are shown as change Δ between post-treatment and baseline levels; * p<0.05.

than the PR group. Pulmonary functions, walking distance, psychological symptoms, and SF-36 scores did not show a significant change in the breathing exercise group, but a decrease in the symptom score was found in SGRQ.

Lung cancer is more common in men than women. A total of 65% of the patients were over 65 years old. There was no significant relationship between BMI and lung cancer. Smoking is the most important risk factor. As the duration of smoking and the number of cigarettes smoked per day increase, the risk of lung cancer increases.^[18]

In this study, consistent with the literature, the median age of the patients was 65 and the percentage of male patients was higher. The median of cigarette packs/years was 50 packs/year. As in the other two studies,^[3,17] no significant difference was observed between the two groups in terms of age, sex, BMI, and cigarette consumption. There was no significant difference between the two groups in terms of the surgery method.

The coexistence rate of lung cancer and COPD is 73% in men and 53% in women.^[9] In this study, the rate of COPD among all patients was 63%.

The operation has negative effects on pulmonary functions.^[5] In addition to parenchymal resection, impairment of diaphragm and chest wall motility cause a decrease in postoperative forced expiratory volume in 1 sec (FEV1).^[19] A decrease in pulmonary functions leads to decreased exercise tolerance, dyspnea, and impaired QoL.^[5,7] In our study, FEV1 values and walking distance of the patients were found to be low, and their dyspnea perception was found to be high. Their QoL was adversely affected.

The main goal of the PR program is to optimize lung function and, as a result, the patient's ability to function despite the disease.^[8] The PR program may decrease functional deterioration due to thoracic surgery.^[9,10] Some studies indicate that both FEV1 and FVC values increase after PR,^[19] while some studies show that only FVC values^[20] or FEV1 and the vital capacity values increase.^[3] In our study, while FEV1 and FEV1/FVC values did not change significantly, FVC values significantly increased in the PR group.

In many studies, the exercise capacity of the PR program implemented after lung resection has been shown to increase.^[5,19,21] In our study, a significant increase in walking distance was observed only in the PR group. It is reported that both the PR program^[20] and respiratory exercises^[21,22] decrease the perception

of dyspnea in patients with lung cancer. In this study, the perception of dyspnea significantly decreased in both groups.

Although QoL is not always the obvious endpoint for treating patients with lung cancer, improving QoL is much more important than other treatment goals.^[23] It is observed that the QoL of patients with lung cancer who participated in PR after lung resection improved.^[21,24] In this study, a significant improvement was observed in all disease-specific QoL scores in the PR group and only in the symptom score in the control group. The decrease in the symptom score after PR in the control group may be due to the decreased perception of dyspnea.

Patients with lung cancer have higher rates of psychosocial symptoms than other types of cancer, regardless of the type of treatment they receive.^[24] After the PR program, patients' self-efficacy and exercise capacity increase, and psychological symptoms decrease as a result of the decreased dyspnea perception.^[4] In this study, a significant decrease was found in the anxiety scores in the PR group, except for the depression score. In addition to the physical and functional gains, the implementation of the program in groups might have contributed to the improvement of the psychological state. However, it is thought that patients with more severe psychological problems should definitely get individual psychological support.

In this study, where we shared our findings following the PR program in patients with lung cancer who underwent lung resection, the relatively low number of patients prevented us from performing further analysis. Besides, the fact that the PR program was implemented for a period of three months to two years after surgery might have affected the results. Furthermore, we believe that the poor QoL scores in the PR group before the program might have affected our findings.

In our study, we presented the results of the PR program after lung surgery in detail. There are no other studies in the literature that provide detailed PR program results, particularly the psychological symptoms. This may be considered as the superior aspect of our study.

In conclusion, both the diagnosis and treatment of lung cancer negatively affect patients in terms of physical, psychological, and mental well-being. The pulmonary rehabilitation program implemented by an interdisciplinary team offers a unique and important opportunity to improve the health status of patients. It should be ensured that patients with lung cancer who underwent lung resection are referred to the pulmonary rehabilitation program and benefit from this opportunity. Providing breathing exercise training to patients who cannot participate in the program for any reason would reduce the perception of dyspnea.

Ethics Committee Approval: The study protocol was approved by the Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee (No: 49109414-604.02). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Main idea, planning and writting - H.Ş.; Analysis, comment - İ.N.; Data collection - N.A., F.G., M.G.; Review and correction - S.Y.; Review and correction -K.C.C.

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