

## Special Article – Pulmonary Rehabilitation

## Efficacy of Preoperative Comprehensive Pulmonary Rehabilitation in Patients with Lung Cancer

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Lung cancer is a catastrophic and progressive disease that carries excessive social and economic burden. Eventhough the overall five year survival is poor, targeted therapeutics, early detection and multidisciplinary approaches to diagnosis and management have trend to improve outcomes. One of the recent interdisciplinary approach is pulmonary rehabilitation (PR) in perioperative period. PR has been shown to decrease post-operative complications as well as hospital length of stay in patients who underwent lung resection [1]. Low exercise tolerance is associated with poor thoracic surgical outcomes. Preoperative pulmonary rehabilitation (PPR) can optimize individuals' exercise tolerance and overall medical stability before lung cancer resection surgery. Pulmonary resection is the treatment of non small lung cancer (NSCLC) in early stage. The measurement of peak oxygen consumption (VO<sub>2</sub> peak) has been shown to be the strongest independent predictor of surgical complication rate. Specifically, NSCLC patients with a preoperative VO<sub>2</sub> peak ≥ 15 mL.kg<sup>-1</sup>.min<sup>-1</sup> are at comparatively low risk of complications, whereas patients with ≤15 mL.kg<sup>-1</sup>.min<sup>-1</sup> and ≤10 mL.kg<sup>-1</sup>.min<sup>-1</sup> are at increased and very high risk of complications, respectively [2,3].

The aim of this study was to evaluate compact, short-term

comprehensive PR program effectiveness in NSCLC patients during preop period.

**Materials and Methods**

This study was performed in our Pulmonary Rehabilitation Center. Fifteen consecutive patients with potentially resectable NSCLC (14 men) of mean age 66.6±5.87 (range 56-77) were included to this study. Characteristics of the participants are shown in Table 1. For evaluation of exercise capacity of these patients, field tests [Incremental Shuttle Walking Test (ISWT)] was used. Peak VO<sub>2</sub> was calculated with a formulation of [4.19 + (walking distance x 0.025)] (mL.min<sup>-1</sup>.kg<sup>-1</sup>) [4,5].

Dyspnea sensation was assessed with MRC scale [6] and psychological status with Hospital Anxiety and Depression scale [7], the bioelectrical impedance analysis (BIA) was performed for the estimation of body composition [8] on admission and after PPR. Pulmonary rehabilitation programme was multidisciplinary, comprehensive, compact (5 consecutive days in a week) and lasted two weeks, totally 10 sessions. In patients with transportation problem, the programme was undertaken inpatient manner. PPR programme consisting of: (a) educational support, medication advices, bronchial hygiene techniques, and breathing control techniques, energy

**Table 1:** Characteristics of the Participants (n=15).

| Variable   | No            | %    |
|--|---------------|------|
| Age, mean±SD, year   | 66.6±5.87     |      |
| Male, %  |               | 93.3 |
| FFMI, mean±SD, kg/m <sup>2</sup>                             | 19.1±1.6      |      |
| Smoking, mean±SD, pack/year                                  | 50.27±29.08   |      |
| Diagnosis  | 15            | 100  |
| Nonsmallcelllungcancer                                       |               |      |
| Extent of resection  |               |      |
| Lobectomy  | 5             | 33.3 |
| Pneumonectomy  | 1             | 6.66 |
| Pulmonary Function Data                                      |               |      |
| FEV1 liters,   | 42±14         |      |
| FVC liters,  | 55±19         |      |
| FEV1/FVC   | 58±14         |      |
| Exercisecapacity data  |               |      |
| VO <sub>2</sub> peak, mL.kg <sup>-1</sup> .min <sup>-1</sup> | 11.16±2.71    |      |
| ISWT, meters   | 279.07±110.30 |      |

SD: Indicates standard deviation; FFMI: Fatfree mass index; FEV1: Forced expired volume; VO<sub>2</sub> peak: Peak oxygen consumption; ISWT: Incremental Shuttle Walk Test.

**Table 2:** PPR values of medically inoperabl patient's.

| n=4  | Before PPR program | After PPR program |
|--|--------------------|-------------------|
| ISWT (m)   | 199±108.6          | 272±69.9          |
| VO <sub>2</sub> Peak(mL .kg <sup>-1</sup> .min <sup>-1</sup> ) | 9.17±2.7           | 11±1.7            |

**Table 3:** The values before and after PPR.

| n=15  | Before PPR program | After PPR program | p            |
|---|--------------------|-------------------|--------------|
| MRC   | 2.67±0.81          | 2.20±0.56         | <b>0.004</b> |
| ISWT(m)   | 279.07±110.30      | 347±106.53        | <b>0.000</b> |
| VO <sub>2</sub> PeakmL .kg <sup>-1</sup> .min <sup>-1</sup> | 11.16±2.71         | 12.85±2.66        | <b>0.000</b> |
| FFMI (kg/m <sup>2</sup> )                                   | 19.1±1.6           | 19.2±1.5          | 0.184        |
| Anxiety   | 10.50±1.34         | 8.79±2.0          | <b>0.002</b> |
| Depression  | 9.64±1.49          | 7.21±2.39         | <b>0.001</b> |

conservation, relaxation, and dietary advices. Educational sessions were delivered by two chest physicians, two physical therapists, a dietician, one respiratory nurses, and a psychologist. (b) exercise training, (c) a nutritional intervention, and (d) psychological counseling, if needed. The exercise training program was individually tailored to each patient. All exercise training sessions were supervised by physical therapist. Exercise included cycle ergometer training (15 min), treadmill training (15 min), upper and lower extremity strength training (5-10 min), breathing therapies (10-20 min), and relaxation therapies (5-10 min) for total 50-70 min/day. Patients underwent both cycle ergometer and treadmill training. Both workload for cycling and walking speed for treadmill ergometer were calculated from incremental shuttle walking test (ISWT) results using formulations and BORG dyspnea scores 4-6 were also used for prescribing exercise [9]. Patients were trained at 50% of peak workload and 50-80% of peak VO<sub>2</sub>. Quadriceps resistance training was applied using free weights for 5 consecutive days in a week according to 1-repetition maximum starting at 50% for three sets and 10 repetitions per set in the 10 sessions. Upper extremity training consisted of one set, 10 repetitions per set totally 10 sessions. Loads were recorded as kilograms.

Exercises intensity increased according to the patient progress. Pulse oximetry was used to supervise patients during exercise. If

the SpO<sub>2</sub> fell below 90%, oxygen supplementation was provided to maintain SpO<sub>2</sub> ≥ 90%.

**Outcomes**

The primary outcome was change in VO<sub>2</sub> peak mL.kg<sup>-1</sup>.min<sup>-1</sup> between baseline and immediately before pulmonary resection (presurgery). Secondary outcome was the evaluation of PPR efficacy in patients with lung cancer

**Statistical analysis**

The statistical analysis was performed using Statistical Package for Social Sciences (SSPS) version 15.0 (Statistical Package for Social Sciences (SSPS), Chicago, IL, USA). Data were given as mean±standard deviation. First, the variables were analyzed with Shapiro–Wilks test for normal distribution. Then, the pairedt test was used for variables with normal distribution and Wilcoxon signed rank test used for those variables without normal distribution. Spearman correlation analyses were performed. Statistical significance was determined as probability value of <0.05 was considered to be statistically significant.

**Results**

Five (33%) of the patients underwent lobectomy where one (6.66%) of them had pneumonectomy. In one patient who had metastasis in lenf node dissection by mediastinoscopy, has given cheomoradiotherapy. Four (26.7%) of them refused the operation. In four (26.7%) patients mean VO<sub>2</sub> peak was 9.2±2.7 mL .kg<sup>-1</sup> .min<sup>-1</sup> so they were accepted as medically inoperable with a FEV1 790±223 mL before PPR (Table 2). In this group of patients even VO<sub>2</sub> peak increased to a level of 1.84±0.9, they did not have surgical resection. The mean FEV1 and FVC of all patients were 1164±470 mL, 42±14% predicted, 2020±714 mL, 55±19 % predicted respectively. ISWT distances ranged from 46 m to 450 m (mean 279.07±110.30 m). The mean VO<sub>2</sub> peak calculated by using ISWT was 11.16±2.71 mL.kg<sup>-1</sup> .min<sup>-1</sup>, Δ.VO<sub>2</sub> peak; 1.69±0.1 mL .kg<sup>-1</sup> .min<sup>-1</sup> (p <0.001) and Δ ISWT ; 68.26±4 m (p <0.001). Significant beneficial changes were also observed in VO<sub>2</sub> peak (p=0.000), ISWT( p=0.000), MRC (p=004) , anxiety (p=0.002), depression (p= 0.001) scores. According to the results of evaluation of body composition mean FFMI was 19.1±1.6 Kg/m<sup>2</sup> where it was 19.2±15kg/m<sup>2</sup> at the end of PPR (Table 3).

There was no statistically significant correlation between baseline lung function tests (FEV1 %, ml) and either baseline or changes in VO<sub>2</sub> peak, ISWT distance values.

**Discussion**

Surgery is the only curative-intent treatment for patients with resectable NSCLC. The principal finding of this study was that a short-term,compact, comprehensive, supervised PPR program was effective, feasible and safe among newly diagnosed NSCLC patients before lung cancer resection surgery.

Jones et al has shown that preoperative exercise could increase the numbers of candidates eligible for curative-intent pulmonary resection [10]. In their study they showed an increase in VO<sub>2</sub> peak according to cardiopulmonary exercise test (CPET). Eventhough CPET is gold standart for evaluating exercise capacity, in most countries often poorly available and it should be performed by expericenced stuff. ISWT which is readily available in most hospitals correlates well with

VO<sub>2</sub> peak in (CPET) [4] and has been widely used as a measure of exercise capacity in many clinical studies. The shuttle walk is a useful exercise test to assess potentially operable lung cancer patients with borderline lung function [10]. In our study after PPR, VO<sub>2</sub> peak which was calculated by using ISWT was increased significantly and by having risk modification six patients (40%) could be operated. In patients with lung cancer performance status is one the most important factor that influence the therapeutic choice. In our study in four (26.7%) patients mean VO<sub>2</sub> peak was 9.1±2.7 mL.kg<sup>-1</sup>.min so they were accepted as medically inoperable with a FEV1 of 790±223 mL. After PPR eventhough risk level of these patients decreased VO<sub>2</sub> peak did not reach an acceptable level for surgery. So two of them underwent steriotactic radiotherapy, and two of them decided to have supportive therapy. Though surgery remains the treatment of choice for resectable lung carcinoma, postoperative complications of lung resection appear to be a major problem especially in patients with co-existing disease [11]. Incidence of postoperative complications after lung resection was reported as 24-48% while the mortality rates of lobectomy and pneumonectomy were 4% and 14%, respectively [11,12]. The most common complications and the main determinant of mortality and morbidity after lung resection are cardiopulmonary complications. Beckles et al stated that the pre-operative physiologic assessment of patients being considered for surgical resection of lung cancer must consider the immediate peri-operative risks from comorbid cardiopulmonary disease, the long-term risks of pulmonary disability, and the threat to survival due to inadequately treated lung cancer [11]. In our study one patient experienced 3 complications (respiratory failure, pulmonary embolism and death) whereas one patient experienced 1 complication (air leak). The average duration of hospital stay was 18,8 days. In this present study the complication rates in patients underwent surgical resection was 33.3%. Knowing that these patients also had the diagnosis of COPD as a comorbidity, we can say that PPR reduced the risk of complications. In comprehensive pulmonary rehabilitation programmes supervised exercise combined with stress management education in pulmonary rehabilitation may offer management strategies for persons with anxiety and depression. The prevalence rates of anxiety and depression in lung cancer survivors are 34% and 33%, respectively [13]. In a study exercise training has been shown positive effects on anxiety and depression in patients with lung cancer [14]. Our PPR programme was short, compact but comprehensive. The decrease in anxiety and depression scores of our patients ( $\Delta$  Anxiety score=1.71,  $\Delta$  Depression score=2.43 was statistically significant and over the level of MCID [15]. Most lung cancer patients suffer from nutritional issues. Although our patients FFMI values did not change at the end of the PPR, patients were able continue a healthy diet and educated on strategies to improve their nutritional needed if necessary.

There is some limitations of this study. First of all designing a randomised controlled study for candidates of lung cancer resection surgery is not ethical. Relatively small sample size of the patients underwent surgical resection is one the handicap of assessing the complication rates.

## Conclusion

In conclusion short term, compact, comprehensive pulmonary rehabilitation programmes before lung cancer surgery is potentially an attractive technique for optimizing preoperative exercise capacity, risk modification and conceivably, in turn, reducing postoperative respiratory complications.

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