

Research Article

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Rosario Salvi[#], Ilernando Meoli[#], Antonio Cennamo, Fabio Perrotta, Francesco Saverio Cerqua, Raffaele Montesano, Carlo Curcio, Francesco Lassandro, Francesco Stefanelli, Edoardo Grella, Domenico Tafuri, Gennaro Mazzarella, Andrea Bianco*

Preoperative high-intensity training in frail old patients undergoing pulmonary resection for NSCLC

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Abstract: Thoracic surgery remains the better therapeutic option for non-small cell lung cancer patients that are diagnosed in early stage disease. Preoperative lung function assessment includes respiratory function tests (RFT) and cardio-pulmonary exercise testing (CPET). Vo₂ peak, FEV₁ and DLCO as well as recognition of performance status, presence of co-morbidities, frailty indexes, and age predict the potential impact of surgical resection on patient health status and survival risk. In this study we have retrospectively assessed the benefit of a high-intensity preoperative pulmonary rehabilitation program (PRP) in 14 patients with underlying lung function impairment prior to surgery. Amongst these, three patients candidate to surgical resection exhibited severe functional impairment associated with high score of frailty according CHS and SOF index, resulting in a substantial mortality risk.

Our observations indicate that PRP appear to reduce the mortality and morbidity risk in frail patients with concurrent lung function impairment undergoing thoracic surgery. PRP produced improvement of VO₂ peak degree and pulmonary function resulting in reduced postoperative complications in high-risk patients from our cases. Our results indicate that a preoperative training program may improve postoperative clinical outcomes in frail lung cancer patients with impaired lung function prior to surgical resection.

Keywords: Respiratory function tests; Non-small cell lung cancer; Thoracic Surgery; Pulmonary rehabilitation program; Frail patients; Aging

1 Introduction

Thoracic surgery remains the better curative option for non-small cell lung cancer treatment as chemotherapy is not satisfactory in terms of response rate and survival [1-6]. Despite improvements in diagnostic procedures [7-13], only a few patients are eligible for surgical treatment [14]. As lung cancer shares common risk factors with other respiratory diseases [15-19] abnormal pulmonary function is a frequent finding. Several functional and clinical assessments are required before surgery is decided upon. An algorithm proposed in clinical guidelines by Brunelli et al. represents a well-established tool for the assessment of cardiopulmonary reserve before lung resection in lung cancer patients [20]. The preoperative assessment of respiratory lung function, including respiratory function tests (RFT) and cardio-pulmonary exercise testing (CPET), is fundamental to predict the impact of surgical resection

*Corresponding author: **Andrea Bianco**, Department of Cardiothoracic and Respiratory Sciences, Second University of Naples/ Hosp. Monaldi, Piazza Miraglia, 2, 80138 Naples, Italy, Phone: +390815665228, Fax: +390815665230, E-mail: andrea.bianco@unina2.it, andrea_bianco_1962@yahoo.it

Rosario Salvi, Carlo Curcio, Unit of Thoracic Surgery, A.O. Dei Colli - Monaldi Hospital, Naples, Italy

Ilernando Meoli, Francesco Stefanelli, Unit of Pneumology, A.O. Dei Colli - Monaldi Hospital, Naples, Italy

Antonio Cennamo, Fabio Perrotta, Francesco Saverio Cerqua, Raffaele Montesano, Edoardo Grella, Gennaro Mazzarella, Department of Cardiothoracic and Respiratory Sciences, Second University of Naples, A.O. Dei Colli - Monaldi Hospital, Via Leonardo Bianchi, 80131, Naples, Italy

Francesco Lassandro, Unit of Radiology, A.O. Dei Colli - Monaldi Hospital, Naples, Italy

Domenico Tafuri, Department of Sport Sciences and Wellness, University of Naples "Parthenope", Naples, Italy

[#]These authors contribute equally to this work

on the health status of the patient [21-23]. An integrated pre-operative evaluation of residual pulmonary function after surgical removal of lung parenchyma allows the definition of the treatment options and risks, to achieve the best therapeutic option [20]. According to this recommendation, VO₂ peak evaluation, assessed using CPET, represents the best independent predictor of surgical complication rate [24]. CPET, indeed, is mandatory in the presence of any slight functional abnormalities, including forced expiratory volume in one second (FEV₁) and/or diffusion lung capacity of CO (DLCO) < 80% of the predicted value. However, other clinical assessments are required for final decision-making. Age, performance status, presence of co-morbidities and frailty indexes should also be considered for an accurate selection of patients suitable to surgery. Preoperative physiologic assessment serves to identify patients with elevated risk of peri-operative complications and long-term pulmonary disability in order to optimize peri- and post-operative management. A high-intensity preoperative pulmonary rehabilitation program (PRP) improved the degree of VO₂, increased physical performance, reduced the perception of dyspnea and increased quality of life in patients with COPD and NSCLC undergoing surgical resection. [25-28]. These effects continue to be observed after surgery. Adherence to medical treatment and rehabilitation is important to achieve synergistic effects. In this study we have retrospectively assessed the impact of a preoperative high-intensity training program in frail and elderly patients undergoing thoracic surgery for lung cancer.

2 Material and methods

2.1 Patients

We retrospectively reviewed 14 patients (10 males – 4 females; median age 68±7,1 years) with Stage I/II NSCLC and underlying respiratory function impairment due to COPD who underwent a preoperative high-intensity training program. The criteria for operability and resectability were based on the preoperative staging test and the recommendations of the ERS/ESTS guidelines. All patients enrolled in this cohort were treated with long-term bronchodilators (beta-2 agonists and/or anticholinergics), with or without use of inhaled corticosteroids. Within the cases selected, we have evaluated three patients prior to surgical resection who exhibited severe respiratory function limitations associated with high score of frailty according to CHS and SOF index [29, 30], resulting in a considerable

mortality risk focusing the impact of pulmonary training on mortality and morbidity risk.

2.2 Pulmonary Rehabilitation Program

The high intensity training was conducted for 3 consecutive weeks. The program included respiratory exercises on the bench, mattress pad and wall bars. Rowing ergometer, treadmill and bicycle were used for upper and lower limb training. The starting exercise work load was set with 70% of the maximum score reached at the CPET and increased by 10 W according patient conditions.

2.3 Surgical technique

All patients underwent lobectomy associated with mediastinal lymphadenectomy. In one case, upper right lobectomy was performed by three-portal access Video-assisted thoracoscopic surgery (VATS). The other two lobectomies (upper right lobe and lower left lobe) were obtained by axillary vertical muscle – sparing thoracotomy.

2.3.1 Case 1

A 69-year old male, heavy smoker, with a medical history of pulmonary emphysema was referred to our department for the evaluation of a single nodule in right upper lobe. Pre-operative pulmonary function assessment showed a severe obstruction and moderate reduction in DLCO (FEV₁: 1.070 L; FEV₁%th: 29%; DLCO: 14.3 mL/mmHg/min; DLCO%th: 46%). A CPET was performed, resulting in a severe reduction in VO₂ peak (VO₂ peak: 13.6; VO₂ peak%th: 48%). The post-operative predictive value resulted in a significant risk of mortality and morbidity according to the SFAR score. The patient was admitted to a pulmonary rehabilitation program during the 3 weeks preceding the surgical treatment. A functional post-rehabilitative program reassessment was conducted reporting an improved lung function. The ppo-FEV₁ and ppo-VO₂ peak hugely increased (pre-rehabilitation ppo-FEV₁ vs post-rehabilitation ppo-FEV₁: 25% vs 38%; pre-rehabilitation ppo-VO₂ peak vs post-rehabilitation ppo-VO₂ peak: 40% vs 56%); conversely, ppo-DLCO value was unaltered after the training program. The improved pulmonary function resulted in a reduction of mortality and morbidity risk assessed by SFAR index (pre-rehabilitation mortality risk vs post-rehabilitation mortality risk: 8% vs 5%; pre-rehabilitation morbidity risk vs post-rehabilitation morbidity

risk: 24% vs 20%). Lobectomy by thoracotomy confirmed the diagnosis of squamous cell carcinoma. No perioperative complications were observed.

2.3.2 Case 2

A 66-years old male was referred to our hospital to undergo a VATS right upper lobectomy (Figure 1). Pre-operative pulmonary function assessment showed a severe obstruction and severe reduction in DLCO (FEV1: 0.910 L; FEV1%th: 32%;DLCO: 8,40; DLCO%th: 34%). Patient underwent CPET, which showed a moderate reduction in VO2 peak (VO2 peak: 15.7; VO2peak%th: 63%). Before VATS lobectomy the patient underwent a pulmonary rehabilitation program. All functional parameters improved (pre-rehabilitation ppo-FEV1vs post-rehabilitation ppo-FEV1: 29% vs 45%; pre-rehabilitation ppo-VO2 peak vs post-rehabilitation ppo-VO2 peak: 53% vs 54% and pre-rehabilitation ppo-DLCO vs post-rehabilitation ppo-DLCO: 28% vs 32%). A reduction of mortality and morbidity risk assessed by SFAR index was achieved(pre-rehabilitation mortality risk vs post-rehabilitation mortality risk: 9% vs 6%; pre-rehabilitation morbidity risk vs post-rehabilitation morbidity risk: 24% vs 20%). Surgical procedure was performed safely without complications.

2.3.3 Case 3

A 65-year-old female with no significant past medical history was evaluated for the detection a single nodule in right lower lobe. Pre-operative diagnosis of adenocarcinoma was made by FNAB. Pulmonary function tests showed a moderate - severe obstruction with severe

reduction in DLCO (FEV1: 1.293 L; FEV1%th: 52%; DLCO: 9.30; DLCO%th: 39%). Subsequently, CPET was performed, resulting in a moderate reduction in VO2 peak (VO2 peak: 16.04; VO2peak%th:54%). Pulmonary rehabilitative training was carried out and the patient was evaluated after 3 weeks. Spirometry documented an improved lung function resulting in an increase of ppo-FEV1 and ppo-VO2 peak value (pre-rehabilitation ppo-FEV1 41% vs post-rehabilitation ppo-FEV1 51%;pre-rehabilitation ppo-VO2 peak vs post-rehabilitation ppo-VO2 peak: 43% vs 50%);ppo-DLCO value was unaltered after the training program. The improved pulmonary function resulted in reduction of mortality and morbidity risk assessed by SFAR index (pre-rehabilitation mortality risk vs post-rehabilitation mortality risk: 4% vs 1%; pre-rehabilitation morbidity risk vs post-rehabilitation morbidity risk: 15% vs 11%). Therefore the patient underwent lower left lobectomy by thoracotomy without experiencing complications (Figure 2).

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available from review by the Editor-in-Chief of this journal.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee

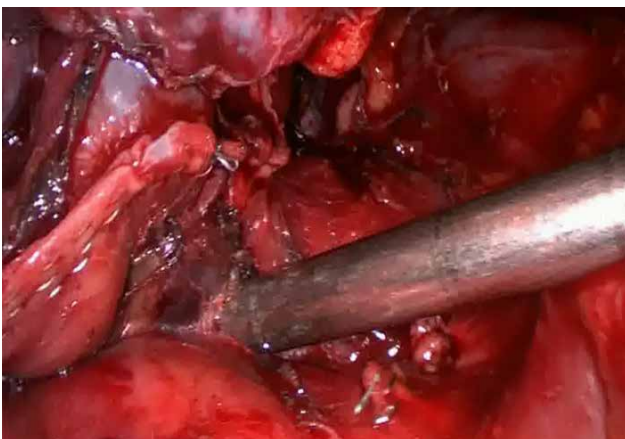


Figure 1: VATS lobectomy plus mediastinal lymphadenectomy.

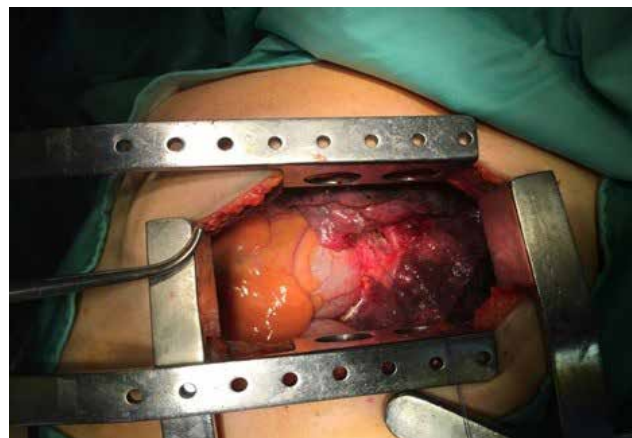


Figure 2: Lower left lobectomy in Thoracotomy.

3 Discussion

Our cases indicate that a pre-operative pulmonary high-intensity program, in NSCLC patients undergoing surgical resection, improves physical performance even in frail patients with compromised lung function caused by COPD. Despite progress in understanding cancer biology [31-52] and a promising novel therapeutic approaches like cell-based therapy [53-56], just postulated in frail old patients [57,58], surgery remains the best option to offer to patients. However, the presence of comorbidities such as cardiovascular and respiratory disorders [59-61] are limiting factors to perform surgery also in technically resectable lung lesions. Improvement in lung function, including several parameters such as FEV1, DLCO and VO2 peak, may lead to a reduction in mortality and morbidity risk. In fact, as is widely acknowledge, lung function assessment is the best independent factor able to predict patients' outcomes following thoracic surgery. The integrated evaluation of ppoFEV1 ppoDLCO and ppoVO2 peak could offer to clinicians a reliable index of pulmonary function after surgical resection. In this scenario, high-intensity rehabilitation programs may represent fundamental tools, especially in older frail patients. In this subgroup, the impact of comorbidities (CHF, COPD, diabetes, chronic kidney failure) may result in a high risk of mortality. Also, pulmonary peri and post-operative complications (atelectasis, obstructive pneumonia, infections) occur more frequently in frail patients [22]. For this reasons, older patients undergoing pulmonary resection require a multidisciplinary pre-operative management. Smoking cessation and pulmonary rehabilitation program may represent the best approach to optimize surgical outcomes [26, 27]. Finally, the correct management should include a comprehensive geriatric assessment focused on the impact of comorbidities in order to optimize medical treatment. Further studies are required to confirm the impact of high-intensity rehabilitation programs also in elderly frail patient who present higher surgical risks.

Conflict of Interests: The authors declare that they have no conflict of interests.

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