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Journal of Infectious Pulmonary Diseases

ISSN 2470-3176 | Open Access

MINI REVIEW

Volume 5 - Issue 1

Fitness Assessment for Treatment of Lung Cancer

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Received: 20 Apr, 2020 | **Accepted:** 09 Jun, 2020 | **Published:** 15 Jun, 2020

Citation: Kastelik JA (2020) Fitness Assessment for Treatment of Lung Cancer. J infect Pulm Dis 5(1): dx.doi.org/10.16966/2470-3176.139

Introduction

Lung cancer is one of the most commonly occurring neoplasms. Overall 5 year survival for lung cancer is around 16% but that for the advanced disease is merely 4% [1]. The evidence suggests that only around a fifth of patients are diagnosed at an early stage of lung cancer, which may be amenable to surgery [1]. Most of the patients with suspected lung cancer undergo systematic investigations in order to confirm histological diagnosis and to establish the stage of the disease. Imaging in the form of a Computed Tomography (CT) of the thorax or a Positron Emission Tomography (PET) scan, provides important staging tools. Positron Emission Tomography has higher accuracy for assessing the mediastinal lymph nodes involvement and detecting of the distal metastatic disease and therefore providing more accurate staging [2]. The assessment of the mediastinal lymph nodes forms an important aspect of staging as this may differentiate whether the patient may be a candidate for surgical treatment. From the diagnostic perspective when assessing mediastinal lymph nodes there are options of performing a mediastinoscopy, which is perceived as gold standard oran Endobronchial Ultrasound (EBUS) and Endoscopic Ultrasound (EUS) [3]. Combined EBUS and EUS were reported to have a very good diagnostic yield and sensitivity comparable with that reported for mediastinoscopy [4]. Other diagnostic tools include navigational bronchoscopy, radial EBUS or CT guided biopsy, which are used for sampling of the peripheral lung lesions [5]. Once the investigations confirm an early stage of lung cancer, which may be amenable to surgery, the next step would be to assess whether the patient is fit to undergo surgical resection. Smoking status requires to be assessed and if the patient is a current smoker, smoking cessation should be undertaken as smoking has adverse effects on the surgical outcomes. Performance status assessment using tools such as the World Health Organisation (WHO) scale allows for the initial estimation of the patients' fitness. Patients' co-morbidities also determine what therapeutic options may be available. The performance status and the presence of co-morbidities are of particular importance not only when assessing for surgery but also in the context of determining patients' fitness for systemic anti-cancer therapy and radical radiotherapy. When assessing the fitness for surgery, tools such as Thoracic Revised Cardiac Risk score ThRCRI help to estimate risks of major cardiac complications [6]. These tools, in order to further stratify the risk of cardiac complications, can be used in conjunction with Electrocardiogram (ECG) and echocardiogram especially in patients who are considered for pneumonectomy [6]. However, there will be a subgroup of patients who have active cardiac condition, risk factors and poor cardiac function. For these patients current guidelines recommend formal assessment by a cardiologist [7]. The patients with cardiac disease should have their medication maximised. In some patients coronary revascularisation may be required including the percutaneous coronary intervention or coronary artery bypass grafting [7].

From the respiratory aspects, all patients should have at least spirometry performed to measure their forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC), which estimate the airflow. Moreover a full lung function testing including lung volumes and the diffusing capacity for carbon monoxide (DLCO) to measure alveolar capillary transfer should be undertaken. For patients considered for radical radiotherapy lung function with FEV_1 and DLCO is required in order to assess whether they are fit to tolerate this type of treatment. It is accepted that patients considered for radical radiotherapy should have DLCO above 40% of predicted. However the current guidelines acknowledge that there is not enough evidence to determine the safe lower level of FEV_1 and DLCO in the context of radical radiotherapy and patients' performance status as well as their co-morbidities need to be taken into account [7]. Nevertheless the most important measurements that affect the decision regarding the fitness for lung cancer surgery are FEV_1 and DLCO as they allow to calculate postoperative FEV_1 and DLCO, which is an estimate of potential mortality and morbidity [8-10]. In fact there are formulas that allow for calculations of estimated post-operative FEV_1, which

involve multiplying the preoperative FEV_1 by (19-number of functional segments to be removed) and dividing this by 19 [7-10]. It is universally accepted that the calculated post-operative FEV_1 of less than 40% is associate with a high risk post lung resection surgery. In those patients surgery is not usually recommended. However, these decisions require to be made on the individual basis. Current guidelines suggest that the decision could be made based on an individual patient's wishes, their expectations and the level of acceptance for possible associated morbidity and level of dyspnoea and disability post lung cancer surgery [7]. This would permit for lowering the lung function threshold and therefore allowing for more patients being considered for surgery. In the sub-group of patients who are borderline for surgery further tests can be undertaken in the form of a perfusion scan or quantitative CT, which can provide more accurate assessment for the predictive post operative values. In contrast, the pre-operative FEV_1 and DLCO over 80% of predicted is associated with low surgical risk [7,10]. Similarly, patients are deemed of low operative risk if their calculated predictive post-operative FEV_1 and DLCO is greater than 60% of predicted [8,11]. Another subgroup that needs to be mentioned includes patients with post-operative predicted FEV_1 and DLCO of less than 60%, which may not necessary prevent them from surgery but would require further assessment. In this subgroup of patients' additional tests such as a shuttle walk or Cardio Pulmonary Exercise Testing (CPET) should be considered [8,11]. Those tests should also be performed in patients with normal FEV_1 but reduced DLCO as they were reported to have increased peri-operative complications [12]. Another deleterious finding that is associated with poor surgical outcome is desaturation on 4% or more on exercise [8].

There are different methods to assess exercise capacity. These include shuttle walk, 6 minute walk, stair climbing and CPET. Comparison between the tests may be not straight forward. However, there is evidence that the stair climb of 22 meters may be equivalent of 400 meters distance of a shuttle walk [8,11]. Moreover these two measurements may equate to maximal oxygen consumption (VO_2 max) of 15 ml/kg/min [7,10]. In fact,VO_2 max of greater than 15 ml/kg/min has been reported as adequate to consider pneumonectomy [8,11]. CPET is the most sophisticated method of assessing fitness for lung cancer surgery. The patients who achieve VO_2 max of more than 20 ml/kg/min are graded as low risk for surgery [8,11]. Those with VO_2 max of 10 to 12 ml/kg/min or less are deemed as high risk for surgery. In the patients who achieved VO_2 max of 10 to 15 ml/kg/min, surgery may be considered but usually in the form lung sparing surgery such as wedge resection rather than lobectomy [8,11]. In addition, in patients withVO_2 max of 10 to 15 ml/kg/min other than surgical therapeutic option may need to be considered such as stereotactic radiotherapy or radiofrequency ablation Intensity-Modulated Radiotherapy (IMRT) [8,12]. There are other parameters of CPET that may be of importance such as the minute ventilation-to-carbon dioxide output (VE/VCO_2) slope, which is associated with a higher incidence of respiratory complications and mortality post lung cancer surgery when it exceeds value of 35 [13]. There are a number of different algorithms on how to assess fitness for lung cancer surgery. For example, the European Society for Thoracic Surgery (ESTS) guidelines suggest that all patients with FEV_1 or DLCO less than 80% should have CPET [8]. Others recommend lung function testing and then low cost exercise testing such as shuttle walk before performing the CPET [14]. However, physiological parameters and exercise testing should not be the only tool applied when assessing the post-operative risks. Therefore the current guidelines suggest using tools such as Thoracoscore, which is a global risk score that estimates the risk of mortality in relation to lung thoracic surgery [7]. The patients who are at high risk need to be made aware of those risks in relation to potential severe dyspnoea, the need for long term oxygen following surgery or radical radiotherapy. In addition in this group of patients' lung sparing surgery may be more appropriate.

In the current pandemic situation many of the options for assessing fitness for lung cancer surgery may not be appropriate. Firstly, the diagnostic protocols that we are accustomed to have changed [15]. New strategies have been employed such as screening of the referrals and excluding low risk patients, telephone consultations rather than hospital visits and the use of interval imaging when findings are indeterminate [15]. Similarly, early decisions whether the investigations are appropriate and whether they may affect the treatment and considerations whether not to perform investigations if treatment is not likely have become more common [15]. PET scanning may be a more appropriate initial imaging tool especially for the early stages of lung cancer. Moreover bronchoscopic biopsies including EBUS require now careful consideration due to the risk of infection [15]. Therefore, PET scan may be of help in identifying alternative site of biopsy. Similarly if the PET scan excludes mediastinal involvement, CT scan guided biopsy of the lesion may be more appropriate for histological diagnosis [15]. In the context of patients considered for surgery similar compromises have been suggested. Thus if spirometry is satisfactory, full lung function testing may not be required, providing that the surgeons are satisfied [15]. Similarly CPET may not be required if the patient has good performance status and the predictive post-operative FEV_1 is greater than 40% [15]. If functional assessment is required rather than performing CPET other options such as shuttle walk or stair test should be considered.

Conclusion

In conclusion, fitness assessment prior to a lung cancer surgery forms an important aspect of an investigating pathway for patients with lung cancer. In the context of systemic anti-cancer therapy and lung cancer surgery, performance status together with the patient's co-morbidities is an important fitness decision making tool. The physiological assessment with spirometry and formal lung function including DLCO allows to decide whether the patients are fit to undergo lung cancer surgery or radical therapy or whether they require additional tests. The exercise capacity assessment such as CPET will allow to measure other physiological parameters including VO_2 max, which stratifies patients' risk for lung cancer surgery. Therefore, when assessing patients' fitness for surgery and other anti-cancer treatment modalities a systematic approach is required in order to make sure that the appropriate patients are chosen for surgery. At the same time the strategies used to assess fitness for surgery should be robust enough to make sure that the patients are not denied surgical intervention. For these reasons, physicians and surgeons investigating and managing patients with lung cancer should be aware of the array of investigational tools that are used for fitness assessment.

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