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http://dx.doi.org/10.1016/j.rppnen.2016.12.008
2173-5115/

Concomitant lung cancer and interstitial lung disease: A challenge in clinical practice

Dear Editor,

Lung cancer (LC) risk is increased in patients with interstitial lung disease (ILD) and sometimes both occur concomitantly.[1] LC incidence is increased 4.96-fold in patients with idiopathic pulmonary fibrosis (IPF) compared with the general population even after adjusting for age, gender and smoking habit.[2] Idiopathic interstitial pneumonias are also associated with increased LC risk and connective tissue disease-associated ILD (CT-ILD) may be a predisposing factor for pulmonary malignancy.[2]

A retrospective analysis of ILD patients diagnosed with LC at our centre in the past 5 years was performed. Characteristics of this cohort were described and outcomes were also reported.

Eleven patients were included [median age 68 (range 36 to 78) years; mostly men ($n=9$; 81.8%)]. Almost all patients had smoking history (81.8%; ex-smokers $n=7$; active smokers $n=2$). The ILDs identified were CT-ILD ($n=5$; 45.5%), combined pulmonary fibrosis and emphysema (CPFE) ($n=2$; 18.1%), IPF ($n=1$; 9.1%), sarcoidosis ($n=1$; 9.1%), cryptogenic organising pneumonia ($n=1$; 9.1%) and silicosis ($n=1$; 9.1%). The most prevalent LC histological type was adenocarcinoma ($n=5$; 45.5%), followed by squamous cell carcinoma ($n=2$; 18.1%) and small cell carcinoma ($n=2$; 18.1%). Most patients were diagnosed at advanced stages (IIIB and IV) ($n=7$; 63.6%), mainly during clinical and radiological follow-up for the ILD. The tumours were predominantly in the peripheral lung fields, in relation to fibrotic areas. Median time from the onset of ILD to the onset of LC was 4 (range 0.3 to 249.7) months. Surgical resection was performed in 3 patients (27.3%) with stage IIA and IIIA LC; chemotherapy and/or radiotherapy were given to 6 patients (54.5%) with advanced disease (stage III and IV). One patient was refused for radiotherapy due to concern about the adverse effects and prognosis. Three patients (27.3%) had acute exacerbations of the ILD after LC treatment: 1 patient with CPFE and another with sarcoidosis presented acute exacerbation after radiotherapy and 1 patient with IPF presented acute exacerbation after chemotherapy with pemetrexed. Two of these patients died due to respiratory failure. Median survival time from the diagnosis of LC was 6.6 months (range 1.2 to 55.6). Three patients died due to progression of LC.

In our sample the majority of patients had a smoking history. Cigarette smoking is a recognised risk factor for the development of ILD[1] but the pathogenesis of LC in patients with ILD is still unclear. IPF has been considered a neoproliferative lung disorder since both IPF and cancer share similar pathogenic hallmarks such as genetic alterations, uncontrolled mesenchymal cell proliferation and tissue invasion behaviour, and dysregulated intracellular signalling pathways.[3]

The treatment choice for ILD patients presenting LC is a challenge to the physicians. In our sample some patients benefited from LC treatment but the pre-existence of ILD also influenced negatively the prognosis. Voltolini et al. showed that major lung resection in patients with early stage non-small cell LC and ILD was associated with increased postoperative morbidity and mortality, mainly in patients presenting lower preoperative FVC% and DLCO%. There was a higher postoperative mortality for pneumonectomy and lobectomy. No patients died after sublobar resection. Thus, anatomic surgical resections can be an option in appropriately selected LC-ILD patients.[4] When planning radiotherapy, it is important to determinate the radiation pneumonitis risk. A recent study showed that fatal radiation pneumonitis tended to be more common in patients with subclinical ILD and that the presence of extensive fibrosis on CT may be a contraindication for thoracic radiotherapy.[5] Stereotactic body radiation therapy (SBRT) could also be an option in LC-ILD patients because of its less invasive nature, nevertheless there is an increasing body of evidence suggesting that even SBRT can induce acute exacerbation of ILD. None of our patients were submitted to SBRT.

Chemotherapy plays an irreplaceable role against LC, but LC-ILD patients receiving chemotherapy may face risks of chemotherapy-related acute exacerbation of ILD. The question arises as to whether chemotherapy regimens are efficacious and safe for the co-morbidity population. So far, no consensus has been reached nor has enough evidence been presented to support an optimal treatment strategy for LC–ILD patients – these patients are usually excluded by most clinical trials and the relevant studies are largely single-armed. A previous meta-analysis performed to evaluate the safety and efficacy of chemotherapy in non-small cell LC–ILD patients suggested that chemotherapy might be an effective therapy for these patients, but it also might be associated with higher incidence of acute exacerbations of ILD.[6] Recently, the role of anti-fibrotic drugs in LC treatment was studied and the results were promising, opening new perspectives on therapeutic options for these complex patients.[7]

In conclusion, LC treatment should be considered in patients presenting both LC and ILD, but interdisciplinary evaluation of therapeutic options is mandatory and the patient opinion should also be considered for the final decision. Prospective studies about LC treatment in ILD patients are urgently needed.

Authorship

This paper has 5 authors, because all of them had contributed to this study: Rita Linhas, Sérgio Campainha, Sofia Neves and Ana Barroso participated in study conception and drafting of the manuscript. Daniela Machado collected the data. All authors read and approved the final manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

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http://dx.doi.org/10.1016/j.rppnen.2016.11.008
2173-5115/

Collective teaching of transverse flute as a component of a pulmonary rehabilitation program: An innovative study

Patients with chronic obstructive lung diseases often remain symptomatic even though optimal standard care, including pharmacological and non-pharmacologic treatment such as oxygen therapy and pulmonary rehabilitation, is provided.[1] Recent studies in these patients demonstrated that several music interventions, such as singing, listening and playing music, resulted in improvement in psychological outcomes (quality of life, dyspnea and anxiety) and mixed results in physiological outcomes.[2] From the pathophysiological stand point, among patients with obstructive lung diseases, the use of wind musical instruments may be an appropriate intervention as their use replicates one of the traditional standardized treatments, the pursed lips breathing technique. This is especially so for instruments that utilize low breathing pressure, such as the harmonica, recorder or flute.[3,4]

The aim of the study was to investigate the impact of collective teaching and practice of transverse flute, as a component of a pulmonary rehabilitation program (PRP), on respiratory functional capacity and quality of life among patients with chronic obstructive lung diseases.

A prospective study was conducted, between October 2015 and April 2016 (28 sessions), at the Physical Medicine and Rehabilitation Department of the Hospital Pedro Hispano – Portugal. Patients with clinically stable chronic obstructive lung diseases who had participated in at least six weeks of a PRP and with availability for the project were selected; written informed consent was obtained from each patient. The patients then enrolled in weekly classes, coordinated by a flute teacher, each class lasting approximately 1 h. Initially, the patients learned the music notes and how to play the transverse flute. Subsequent classes consisted of warm-up exercises with single notes, followed by playing songs of increasing difficulty. The patients were encouraged to practice at home during the week. Patient demographics and clinical histories were recorded, and patients were evaluated at the beginning and at the end of the study period with a six minute walk test (6MWT), maximal respiratory pressures and several questionnaires: Saint George's Respiratory Questionnaire, COPD Assessment Test, EuroQoL-5D Test, Hospital Anxiety and Depression Scale, London Chest Activity of Daily Living Scale and Medical Research Council Dyspnea Questionnaire. On the final evaluation, patients also responded to a self-perceived