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Non-small cell lung cancer in young patients – A retrospective analysis of 10 years in a tertiary university hospital

Dear Editor,

Non-small cell lung cancer (NSCLC) in young adults is uncommon. Although there is limited data about clinical presentation and outcomes, it does seem that this population has some distinct clinicopathological characteristics and given the significant socio-economic implications NSCLC in young adults is increasingly important.[1–3]

The authors report the incidence, clinical characteristics, treatment and prognosis of NSCLC in young patients (≤45 years), in a tertiary academic hospital in Oporto. We retrospectively evaluated 2430 patients newly diagnosed with lung cancer, from January 2005 to December 2014. Our study identified 78 (3.2%) young adults. For analysis purpose, it only included patients with NSCLC who were followed up in our center.

Fifty-nine (75.6%) young adults were included: 37 (62.7%) were male with a mean age of 40.8 years (SD ± 3.8). 40 (67.8%) patients of the patients had a history of smoking. The median time from symptom onset to diagnosis was 1.0 months (0–12.0). Adenocarcinoma was the most common histopathological type, recorded in 44 (74.6%) patients, followed by squamous cell carcinoma in 7 (11.9%). EGFR mutations and ALK translocation were recorded in only 11 (18.7%) patients, and EGFR activating mutations were found in 2 (18.2%). The clinical staging revealed 5 (8.5%) patients with NSCLC in stages I and II, 6 (10.2%) III-A and 48 (81.4%) III-B and IV. The initial *Performance Status* (PS) was 0 and 1 in 41 (69.5%) patients, 2 in 6 (10.2%), and 3 and 4 in 8 (13.6%).

Surgical resection was performed in 9 (15.3%) patients, of whom 7 received chemotherapy and 2 received chemo-radiotherapy. In patients undergoing to surgery, lobectomy and mediastinal lymph node dissection was performed in 7 and pneumonectomy in 2. Chemotherapy alone was given to 32 (54.2%) patients and combination chemo-radiotherapy to 11 (18.6%). *Platinum-based doublet regimens* were used as first-line chemotherapy in more than two thirds of patients ($n = 41$). After progression, half of the patients ($n = 29$) were treated with second-line chemotherapy and 18.6% ($n = 11$) patients to third-line. A minority (11.9%) of patients received best supportive care (BSC) as initial treatment. Regarding response to first-line treatment, 5 (8.5%) patients obtained a complete response, 8 (13.6%) obtained a partial response, 3 (5.1%) stabilized, and the majority (72.9%) progressed. The median progression-free survival was 4.0 months (0–39.0).

During the follow-up period only 12 (20.3%) patients were still alive. In Kaplan–Meier analyses, the median survival rate was about 1.5 months in BSC group and 9.0 months in those submitted to other non-surgical treatments. Six (66.7%) operated patients are still alive (Fig. 1).

Lung cancer is considered a disease of the elderly. The incidence among young adults has been found to be

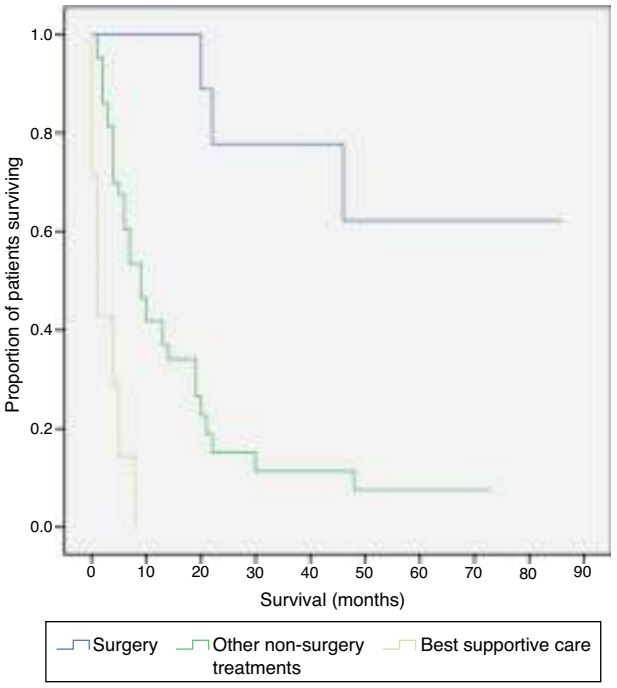

Fig. 1 Kaplan–Meier survival curves according to treatment performed (surgery, other non-surgical treatments and best supportive care).

around 5.3%; however, previous reports have shown trends of increasing incidence rates.[4] However, in our study we found a lower incidence (3.2%). Patients who developed NSCLC at a young age may have other unknown risk factors in addition to inherited risk.[3]

Adenocarcinoma was the most common histopathological type in this group, confirming previously published series.[1–5] The majority of patients presented with advanced stage disease at diagnosis, despite a good PS. Unfortunately, for most of the study period the patients were not screened for driver mutations so the *platinum-based doublet* was the most frequently used treatment scheme. There are conflicting data regarding prognosis in this group when comparing them with older adults.[1–5] In our study, despite the aggressive treatment, the prognosis was poor.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Not yet known side effects of pirfenidone in the treatment of idiopathic pulmonary fibrosis?

To the Editor,

Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive fibrosing pneumonia of unknown cause, occurring primarily in older adults and limited to the lungs,[1,2] with a very poor prognosis.

There were no therapeutic options with proven efficacy until recent randomized controlled trials have shown the efficacy of pirfenidone and nintedanib in reducing the decline rate of forced vital capacity (FVC).[3,4]

Like any other recently introduced drug, the whole spectrum of the side effects of pirfenidone is still unknown. The most frequent side effects reported from the CAPACITY and ASCEND trials,[3,5] the follow-up extension study RECAP[6] and PASSPORT registry interim results,[7] are gastrointestinal (nausea, diarrhea, dyspepsia and vomiting), cutaneous (rash, photosensitivity), headache, dizziness and fatigue. Although cough, upper airway tract infection and worsening of IPF were also reported, these could be attributed to the pathophysiology of IPF *per se*.

We report the cases of 2 patients diagnosed with IPF according to the American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society/ALAT consensus statement on IPF[1] and the 2013 ATS/ERS update of the International Multidisciplinary Classification of the Idiopathic Interstitial Pneumonias statements,[2] who experienced probable toxicity induced by pirfenidone.

The first case reports a 62-year-old female non-smoker diagnosed with IPF (Possible UIP HRCT and UIP pattern in surgical lung biopsy) in 03-2011, being started on N-acetylcisteine 600 mg tid. The patient was started on pirfenidone in 05-2014; at that time a mild restriction was observed (FVC: 75%, 1760 mL, TLCO: 76.3%). From the time she was started on pirfenidone, she complained of dyspepsia, increasing dyspnea (modified Medical Research Council dyspnea scale [mMRC] 2–3), cough and wheezing. On physical examination, bilateral basilar crackles and expiratory wheezing were observed. Blood analysis was unremarkable and sputum microbiological exams were negative. Chest radiography was similar to the previous ones. Cardiac heart failure and pulmonary hypertension were pursued and excluded by echocardiogram, and NT pro-BNP was within normal range. After 4 months on pirfenidone the patient kept complaining of wheezing since the beginning of the drug and troublesome cough not alleviated by opioids; functional decline was observed (relative FVC drop of 10%, with maintained TLCO value). Pirfenidone was interrupted, with resolution of symptoms after one month and improvement of FVC back to basal values. Reintroduction of pirfenidone was attempted, but recurrence of symptoms led to its definitive suspension.

The second case reports a 66-year-old non-smoker woman diagnosed with IPF in 07-2014 (Possible UIP HRCT,