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FDG-PET/CT in the prediction of pulmonary function improvement in nonspecific interstitial pneumonia. A Pilot Study

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ABSTRACT

Purpose: Our study aimed to analyse the characteristics of nonspecific interstitial pneumonia (NSIP) using FDG-PET/CT (PET) and to evaluate its ability to predict the therapeutic response.
Procedures: Eighteen NSIP patients were included. Maximum standardized uptake value (SUV_{max}), FDG uptake extent (in percentage of lung volume), high resolution CT scan (HRCT) elementary lesions, and HRCT fibrosis score were recorded. The predictive value of the parameters for lung function improvement was evaluated using logistic regression and Receiver Operating Characteristic (ROC) curve analysis (n = 13/18).
Results: All patients had an increased pulmonary FDG uptake (median SUV_{max} = 3.1 [2–7.6]), with a median extent of 19% [6–67]. Consolidations, ground-glass opacities, honeycombing and reticulations showed uptake in 90%, 89%, 85% and 76%, respectively. FDG uptake extent was associated with improvement of pulmonary function under treatment (increase in forced vital capacity > 10%, p = 0.03), whereas SUV_{max} and HRCT fibrosis score were not (p > 0.5). For FDG uptake extent, ROC analysis showed an area under the curve at 0.85 ± 0.11 and sensitivity/specificity was 88%/80% for a threshold fixed at 21%.
Conclusions: Increased FDG uptake was observed in all NSIP patients, both in inflammatory and fibrotic HRCT lesions. The quantification of FDG uptake extent might be useful to predict functional improvement under treatment.

1. Introduction

Interstitial lung diseases (ILD) are a heterogeneous group of afflictions. Among them, the clinical courses of idiopathic pulmonary fibrosis (IPF) and nonspecific interstitial pneumonia (NSIP) are heterogeneous. These entities have a characteristic CT pattern that contributes to the initial diagnosis but is limited in terms of disease activity and prognosis.

Nonspecific interstitial pneumonia (NSIP) is a distinct entity in which diagnosis is achieved through a multidisciplinary approach [1,2]. This entity is distinguished from other ILD because NSIP displays a different clinical course [1]. Although it is most often idiopathic, the histologic pattern of NSIP has been observed in a wide variety of clinical settings, including connective tissue diseases (CTD), chronic hypersensitivity pneumonitis, drug toxicity and slowly resolving diffuse alveolar damage [3]. The high resolution CT scan (HRCT) findings in NSIP are bilateral, symmetric ground glass opacities; predominantly basal reticular opacities with traction bronchiectasis; and volume loss [1]. Pathological analysis through a lung biopsy is recommended for idiopathic forms of the disease [1]. NSIP is characterized histologically by varying degrees of interstitial inflammation and fibrosis that are temporally and morphologically homogeneous. The histological spectrum of NSIP ranges from a predominantly cellular process (i.e., cellular NSIP) to paucicellular lung fibrosis (i.e., fibrotic NSIP). Cellular forms exhibit uniform alveolar septal infiltrates of lymphocytes and plasma cells, whereas fibrotic forms exhibit a uniform collagen accumulation resulting in expansion of alveolar septa, peribronchiolar interstitium, interlobular septa, or visceral pleura. [1].

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Evaluating the prognosis of NSIP remains difficult. NSIP with a cellular pattern has a better clinical course than does NSIP with a fibrotic pattern [4,5]. Recent data suggest that the prognosis of NSIP is influenced by the underlying disease as well as by the histological variants [3,6]. However, the absence of a response to a specific therapy is considered to be the strongest determinant of mortality [3].

Several previous studies have reported increased FDG uptake with positron emission tomography and computed tomography in ILD, focusing on IPF [7–13]. One study suggested than FDG-PET/CT (PET) could be more sensitive than CT for the detection of interstitial infiltration in IPF patients because those authors found increased FDG uptake in normal parenchyma on CT scans [7]. In addition, two studies found that high maximum standardized uptake (SUV_{max}) values in IPF parenchyma were associated with a poorer functional prognosis [11,14]. Data regarding FDG-PET in NSIP patients are very limited, and increased FDG uptake in the lungs has been described [8,13].

However, data about correlations between anatomical interstitial lesions and glucose metabolism are lacking. PET is considered to be a very sensitive method for detecting inflammatory lung infiltrates, as shown in the literature [7,15]. During ILD, FDG PET imaging can allow for a comprehensive evaluation of the whole lung volume, with the potential to assess the presence of inflammatory infiltrate, which is located in lung regions with FDG uptake. These hypermetabolic regions can be related to active disease, and therefore to potential reversible lesions. In this work, we assumed that FDG uptake in NSIP can be related to the prognosis and potential functional improvement under immunosuppressive (IS) treatment. So, the objective of this study was to describe the FDG PET findings in NSIP patients and to the correlate FDG uptake with treatment response.

2. Patients and methods

2.1. Patients

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

We conducted a retrospective study of patients with NSIP from two university departments of pneumology and internal medicine (Avicenne Hospital, a tertiary reference centre for ILD, and Jean Verdier Hospital) between October 2000 and October 2012. Inclusion criteria were: (1) patients with idiopathic or secondary NSIP (according to American Thoracic Society/European Thoracic society guidelines); (2) a PET scan during the disease course; and (3) pulmonary function tests (PFT) at the time of the PET scan and repeated between 6 and 12 months after the PET. Patients with sarcoidosis, lung cancer or an active *pulmonary infection* at the time of the PET scan were excluded from the study. Patients' characteristics, clinical data, smoking history, comorbidities, NSIP course, and PFT were analysed. NSIP was confirmed by a surgical lung biopsy in patients with the idiopathic form. In those with connective tissue diseases, the diagnosis of NSIP was based on HRCT showing a typical picture. For each patient, the treatments for NSIP before, at the time of and after PET scanning were recorded. The specific treatment for NSIP was defined as steroid (oral or intravenous) use and/or other IS drugs. Overall, 18 patients fulfilled the inclusion criteria and were analysed.

2.2. Pulmonary function test

For each patient, PFT, including the following parameters, was recorded: diffusing capacity of the lung for carbon monoxide (D_{LCO}), forced vital capacity (FVC), FEV1 (forced expiratory volume in the first second), FEV1/VC (FEV1/vital capacity), and total lung capacity (TLC). *Improvement of lung function was defined as ≥10% increase in the percentage of predicted FVC or ≥15% increase in the percentage of predicted* D_{LCO} [16].

2.3. HRCT protocol and analysis

The CT scans were acquired using a high-resolution protocol. The CT devices were a Philips Mx 8000 (Philips Medical Systems, Eindhoven, The Netherlands) from 2000 to 2006 and either a GE Lightspeed Pro 16 (GE Medical System, Milwaukee, Wisconsin, USA) or a Philips Brilliance 64 (Philips Medical Systems, Eindhoven, The Netherlands) from March 2006 to October 2012. The images were reconstructed in millimetric slices with a hard filter. During the acquisitions, patients were in maximal inspiration, and iodine contrast was not used in most cases. Images were read using a pulmonary window/level (1600 HU, -600 HU) (Philips workstation EBW). The median time interval between HRCT and PET scans was 30 days.

Visual analysis of PET was performed by a radiologist (V.J.) and an experienced double board-certified specialist in thoracic imaging (M.S.), who independently recorded the presence or absence of the following elementary lesions in each of the 6 zones: honeycombing, reticular opacities, bronchiectasis, nodules, consolidation, ground glass and cysts.

In addition, the percentage of pulmonary tissue affected by fibrosis, using the "HRCT fibrosis score", was recorded. This scoring system has already been used in previous studies and has shown a prognosis value in patients with IPF [17–19]. Pulmonary fibrosis was defined by honeycombing, reticular opacities, traction bronchiectasis, or lung architectural distortion. The extent of lung fibrosis on HRCT was determined by visually estimating the percentage (to the nearest 10%) of parenchymal involvement in each zone. The final percentage of fibrosis was the mean of the mean fibrosis score as scored by the two observers in each of the six zones.

2.4. FDG-PET/CT protocol and analysis

All PET images were acquired with a 16-slice PET/CT system (Gemini TF, Philips Medical Systems, The Netherlands), 60 ± 10 min after an intravenous injection of 3–3.5 MBq/kg of FDG. Acquisition duration was 2 min per bed position, with a total of 9–11 bed positions used. The serum glucose level was under 140 mg/dl at the time of injection for all patients. PET images were reconstructed by using a blob ordered subset–time of flight list-mode iterative algorithm with two iterations and 33 subsets, including attenuation and scatter corrections. No post reconstruction smoothing filter was used. SUVs were calculated from the reconstructed activity concentration values and were normalized to body weight. The CT raw data were reconstructed to 3-mm thick axial slices with a soft-tissue reconstruction algorithm and 1-mm thick slices with a lung reconstruction algorithm. PET images were interpreted by a resident and reviewed (Philips workstation) by a nuclear medicine physician (M.S.) who was blinded to the clinical and biological parameters.

Visual analysis of PET was performed by a radiologist (V.J.) and an experienced double board-certified specialist in thoracic imaging (M.S.), who independently recorded the extent of pulmonary FDG uptake. Increased FDG uptake was visually defined as being greater than the normal lung background. Slight uptake associated to normal lung parenchyma, confirmed on HRCT, was used to determine the background lung uptake [13]. The extent of pathological