18F-fluorodeoxyglucose positron-emission tomography/CT and lung involvement in systemic sclerosis

Systemic sclerosis (SSc) early lung involvement (interstitial lung disease (ILD)) is characterised by ground glass opacities (GGO) at high-resolution CT (HRCT).[1 2] The literature provides conflicting interpretations of GGO's clinical significance,[3–5] and whether it represents inflammation or early fibrotic changes is a dilemma. In fact, HRCT cannot discriminate between 'active inflammatory' and 'established fibrotic' GGO.[6] Instead, 18-F fluoro-deoxy-d-glucose positron-emission tomography/CT (18F-FDG-PET/CT) locates areas of increased metabolic activity,[7 8] but no data on the 'established fibrotic' GGO metabolic activity has been demonstrated yet. We aimed at evaluating if 18F-FDG-PET/CT scan may identify GGO inflammatory component in SSc-ILD.[9]

Seven patients with SSc (six females; mean age 59.56±9.15 years, median disease duration 5 years) from the Rheumatology Outpatient Clinic, University of Florence underwent a 18F-FDG-PET/CT to rule out the presence of a neoplasia for a lung nodule detected at chest HRCT. HRCT pulmonary segments were classified as 'negative' (normal morphology) and 'positive' (presence of GGO), and the Warrick score was used to quantify ILD at HRCT.[10] 18F-FDG-PET/CT images were retrospectively analysed by two independent blinded nuclear medicine physicians, obtaining mean standardised uptake value (mSUV) for regions-of-interest for each lung segment, using standard PET/CT scanner workstation tools. These values were normalised (nmSUV) by comparison with sex, age, height and weight-matched controls selected from a database of subjects with negative PET/CT scans and no thoracic and systemic diseases (reference value of 1). Clinical features (including smoking exposure), laboratory workup, chest echocardiography and pulmonary function tests were recorded.

All patients with SSc were non-smokers, and cancer (as assessed by PET/CT and follow-up HRCTs until August 2017), cardiac function abnormalities or increased systolic pulmonary artery pressure were ruled out.

In the four patients with a Warrick score=0, the lung segments were all 'negative' (group A) and had an nmSUV (mean 0.97; 95% CI 0.93 to 1.01, p=0.14) which was not different to reference value of 1. In the three patients with Warrick score >0, a significantly higher nmSUV than reference value of 1 was detected both for 'positive' (group C, mean 1.53; CI 1.42 to 1.65, p<0.0001) and for 'negative' (group B mean 1.29; CI 1.22 to 1.37, p<0.0001) lung segments. Group C showed a 24% higher nmSUV than group B (CI 0.13 to 0.33, p<00 001) (figure 1). Interestingly, lung segments of group B had a 32% higher 18F-FDG uptake than in group A (CI 0.17 to 0.48, p<0.0001).

This preliminary study showed that morphologically 'positive' GGO segments present a clear 18F-FDG uptake, suggesting the existence of an increased metabolic activity of GGO. This 18-FDG uptake could be potentially due to inflammation but could also be seen as a reflection of a concomitant active phenomenon due to underlying pathogenetic mechanisms (ie, high fibroblast activity).[11]

Although these data indicate that PET/CT may disclose an underlying inflammatory process not yet evidenced by HRCT, still it remains to be determined whether early parenchymal involvement may be identified before this is evident at HRCT. In fact, the metabolic activity observed in group B could be related to a lung SSc-related 'impairment' not detectable at HRCT, possibly representing a lung reaction to the disease, stronger in those subjects with some segments affected by GGO. In the

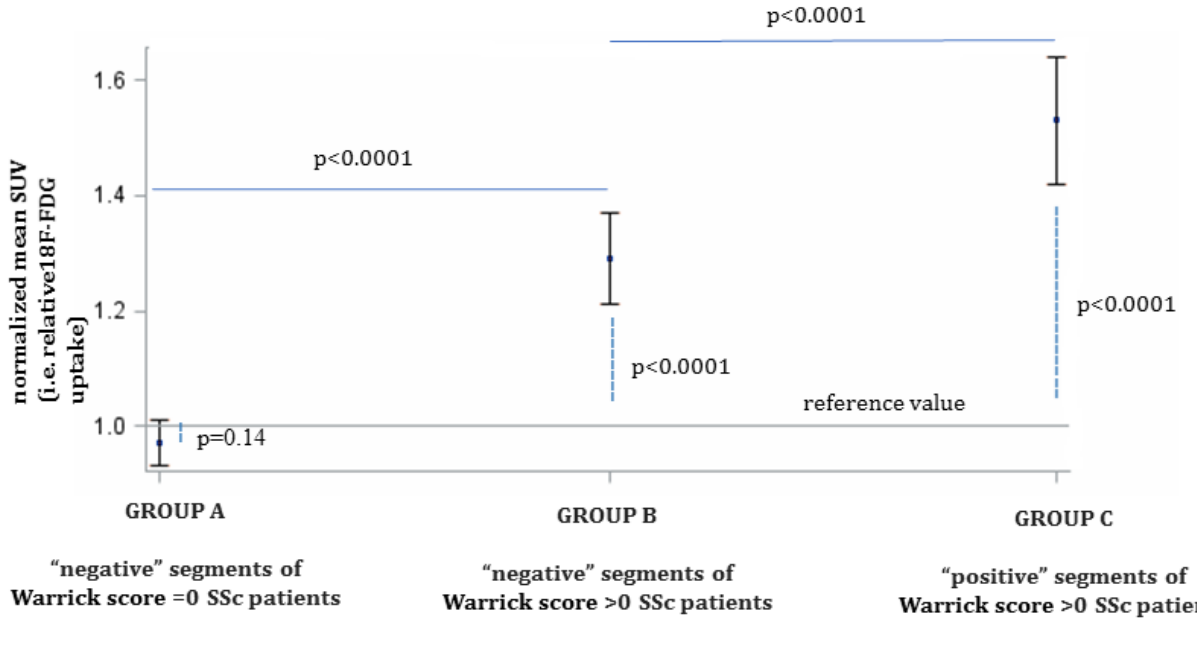

Figure 1 Differences in 18F-FDG uptake between 'positive' segments of Warrick score >0 SSc patients, 'negative' segments of Warrick score >0 SSc patients and 'negative' segments of Warrick score=0 SSc patients versus attended normalised control value (=1). 18F-FDG, 18-F fluoro-deoxy-d-glucose; SSc, systemic sclerosis; SUV, standardised uptake value.

future, the evolution of this specific metabolic activity could be verified with an HRCT follow-up. The fact that 18F-FDG PET/CT might be useful to evaluate the response to treatment during follow-up of patients with SSc, as already used in oncology, remains a working hypothesis because the radiation load is a serious issue which could limit this approach. Further studies on a larger population are warranted to verify our data, preliminary results and possibly provide a prognostic significance of PET/CT positivity in patients with SSc.

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