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Title: Ectopic subpleural fat deposition in idiopathic pulmonary fibrosis correlates with radiographic extension of fibrosis

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Body: Introduction: adipose tissue has been implicated in the pathophysiology of visceral fibrosis, but this has not been studied in idiopathic pulmonary fibrosis (IPF). Methods: we evaluated 39 untreated IPF patients, at diagnosis, and 31 control subjects without lung disease. We measured on chest CT the volume of mediastinal fat and the number of areas where the thickness of subpleural fat was >1mm. Subpleural fat was measured at 3 levels (aortic arch, carina and the right inferior pulmonary vein), in three zones (paravertebral, anterior and posterior quadrants) and on the left and right sides (a total of 18 measures for each patient). Results: patients were older (71 ± 9 vs 64 ± 15 years) with a higher BMI (27 ± 3 vs 24 ± 4 kg/m²). Mediastinal fat volume was increased in IPF patients (391 ± 156 ml vs 261 ± 149 ml, $p=0.0007$), correlated with BMI in IPF and controls. Subpleural fat was detected in all IPF vs 19/31 (61%) controls ($p<0.0001$). The mean (SD) number of areas where subpleural fat could be detected was 11 (3.8) in IPF patients and 1.8 (2.2) in controls ($p<0.0001$). Subpleural fat was more likely to be detected in the posterior quadrants. Mediastinal fat volume and presence of subpleural fat did not correlate with lung function tests (FVC, DLCO, PaO₂). In multivariate analysis, presence of subpleural fat was strongly associated with IPF (OR: 20.9[8.7-50.1]; $p<0.001$), was independent of BMI, and correlated with the extension of fibrosis on CT. Conclusion: IPF is associated with increased mediastinal fat volume and with ectopic subpleural fat deposition, the latter being independent of BMI and correlated to the radiographic extension of fibrosis.