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Title: Idiopathic pulmonary fibrosis: Clinical, radiological and functional significance of biomarkers of proliferation

Dr. Edwin Roger 19334 Parra erparra20003@yahoo.com.br MD [1], Dr. Marcel Lekevicius 19335 Costardi patologia.gamavet@hotmail.com [1] and Prof. Dr Vera 19336 Capelozzi vcapelozzi@lim05.fm.usp.br MD [1]. [1] Pathology, Faculdade de Medicina da Universidade de São Paulo, Brazil, 01246-903 .

Body: Background: Natural course of idiopathic pulmonary fibrosis (IPF) could be predicted by proliferative markers of the fibrotic process, such as myofibroblasts and interleukins (IL)-13 and IL14. Our primary aim was to determine whether these proliferative markers influence the course of IPF course measured by a radiological/functional score. Methods: Twenty-eight patients with biopsy-proven IPF disease, who underwent pulmonary evaluation by high-resolution computed tomography (HRCT) fibrosis score and pulmonary function tests were studied. Five normal lung tissues (NLT) were included Biomarkers in lung tissues were detected by immunohistochemistry and quantified by histomorphometry for myofibroblasts alpha-smooth muscle actin (α-SMA), anti-interleukin (IL)-4 and IL-13. Results: Myofibrobalst amount, IL-4 and IL-13 expression were higher in IPF than in NLT ($p<0.01$). Myofibroblast expression of α-SMA was positively correlated to IL-14 and IL-13 expression. Lung tissue from patients with high HRCT fibrosis scores expressed significantly greater α-SMA+, IL-4 and IL-13 when compared with patients with low HRCT fibrosis scores ($p<0.05$). Negative correlations were found between myofibroblasts α-SMA+ and VC and DLCO. Conclusions: Proliferative markers, detected by immunohistochemistry, in lung tissue allowed recognizing a dichotomous distribution of HRCT fibrosis course and influenced pulmonary function tests, suggesting that they may be promising markers of prognosis in these patients. Financial Support: FAPESP, CNPq.