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"The density histogram-derived computerized integrated index (CII) is a mortality predictor in patients with idiopathic pulmonary fibrosis"

**Background:** The quantitative assessment of the extent of radiological alterations in interstitial lung diseases is a promising application field beyond the qualitative scoring limitations. Among the most studied approaches are the density histograms: skewness, kurtosis, and mean lung attenuation. We recently proposed their integration in a single parameter, the computerized integrated index (CII), to reduce redundancy. The CII has proven effective in detecting subclinical lung involvement in systemic sclerosis patients, and to correlate with lung function/disease activity.

**Aim:** To evaluate the mortality predictive value of the CII in patients with idiopathic pulmonary fibrosis (IPF).

**Study population and Methods:** Seventy-three newly diagnosed and therapy-naive IPF patients (M=50; median age: 70.2 yrs) were prospectively enrolled from January 2014 to December 2022, and followed till December 2023. At baseline, all underwent lung function testing and volumetric high resolution chest CT. Density histograms were analyzed with an open-source automatic platform (Slicer 3D) and CII derived as previously described.

**Results:** During a median follow-up of 5.8 years, 39 (53.4%) subjects died. Median overall survival (OS) was 4.9 years (95% CI: 3.7 yrs-*not estimable*). The CII was significantly associated with OS (HR: 0.49; 95% CI: 0.35-0.68; P<0.001). Patients stratification according to CII tertile, showed a consistent reduction in the hazard of death. After adjusting for BMI, smoking, GAP stage, and anti-fibrotic therapy, the CII preserved a significant association with the hazard of death (HR: 0.35; 95% CI: 0.2-0.63; p<0.001).

**Conclusions:** CII is a proxy marker of IPF severity to be used in clinical evaluation and monitoring.