New Prospects for Diagnosis and Prognosis

We had some news from Dr. Maria Kokosi. She presented on a preliminary data from 38 non-IPF patients and 58 IPF patients recruited from the Royal Brompton hospital and the University of Crete. And she found that all patients presented high values of KL-6, and there was a correlation with the DLCO. The patients have presented a KL-6 level higher than 2000 and were eight in total and six of them presented functional decline. On the other hand, 50 patients showed KL-6 levels below 2000 and from them, only five cases presented functional decline. So, a cut off of 2000 in the KL-6 levels could be evaluated in prospective studies as a potential biomarker for progressive phenotype, very promising data.

While KL-6 is a biomarker that showed correlation with acute exacerbations in IPF, it's a biomarker of alveolar epithelial cell damage. So as you could see in this e-poster, the levels of KL-6 in fibrotic KLD is high because the injury of the other epithelial cells is high. So the thing is that we need prospective studies to evaluate if it could works as a biomarker from the beginning, as a predictive biomarker, or even a diagnostic biomarker, we'll see. But at least this is new data about the potential role of this biomarker or cell marker for the future in progressive phenotype, or in identifying the potential progressive phenotype.

In this study by PON colleagues, they presented data on the use of quantitative CT for the assessment of disease severity in interstitial lung disease. It was a study conducted in the UK, which was really looking to explore the utility of quantitative CT and textural features in IPF. In recent years, quantitative CT has gained more attention as a tool to assess disease, progress and severity. And so the authors use CT scan data from 28 patients with a diagnosis of IPF and process the images using self-developed software to quantify the percentage of honeycombing, reticulation and normal lung tissue. The textual features were then validated against a visual scoring system, which was done by radiologist. They found that the percentage of honeycombing and or reticulation on textural analysis of CT imaging, inversely correlated with the St. George's Respiratory Questionnaire scores, FEV1, FVC and total lung capacity.

The extent of fibrosis on CT correlates with disease severity, mortality, and interstitial lung disease, and this has been shown in other studies, but visual scoring of IPF by radiologist is limited by the availability of specialist radiologists, the high inter-observer variability, and is somewhat subjective. There's only moderate inter-observer agreement among radiologists in identifying honeycombing, which is a diagnostic criteria of IPF. So compared to the visual assessment, quantitative analysis of IPF offers an objective detailed and reproducible measurement of the extent of IPF. This study was small but confirms the previously published data on the correlation of quantitative CT and lung function.

In this poster, Bonella and colleagues actually looked to present data on the enhancement of the gender age physiology index with KL-6 scoring. In this study, the authors measured serum KL-6 levels and investigated whether enriching the GAP staging system with KL-6 improved discrimination of disease progression at one year. KL-6 is a mucinous glycoprotein, which has been found to be elevated in serum, plasma and bio fluid from multiple ILDs, including IPF. The GAP index is a well validated mortality risk

indicator for IPF and has been adapted for use in other ILDs. So this study included 208 ILD patients, 72 of which were IPF and 77 of which had NSIP. They added two points for the baseline GAP score for a KL-6 level greater than 1,000 and two points were added for the diagnosis of IPF. GAP stages were stratified to stage one, which is one to three points and stage two, greater than three points.

The authors did not further stratify the core to delineate gap stage three. Independently, serum KL-6 level greater than a thousand and a diagnosis of IPF were identified as significant predictors of disease progression. There was a non-significant difference in discrimination between progressors and non-progressors with the original GAP score, but when the KL-6 levels and IPF diagnosis were added to GAP staging, and scoring the modified GAP case staging demonstrates significantly improved discrimination of the risk of progression in one year with a log rank p-value of 0.009. The use of biomarkers to help with prognostication is certainly going to be part of future progress, but currently given the limited commercial availability and the ability to routinely check for these biomarkers, its clinical utility at this time remains low and it's not there for prime time.

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The use of biomarkers to help with prognostication is certainly going to be a part of future progress. But currently, given the limited commercial availability and the ability to routinely check for these biomarkers, its clinical utility at this time remains low, and it's not there for prime time.