502. Clinical approach of diffuse parenchymal lung disease

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Prevalence of interstitial lung disease (ILD) in a lung cancer screening program using low-dose computer tomography (CT)

María Sánchez-Carpintero Abad[1], Luis Seijo Maceiras[1], Mónica Ferreira[2], Montes Uxua[1], Alcaide Ana Belén[1], Campo Aranzazu[1], Juan Pablo De Torres[1], Pueyo Jesús[2], Bastarrika Gorka[2], Zulueta Francés Javier[1]. *[1]Pulmonology, Clínica Universidad de Navarra, Pamplona, Navarra, Spain; [2]Radiology, Clínica Universidad de Navarra, Pamplona, Navarra, Spain*

Introduction: The prevalence of ILD in asymptomatic smokers is unknown. Unsuspected ILD can easily be detected by low-dose screening CTs.

Materials and methods: We conducted a retrospective review of CTs from 2418 individuals enrolled in the University of Navarre's lung cancer screening program between 2003 and 2010. Subjects were asymptomatic current or former smokers at least 40 years old, with a cumulative tobacco exposure > 10 pack-years. The prevalence of ILD on baseline CT was assessed initially by 2 independent radiologists. ILD was confirmed and characterized by a panel including a third radiologist and a pulmonologist.

Results: The prevalence of ILD in our study was 1.8%. The median age of subjects with ILD was 57 years (IQR: 51-68). Most were male (70%) and continued to smoke (71%) with a cumulative tobacco exposure of 35 pack-years (IQR: 23-47). The most common radiographic pattern was reticular disease (68%), followed by ground glass opacities (59%), bronchiolitis (15%), honeycombing (11%), and nodular (5%). The majority of subjects had peripheral (77%) and bilateral (96%) disease. Lymphadenopathy was rare (9%). The prevalence of emphysema in subjects with ILD was high (80%). Bronchial wall thickening (59%) and coronary calcifications (46%) were also common. Lung function was preserved in this asymptomatic cohort with a mean FEV1 of 97% (IQR: 78-108).

Conclusions: The prevalence of ILD in our screening population was higher than expected. Most of these individuals ignore the diagnosis, continue smoking, and have preserved lung function.

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Physiology is a better predictor of mortality than HRTC findings in patients with fibrotic idiopathic interstitial pneumonia

Federica Novelli[1], Laura Tavanti[1], Federica Martino[1], Stella Cini[1], Lorenza Melosini[2], Chiara Romei[2], Fabio Falaschi[1], Stefano Solfanelli[1], Alessandro Celi[1], Pierluigi Paggiaro[1]. *[1]Cardiac, Thoracic and Vascular Department, University of Pisa, Pisa, Italy; [2]Radiology Department, University of Pisa, Pisa, Italy*

Background: Prognosis of fibrotic idiopathic interstitial pneumonia (IIP) is influenced not only by the histologic pattern observed in lung biopsy but also by high resolution chest tomography (HRCT) and pulmonary function findings.
Aim: To evaluate if functional parameters are better predictors of mortality that HRCT findings in patients with fibrotic IIP.
Methods: We studied 43 patients with fibrotic IIP during a follow-up of 37.2±31.7 months after diagnosis. Baseline HRCT was evaluated for different abnormalities: honeycombing (HC), reticulation, ground-glass, bronchiectasis and total fibrotic score. Pulmonary function was assessed as baseline FVC and change of FVC after 6 months of follow-up (less or more 10%).
Results: Among the different HRCT scores, a cut-off of 10% in the HC score differentiated patients with different survival (5-yrs survival 41% vs 90%, p=0.04). Patients with HC > 10% had a longer duration of symptoms (p=0.04), a lower baseline DLCO (% of predicted, p=0.006) and higher fibrotic and bronchiectasis score (respectively, p=0.04 and p<0.001) than the other patients. A baseline FVC < 76% (median value) and a worsening FVC at 6 months (vs stable-improved) were associated with lower survival (baseline FVC: 5-yrs survival 57% vs 78%, p=0.03; FVC change: 21% vs 75%, p=0.005). In a multivariate logistic analysis taking in consideration clinical, radiological and functional findings, only baseline FVC and FVC change resulted still significant predictors of mortality.
Conclusion: Functional findings are more important prognostic factors of mortality than HRCT parameters in patients with fibrotic IIP.

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Six-minute-walk test: Desaturation index in diffuse parenchymal lung disease

Dina Visca, Angelo De Lauretis, Giuliana Pasciuto, Giuseppina Gioffrè, Smargiassi Andrea, Riccardo Inchingolo, Francesco Macagno, Giuseppe Maria Corbo, Salvatore Valente. *Respiratory Medicine, Internal Medicine, Rome, Italy*

Six minute walk test (6MWT) is widely used in the functional evaluation of diffuse parenchymal lung diseases (DPLD). To date, distance walked is the most studied 6MWT parameter.
We focused our study on desaturation index (DI) in 6MWT.
We retrospectively evaluated serial lung functions of 59 consecutive DPLD patients: 28 idiopathic interstitial pneumonia (IIP), 11 connective tissue disease (CTD), 13 sarcoidosis and 7 other DPLD.
DI was calculated as the ratio between the area above the curve, which was created using each peripheral oxygen saturation (SpO2) value obtained every 2 seconds, and the distance walked.
Composite physiologic index (CPI) was used to assess disease severity. Disease progression ("time to irreversible decline" in either FVC levels of 10% from baseline or DLCO levels of 15% from baseline) was quantified from the date of the first 6MWT available, by using proportional hazards analysis.
Of the 59 patients, 38 were females, mean age was 66.3 (±11.8 SD), mean FVC was 90% predicted (±24) and mean DLCO was 55% (±24). Median length of follow up was 24.7 months.
Among 6MWT parameters, only DI (p=0.02), lowest SpO2 (p=0.01) and SpO2 at 1 minute of recovery (p=0.02) significantly differed between IIP and sarcoidosis.
DI showed more correlations with other physiologic variables than distance walked; the strongest one was with DLCO (r=-0.53, p=0.0001).
After controlling for age, gender, smoking status, diagnosis and disease severity, DI remained predictive of disease progression (p=0.04).
DI and SpO2 at 1 minute of recovery are two new promising parameters in the assessment of DPLD. DI is associated with disease progression, independently of disease severity.

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Abnormal pulmonary arterial remodelling in patients with combined pulmonary fibrosis emphysema (CPFE) and idiopathic pulmonary fibrosis (IPF)

Elisabetta Balestro[1], Francesca Lunardi[2], Emanuela Rossi[1], Nazarena Nannini[2], Giuseppe Marulli[1], Monica Loy[1], Federico Rea[1], Fiorella Calabrese[2]. *[1]Department of Cardiac, Thoracic and Vascular Science, University of Padova, Padova, Italy; [2]Department of Diagnostic Medical Sciences and Special Therapies, University of Padova, Padova, Italy*

CPFE is a syndrome with distinct clinical, functional and radiological characteristics. Recent works have demonstrated the impact of pulmonary hypertension (PH) on worse survival but little is known about the morphological and molecular substrates. The aim of our study was to evaluate the arterial remodelling and expression of transforming growth factor-beta1 (TGF-β) in the lungs of patients with CPFE compared to IPF without PH. The study was performed on lung samples or native lungs (2007-10 recruitment period): 7 CPFE patients (mean age 59±5.8 yrs), 15 IPF patients (mean age 53±10yrs) and 5 non-implanted donors (mean age 30±10yrs) as a normal control group. In all cases morphometry was used to measure arterial intimal, medial, and total thickening and immunohistochemical evaluation of TGF-β was quantified in macrophages and alveolar epithelial cells. In CPFE, FEV1%pred and FVC%pred were significantly less reduced than in IPF (p=0.004 and p=0.003, respectively), while DLCO%pred was similar. Intimal and total thickening were significantly increased in CPFE than IPF (p=0.004 and p=0.03, respectively). A trend of increased alveolar TGF-β expression was detected in CPFE compared to IPF (p=0.07) while its expression in macrophages was similar. As expected, arterial remodelling and TGF-βexpression were significantly increased in both IPF (p=0.001; p=0.001 respectively) and CPFE (p=0.004; p=0.003, respectively) compared to controls. In conclusion, our study demonstrated that lungs with CPFE display significant arterial remodelling which may represent pathological substrate for the increased occurrence of PH.

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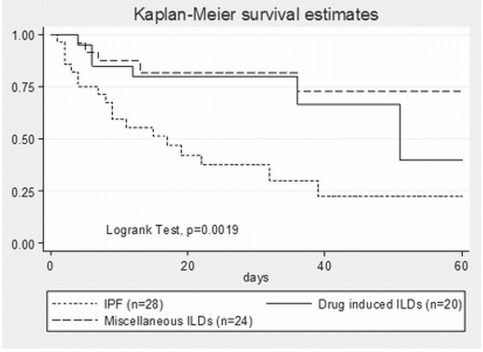
Outcome of patients with interstitial lung disease admitted into ICU

Amandine Vial-Dupuy[1,2], Olivier Sanchez[1,2], Liath Guetta[1,2], Benoit Douvry[1,2], Karine Juvin[1], Delphine Wermert[1], Emmanuel Guerot[3], Dominique Israel-Biet[1,2]. *[1]Faculté de Médecine, Université Paris Descartes, Paris, France; [2]Service de Pneumologie et Soins Intensifs, AP-HP, Hôpital Européen Georges Pompidou, Paris, France; [3]Service de Réanimation Médicale, AP-HP, Hôpital Européen Georges Pompidou, Paris, France*

Background: Limited data are available on the clinical course of patients with Interstitial Lung Disease (ILD) and acute respiratory failure requiring admission to ICU.
Objectives: To investigate the outcome of patients with ILD and acute respiratory failure with special attention to Idiopathic Pulmonary Fibrosis (IPF) or Drug-induced ILD (DI-ILD).
Methods: Retrospective identification of patients with ILD admitted into ICU between 1993 and 2009. Primary end-point was in-hospital mortality.
Results: 72 subjects could be included, divided into 3 groups: IPF, n=28; DI-ILD, n=20 and Miscellaneous, n=24. The in-hospital mortality rates were 68, 40 and 25% for IPF, DI-ILD and Miscellaneous, respectively, (p=0.006) and reached 100, 64 and 60%, respectively, in those receiving mechanical ventilation (p=0.007).



Two month survival analysis: Global Logrank Test, p=0.0019.

On multivariate analysis, the need for invasive or non invasive ventilation (OR= 35; [95% IC, 5-255]), the type of ILD (IPF vs Miscellaneous) (OR=22; [95% IC, 3-147]), and high-dose steroids during ICU stay (OR=0.19; [95% IC, 0.04-0.99]) were found to be independent determinants of in-hospital mortality.
Conclusion: This study highlights the poor prognosis of IPF in ICU particularly if mechanical ventilation is required. DI-ILD and Miscellaneous with comparable severity criteria have a better prognosis than IPF. High-dose steroids appear as a protective factor whatever the type of ILD.

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The King's brief interstitial lung disease quality of life questionnaire (K-BILD) for patients with IPF and other ILDs

Amit S. Patel[1], Richard Siegert[2], Kate Brignall[1], Sabrina Bhajwah[2], Sujal R. Desai[4], Athol U. Wells[2], Irene J. Higginson[1], Surinder S. Birring[1]. *[1]Division of Asthma, Allergy and Lung Biology, King's College London, London, United Kingdom; [2]Department of Palliative Care, Policy & Rehabilitation, Cicely Saunders Institute, King's College London, London, United Kingdom; [3]Department of Respiratory Medicine, Royal Brompton Hospital, London, United Kingdom; [4]Department of Radiology, King's College Hospital, London, United Kingdom*

We set out to develop a brief ILD specific health related quality of life (HRQOL) questionnaire for patients with idiopathic pulmonary fibrosis (IPF) and other ILDs. Items were generated from patient interviews (n=10), literature review and a multi-disciplinary team meeting. A preliminary questionnaire consisting of 71 items and a 7 point Likert response scale was tested in 173 patients (49 IPF). The following items were removed: 1) floor effect: >60% of participants responded

"rare" or "never" (25 items), 2) inter-item correlations of r>0.8 (7 items), 3) Exploratory factor analysis (FA): items loading <0.5 on each factor (5 items). A scree plot suggested a 4 factor solution. 4) Items that did not fit unidimensional scales following Rasch analysis (9 items). The remaining 25 items were pooled together and subjected to further Rasch analysis to eliminate items that did not conform to a unidimensional overall HRQOL scale (10 items removed). A repeat FA was performed to confirm the remaining items conformed to the original factor solution. The fourth factor consisted of 1 item which was considered too small to constitute a health domain but remained in the questionnaire to generate an overall HRQOL score. The final King's Brief ILD questionnaire (K-BILD) comprises of 15 items which generate an overall and 3 health domain QOL scores (Psychological (7items), Breathlessness and Activities (4 items) and Physical Symptoms (3 items). The K-BILD is currently undergoing evaluation of repeatability and responsiveness.

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Demonstration of diagnostic and prognostic benefits of an interstitial lung disease (ILD) multidisciplinary team meeting

Lisa Spencer[2], Seamus Grundy[1], Melanie Greaves[1], Paul Bishop[1], Annette Duck[1], Colm Leonard[1]. *[1]North West Lung Centre, University Hospital of South Manchester NHS Foundation Trust, Manchester, United Kingdom; [2]Respiratory Medicine, Aintree Univesity Hospitals NHS Foundation Trust, Liverpool, United Kingdom*

Introduction: Idiopathic pulmonary fibrosis (IPF), the commonest of the idiopathic interstitial pneumonias, is increasing in incidence/prevalence. Diagnosis can be challenging due to a number of interstitial lung disease with overlapping clinical, radiological or pathological features. Recent guidelines (British Thoracic Society) emphasise the need for multidisciplinary team-based diagnosis, but little published evidence is available to support this recommendation.
Methods: 161 consecutive patients discussed at the ILD MDT meeting at University Hospital of South Manchester were analysed.
Results: In 69 of 161 cases the MDT agreed with the diagnosis of the referring physician. In 67 of 161 cases a single ILD label different to that of the referring centre was given, and in 25 of 161 cases the ILD delivered a differential diagnosis only. Of 67 patients referred with definite IPF only 40 patients (60%) kept their label of IPF, the remaining 27 patients receiving a different diagnosis, predominantly non-specific interstitial pneumonitis (NSIP). At time of follow (3-6 years after MDT discussion) 52% of patients who kept their IPF diagnosis were alive versus 78% of patients alive where a pre-MDT diagnosis of IPF was changed to a more favourable diagnosis, $p<0.05$.
Conclusion: This data is the largest ILD MDT cohort thus far reported and is the first report to clearly link an MDT-based change in diagnosis from IPF to NSIP translating into documented improved survival.