

All procedures were performed with the patient self-ventilating under deep sedation with propofol using a flexible bronchoscope and 2.4 mm cryoprobe (ERBE). All but one procedure was performed under fluoroscopy guidance. All but the first two cases were performed following intubation with an uncuffed ET tube (Bronchoflex, Rusch). We introduced prophylactic IV tranexamic acid 1 g as premedication and endobronchial adrenaline routinely as part of our protocol after the first 5 cases. 1–5 samples were taken per procedure from several sub-segments of one lobe pre-selected by CT imaging.

**Results** 14 procedures were carried out on 13 patients. 9 patients were male. Mean age 63, mean predicted TLCO 50%; mean number of biopsies 2.7; mean aggregate biopsy size 624 mm<sup>3</sup>.

**Complications:** 2 pneumothoraces requiring chest drain insertion; 1 case of moderate bleeding and 1 case of severe bleeding managed with endobronchial adrenaline and suction only.

All cases were performed as outpatient day cases with patients discharged home 2–4 h after the procedure except the 2 patients requiring chest drains.

**Abstract S42 Table 1** Patient characteristics

Case	Sex	Age	Number of biopsies	Aggregate biopsy size in mm <sup>3</sup>	Diagnosis
1	M	66	3	1800	Normal lung parenchyma
2	M	75	2	118	UIP
3	F	60	3	410	NSIP
4	M	66	1	125	Interstitial fibrosis
5	M	64	1	60	HP
6	M	44	1	80	NSIP
7	F	73	4	147	HP
8	M	74	5	1200	CLL
9	M	68	2	1120	Interstitial fibrosis
10	M	41	4	810	Organising Pneumonia
11	M	59	3	168	Interstitial fibrosis
12	F	57	4	2000	UIP
13	M	64	1	75	Non-diagnostic
14	F	67	2	pending	pending

**Conclusions** Our transbronchial cryobiopsy service is comparable in complication rates and diagnostic yield with larger case series from established centres outside the UK. Transbronchial cryobiopsy provides potential for minimally-invasive acquisition of sizeable lung biopsies. Further research is needed to establish whether transbronchial cryobiopsy should replace surgical lung biopsy in selected cases.

#### REFERENCE

- Morris D, Zamvar V. The efficacy of video-assisted thoracoscopic surgery lung biopsies in patients with interstitial lung disease: a retrospective study of 66 patients. *J Cardiothorac Surg.* 2014;9:45

#### S43 MORTALITY FOLLOWING SURGICAL LUNG BIOPSY FOR THE DIAGNOSIS OF INTERSTITIAL LUNG DISEASE IN THE UNITED STATES: 2000–2011

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**Introduction** Surgical lung biopsy can help to achieve a specific diagnosis in interstitial lung disease, but has associated risks. Most currently available mortality data come from case series.

**Objective** We aimed to assess in-hospital mortality following surgical lung biopsy for interstitial lung disease in a national secondary care dataset.

**Methods** Data were obtained from the Nationwide Inpatient Sample, an anonymised yearly sample of US community hospitals developed for the Healthcare Cost and Utilisation Project (HCUP). We identified cases from 2000–2011 using International Classification of Diseases (ICD-9-CM) codes for interstitial lung disease, and procedure codes for surgical lung biopsies. Lung resections and cases of lung cancer were excluded. We estimated numbers of biopsies nationwide and in-hospital mortality, and used multivariate logistic regression to assess risk factors for mortality, adjusting for sex, age, geographic region, co-morbidity, type of operation, and provisional diagnosis.

**Results** We estimated there to be around 12,000 surgical lung biopsies performed annually for interstitial lung disease in the United States, two-thirds of which were performed electively. In-hospital mortality was 1.7% for elective procedures, but significantly higher for non-elective procedures (16.0%). Male sex, increasing age, increasing co-morbidity, open surgery and a provisional diagnosis of idiopathic pulmonary fibrosis or connective tissue disease related interstitial lung disease were risk factors for increased mortality.

**Conclusions** In-hospital mortality following elective surgical lung biopsy for interstitial lung disease is just under 2%, but significantly higher for unplanned procedures. The mortality risk and risk factors for death should be taken into account when counselling patients on whether to pursue a histological diagnosis.

#### S44 PROGNOSTIC SCORING SYSTEMS FOR IDIOPATHIC PULMONARY FIBROSIS: COMPARISON OF THE COMPOSITE PHYSIOLOGIC INDEX (CPI) AND THE GAP SCORE

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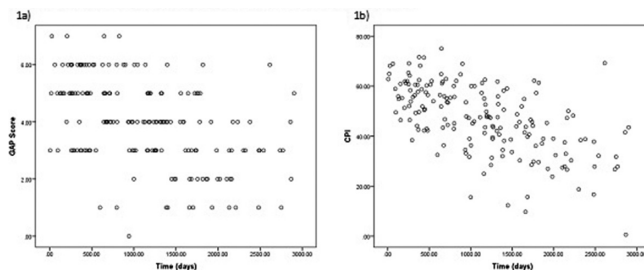
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Idiopathic Pulmonary Fibrosis (IPF) is a progressive, scarring lung disease with a poor prognosis and median survival of 3 years. It is a heterogeneous disorder with varying rates of progression, which presents a challenge for accurate prognostic prediction. The CPI<sup>1</sup> and the GAP<sup>2</sup> score are validated scoring systems for prognostic determination in IPF. However, it remains unclear which is the optimal method for accurate prediction of mortality in IPF. Therefore, a comparison of the predictive ability of the GAP score and CPI was undertaken in a cohort of IPF patients.

**Methods** Baseline data were collected retrospectively from 213 IPF patients (in accordance with ATS/ERS criteria and MDT consensus) from a single centre in the UK between 19<sup>th</sup> April 2007 and 14<sup>th</sup> July 2014. Thirty-eight patients were excluded, either because pulmonary function test results could not be obtained or the patient received a lung transplant during follow-up. Gender, age, FVC and DLCO were used to calculate the GAP score whilst FVC, FEV1 and DLCO were used for the CPI. Spearman's correlation was used to analyse the relationship between GAP score or CPI and survival time. The ability of the scoring systems to predict survival at 1 and 3 years was assessed using ROC curve analysis.

**Results** Of the 175 patients, 131 (75%) were male with a mean age of  $71 \pm 8$  years (mean  $\pm$  SD) at presentation. Overall 3-year mortality was 50%. The CPI demonstrated a better correlation with survival ( $r^2 = 0.37$ ,  $p < 0.01$ ) compared to the GAP score ( $r^2 = 0.24$ ,  $p < 0.01$ ). ROC curve analysis for 1-year mortality found that area under curve (AUC) was 0.726 for the GAP score and 0.783 for the CPI. For 3-year mortality AUC was 0.749 for the GAP score and 0.805 for the CPI.

**Conclusion** These data show that the CPI more accurately predicts survival at presentation and 3-years than the GAP score in a UK IPF cohort.



**Abstract S44 Figure 1** Correlation of GAP score (1a) and CPI (1b) and survival in IPF

#### REFERENCES

- 1 Wells AU, et al. *Am J Resp Crit Care Med.* 2003;**167**:962
- 2 Ley B, et al. *Ann Intern Med.* 2012;**156**:684

#### S45 MUC5B GENOTYPE DOES NOT INFLUENCE COUGH SEVERITY IN IPF

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**Introduction** Cough is a disabling symptom in IPF which causes significant reduction in quality of life. The mechanisms underlying cough in fibrotic lung disease are not well understood. Polymorphisms in the rs35105950 promoter region of the *MUC5B* gene have been shown to relate to risk of developing IPF and, in those with disease, have been shown to increase mucin expression in the small airways. A previous small study linked carriage of the minor T allele at rs35105950 with heightened cough in IPF. We sought to test this observation in a larger cohort of prospectively recruited individuals with IPF.

**Method** *MUC5B* genotyping was performed on 117 prospectively recruited individuals with IPF. All subjects completed the Leicester Cough Questionnaire and full lung function at the time of their blood draw. Survival time from enrolment was censored at 1<sup>st</sup> May 2015. Statistical analyses were performed using SAS software.

**Results** The mean age of subjects at enrolment was  $68 \pm 8.4$  with 79% being male. Subjects had, on average, moderately severe disease with mean FVC  $73.9 \pm 19.7\%$  predicted and DLco  $41.7 \pm 18.1\%$  predicted. At baseline, the median (IQR) LCQ score was 16.0 (11.6–18.6) points. 43 subjects (36.8%) were homozygous at rs35105950 for the G allele, 62 (53.0%) were heterozygous and 12 (11.1%) were homozygous for the T allele. Despite a trend towards worse disease at baseline,

homozygosity of the T allele was correlated with a significant survival advantage (422 days compared to GG,  $p = 0.0063$ ). There was, however, no difference on univariate analysis in LCQ cough severity between groups based on *MUC5B* genotype (GG  $14.6 \pm 4.5$ , GT  $15.3 \pm 3.9$  and TT  $15.1 \pm 3.5$ ,  $p = 0.70$ ). This finding did not change when correction was applied for baseline disease severity.

**Conclusions** The severity of self-reported cough is worse in IPF than in other respiratory diseases. In contrast to one previous small study of 68 subjects, there is no relationship between patient reported cough and *MUC5B* genotype in our cohort. It therefore seems unlikely that the mechanism behind cough in fibrosing lung disease is related to mucin production. Further studies are required to determine the mechanisms underlying the heightened cough response observed in IPF.

#### S46 AN RCT OF 28 DAY TREATMENT WITH FOSTAIR® PMDI 200/12 BD ON PLATELET BIOMARKERS IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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**Introduction and objectives** We have recently studied platelet activation in idiopathic pulmonary fibrosis (IPF) and found that IPF patients exhibit a significant increase in platelet reactivity. This was demonstrated by an ADP (Adenosine diphosphate) concentration dependent increase in platelet-monocyte aggregates (PMA), platelet P-selectin expression, and platelet fibrinogen binding.<sup>1</sup> We have suggested this may have a potentially important role in the initiation and/or progression of tissue injury in IPF.

Systemic corticosteroid treatment may alter platelet adhesion, as seen with suppression of p-selectin expression in the spontaneously hypertensive rat.<sup>2</sup> We hypothesised that peripherally deposited inhaled corticosteroid may have similar activity. In this study we evaluate the effect of beclomethasone/formoterol pMDI (B/F Fostair) on clinical parameters and biomarkers of platelet activation in IPF.

**Methods** Twenty non-smoking patients with IPF and no evidence of COPD were randomly assigned to either Fostair 100/6, 2puffs BD for 28 days or matched placebo inhaler. There was 28 days washout between crossover. Biomarkers, PMA, p-selectin and fibrinogen were measured at baseline and post treatment periods. Clinical outcomes of six minute walk (6MWT), spirometry, average daily activity over 7 days (Sense Wear) and Quality of life (KBILD) were also measured.

**Results** 17 patients (11 males, mean age 71.2 yrs) completed the study. Table 1 shows the 95% CI on differences between the baseline and two treatments on biomarkers of platelet adhesion obtained from ANOVA and using the Tukey *post hoc* test for multiple comparisons.

Change from baseline spirometric measurements of FEV1(L), FEV1/FVC,% pred FEF25–75 were significantly improved following 28 days B/F by (mean  $\pm$ SD),  $0.88 \pm 0.16$  L ( $p = 0.03$ ),  $0.03 \pm 0.03$  ( $p = 0.03$ ),  $12.4 \pm 19.1\%$  ( $p = 0.02$ ) respectively when compared to placebo.

There was no change in quality of life or exercise measures.