

microbial community in the COPD lung contributing to the pathogenesis of COPD.

**Methods** Nine clinically stable COPD patients attending the Freeman Hospital had a bronchoalveolar lavage fluid (BALF) taken. DNA extraction from these samples was performed using an Ultraclean<sup>®</sup> Microbial DNA Isolation Kit. DNA obtained from these samples was then used as template for conventional PCR. Both primer sets used targeted the universal bacterial and fungal V3 variable regions of the 16S rRNA gene and 28S rRNA gene respectively with attachment of a GC-clamp. Amplicons were then run out for analysis by denaturing gradient gel electrophoresis (DGGE) performed on a DCode System (BIO-RAD). Microbial DNA extracted from all nine BAL samples was then sent for 454 pyrosequencing to perform metagenomic analysis.

**Results** Molecular fingerprinting of BAL analysis by DGGE produced a distinct number of bands in each sample strongly indicating the presence of a diverse microbial community in the COPD infected lung. This was also seen in culture negative patients. Migration of bands present at the top of the denaturing gradient suggests that the lungs of COPD patients are heavily colonised with bacteria that have a low GC content such as *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*. Metagenomic analysis of the nine BAL samples by 454 pyrosequencing supports this hypothesis by detecting numerous other bacterial taxa present.

**Conclusions** This preliminary study shows that the lungs of COPD sufferers are colonised with multiple species of bacteria and demonstrates that a complex microbial community is present. Metagenomic analysis performed demonstrates the key bacterial taxa which may be responsible for inducing the damaging inflammatory response and the differences in bacterial diversity shown in the nine patients studied. Thus a complex microbiota may elicit ongoing inflammation leading to lung function loss and destruction of the lung architecture.

## Pulmonary thromboembolism: acute and chronic studies

**S20** **TIME-RESOLVED CT PULMONARY ANGIOGRAPHY CONTRAST TRANSIT TIME IN PATIENTS WITH PULMONARY EMBOLISM: A NOVEL FUNCTIONAL CT METRIC OF RIGHT HEART STRAIN?**

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<sup>1</sup>E R Swift, <sup>2</sup>S Rajaram, <sup>1</sup>O R Byass, <sup>1</sup>K Chiu, <sup>2</sup>A J Swift. <sup>1</sup>Hull and East Yorkshire Hospitals NHS Trust, Hull, UK; <sup>2</sup>University of Sheffield, Sheffield, UK

**Introduction and Objectives** Acute right ventricular (RV) failure is known to cause death in patients with pulmonary embolus due to circulatory collapse. CT pulmonary angiogram (CTPA) is now

considered the gold standard test for the detection of pulmonary emboli, the technique provides excellent structural detail, however provides limited functional information. This aim of this was to assess time-resolved CTPA contrast transit times (TT) as a potential functional CT marker for the detection of right heart strain in patients with PE.

**Methods** We retrospectively reviewed consecutive patients who underwent CTPA at our institution over a 2-month period. Scans were performed on a Phillips Brilliance 16-slice scanner with a 4 ml/s Optiray<sup>TM</sup> 300 pressure injection. TT was defined as the time from the start of the injection to the scan trigger at the threshold of 150 hounsfield units measured from ROI analysis at the main pulmonary artery. Established CT structural imaging metrics were scored for comparison.

**Results** 56 consecutive patients were identified with evidence of pulmonary embolic disease or normal thoracic CT appearances from CTPA scans. One patient with PE was excluded as the CTPA scan was non-diagnostic. TT, RV septum to free wall distance, RV/LV ratio and PA diameter were all significantly elevated in patients with pulmonary embolus compared to patients with a normal CTPA. On analysis of bivariate correlation, TT had a statistically significant positive correlation with hepatic reflux, PA diameter and RV/LV ratio. Notably, the TT and RV/LV ratio demonstrated a significant direct linear correlation ( $p=0.001$ ).

**Conclusions** This study supports previous evidence of existing markers, such as RV/LV ratio, being useful imaging marker in pulmonary embolic disease. It also suggests that TT, could be a new useful functional marker of right heart strain. The importance of further research into this field is highlighted, and particularly into TT as a haemodynamic prognostic indicator in acute pulmonary embolism.

**S21** **OBJECTIVE AND PATIENT REPORTED OUTCOMES OF LONG TERM MANAGEMENT OF PATIENTS WITH CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH): A SINGLE CENTRE EXPERIENCE**

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N J Doughty, J Pepke-Zaba. Papworth Hospital NHS Trust, Cambridge, UK

**Objective** To determine long-term objective and Patient Reported Outcomes at a single centre in patients with CTEPH (distal or residual post Pulmonary endarterectomy).

**Method** A retrospective study of all incident patients with CTEPH (2000–2011). Data obtained from the service database—6-minute walk test (6MWT), CAMbridge Pulmonary Hypertension Outcome Review (CAMPHOR) symptom, activity and Quality of Life (QoL) scores, and NTproBNP. Results obtained at baseline (at the time of diagnosis, pre-commencement of first targeted therapy), 3 months,

Abstract S21 Table 1 Summary of change scores over time for CTEPH cohort

	6MWT	CAMPHOR symptoms	CAMPHOR activity	CAMPHOR QoL	NTproBNP
CTEPH	n=98	n=75	n=77	n=76	n=64
3-month change score mean (SD)	30.03 (77.2)†	1.1 (3.8)*	0.7 (3.4)*	1.1 (4.1)†	714.9 (2342.2)†
CTEPH	n=97	n=80	n=79	n=79	n=60
1-yr change score mean (SD)	37.03 (72.69)†	1.8 (4.6)†	0.7(4.3)	1.6 (4.7)†	891.6 (1815.5)†
CTEPH	n=80	n=62	n=61	n=61	n=50
2-yrs change score mean (SD)	35.1 (76.1)†	0.9 (4.4)	0.1 (4.6)	1.1 (5.1)	904.7 (1832.80)†
CTEPH	n=61	n=56	n=56	n=54	n=39
3-yrs change score mean (SD)	40.4 (74.6)†	1.3 (4.6)*	0.1 (5.2)	0.3 (4.3)	1009.4 (2083.9)†
CTEPH	n=44	n=34	n=34	n=34	n=29
4-yrs change score mean (SD)	18.8 (97.2)	0.9 (3.6)	0.3 (4.8)	0.4 (4.9)	780.1 (1695.1)*

Wilcoxon signed rank test \* Significant ( $p<0.05$ ), † Highly significant ( $p<0.01$ ).

1, 2, 3, and 4 years follow-up. Over this period were managed according to clinical need and NCG guidelines. N=124. Targeted therapy defined as Prostacyclin, endothelin receptor antagonists, and phosphodiesterase 5 inhibitors.

**Results** Changes at 1st and 2nd time points (median 3 months and 1 year) show statistically significant improvements in patient reported outcomes and objective measures. The NTproBNP improvement peaks at 3 years and begins to tail off at 4 years. The 6MWD improvement plateaus out between 2 and 3 years. The CAMPHOR symptom score shows significant improvement including year 3. The 4-year 6MWD does not achieve statistical significance compared to baseline. Further investigation revealed that between the third and fourth year 22 subject's follow-up was not performed; 3 died, 1 transferred to another centre, 18 are awaiting their 4-year follow-up.

**Conclusion** Objective and patient reported measures of change over time show improvements for CTEPH patients up to 3 years. After 3 years it becomes more difficult to determine a categorical change. More 6MW and CAMPHOR data for the 4 year time point is needed to determine if initial improvements are sustained after 3 years in this patient group, or if the improvement seen really has begun to tail off as the results here may suggest. The 4-year follow-up data for the remaining 18 patients will be available later this year.

## S22 IMPROVED SYMPTOMS AND QUALITY OF LIFE AFTER PULMONARY ENDARTERECTOMY (PEA) IN PATIENTS WITH CHRONIC THROMBOEMBOLIC DISEASE (CTED) AND BORDERLINE PULMONARY HYPERTENSION (PH)

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D Taboada, C Treacey, D Jenkins, J Pepke Zaba, K Sheares. *Papworth Hospital NHS trust, Cambridge, UK*

**Background** Chronic thromboembolic pulmonary hypertension (CTEPH) is defined by a mean pulmonary artery pressure (mPAP) =25 mm Hg at right heart catheterisation in patients with multiple chronic/organised occlusive thrombi in the pulmonary arteries. PEA is potentially curable and is the treatment of choice for patients with CTEPH. There is a small group of patients with CTED and exertional dyspnoea but with a resting mPAP that does not fulfil criteria for PH in whom PEA may be considered. The outcome of PEA in these patients has not been previously assessed.

**Objective** To assess the post PEA functional and haemodynamic outcomes in patients with symptomatic CTED and borderline PH.

**Methods** Retrospective data were collected on patients with baseline mPAP of =25 mm Hg who underwent PEA at the UK and Ireland national referral centre between 2002 and 2010. Patients were reassessed 3 and 12 months after surgery. Right heart catheterisation was performed at baseline and 3 months post PEA.

### Abstract S22 Table 1

	Baseline (n = 16)	3 months post PEA (n = 16)	12 months post PEA (n = 11)
WHO class I/II/III/IV (%)	0/50/50/0	50/50/0/0	60/40/0/0
6MWT distance (m)	403±113	417±111	438±88*
6MWT min SatO2 (%)	88±7	91±8*	93±4*
mPAP (mm Hg)	22±3	16±3*	
Cardiac Index (l/m/m <sup>2</sup> )	2±0.5	2.5±0.4	
PVR (dynes.s.cm-5)	239±116	126±33*	
CAMPHOR symptoms	10	2*	1*
Activity	6	3	0*
Quality of life	9	3*	1*

\*p<0.05.

**Results** 558 patients underwent PEA at Papworth Hospital between 2002 and 2010. From those, 16 had symptomatic operable CTED and mPAP of =25 mm Hg. Mean age was 45±17 and 69% were female. All survived surgery and are currently alive at follow-up. The median length of stay was 13 days (IQR 6). Results are displayed in the Abstract S22 table 1 as mean ± SD. WHO class data are expressed as percentages. CAMPHOR (Cambridge Pulmonary Hypertension Outcome Review) is a disease specific quality of life questionnaire and scores are expressed as median.

**Conclusion** In this small series of patients with CTED and borderline PH, there was a significant symptomatic, haemodynamic and functional benefit from PEA at 1-year. Further research is required to assess the prognostic benefit in this population. We would like to acknowledge the national pulmonary hypertension centres in the UK and Ireland, and support by the Cambridge NIHR Comprehensive Biomedical Research Centre.

## S23 ACCURACY OF CONTRAST ENHANCED MR LUNG PERFUSION COMPARED TO PERFUSION SCINTIGRAPHY IN DIAGNOSING CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

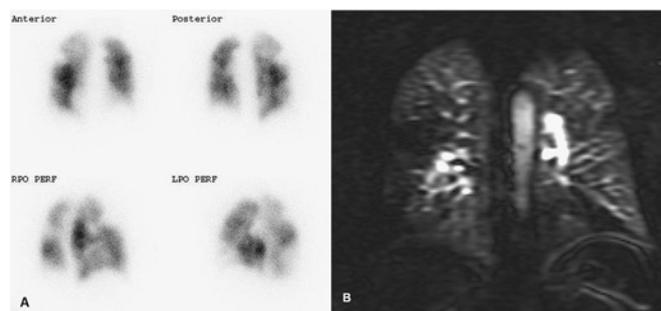
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<sup>1</sup>S Rajaram, <sup>1</sup>A J Swift, <sup>1</sup>D Capener, <sup>2</sup>C Hill, <sup>2</sup>C Davies, <sup>3</sup>R Elliot, <sup>3</sup>J Hurdman, <sup>3</sup>R Condliffe, <sup>1</sup>J M Wild, <sup>3</sup>D G Kiely. <sup>1</sup>Academic Unit of Radiology, University of Sheffield, Sheffield, UK; <sup>2</sup>Department of Radiology, Royal Hallamshire Hospital, Sheffield, UK; <sup>3</sup>Pulmonary Vascular Disease Unit, Sheffield, UK

**Purpose** The purpose of our study was to assess the diagnostic accuracy and reliability of contrast enhanced MR lung perfusion compared to perfusion scintigraphy in patients with CTEPH.

**Methods and Materials** Retrospective analysis of patients investigated for CTEPH who had MR lung perfusion, perfusion scintigraphy and CTPA performed within a time interval of 5 days. The MR images were acquired using a time resolved 3D spoiled gradient echo sequence. The sequence parameters: TE 1.1 ms, TR 2.5 ms, flip angle of 30°, FOV=48 cm<sup>2</sup>, slice thickness of 5 mm, average of 32 slices and frame rate was 2 acquisitions per second. This was a breathhold sequence obtained after 0.05 ml/kg of Gadovist injection at 5 ml/s followed by a 20 ml saline flush. The subtraction images and positive enhancement dataset were analysed in the coronal plane. Four static views perfusion scintigraphy views were obtained. Final diagnosis of CTEPH or non-CTEPH was made at a multi-disciplinary meeting following detailed multi-modality assessment.

**Results** 27 patients had a diagnosis of CTEPH and 55 patients were diagnosed as non-CTEPH. In the CTEPH group, MRI lung perfusion diagnosed 26 patients as CTEPH and 1 patient with distal surgically inaccessible disease as non-CTEPH. In the non-CTEPH group, four patients were diagnosed as CTEPH and 48 patients were identified



Abstract S23 Figure 1