follow-up measurements. Baseline characteristics of 229 patients with complete data on pulse wave analysis are shown in the table (values are mean (SD) were applicable). CPAP improved endothelial function (FMD at follow-up +1.97% with CPAP compared to control group, 95% CI +0.84 to +3.09%, p=0.001), but there was no evidence of an effect on arterial stiffness (AIx at follow-up −0.56% with CPAP compared to control group, 95% CI −2.87 to +1.75, p=0.64). CPAP improved daytime sleepiness as assessed by the Epworth sleepiness score (mean (SE) change −1.91 (0.30) with CPAP; control group +0.08 (0.26), mean difference −1.99, 95% CI −2.77 to −1.21, p<0.0001, assessed using an unpaired *t*-test).

**Conclusions** 6 months of CPAP is associated with improved endothelial function, but does not reduce arterial stiffness in minimally symptomatic OSA. Thus patients with minimally symptomatic OSA may benefit from CPAP therapy in terms of cardiovascular risk reduction.

Abstract S14 Table 1

| Variable | CPAP group | Control group |
|---|---|---|
| Age (years) | 58.24 (7.21) | 57.90 (7.55) |
| Male/females | 97/19 | 97/13 |
| BMI (kg/m$^2$) | 32.69 (5.57) | 32.58 (5.37) |
| ESS | 8.39 (4.12) | 8.55 (4.31) |
| ODI (events/h) | 13.98 (14.14) | 13.40 (11.38) |
| FMD (%) | 3.41 (3.41) | 3.42 (2.36) |
| AIx (%) | 27.56 (9.32) | 29.09 (10.54) |

## S15 AN OFFICE BASED ADVANCED DRIVING SIMULATOR TO ASSESS DRIVING PERFORMANCE IN OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS): A PILOT STUDY

doi:10.1136/thx.2010.150912.15

[1]D Ghosh, [2]S Jamson, [1]M W Elliott. *[1]St James' University Hospital, Leeds, UK; [2]Institute for Transport Studies, University of Leeds, Leeds, UK*

**Introduction** Advising patients with Obstructive Sleep Apnoea Syndrome (OSAS) about whether they are safe to drive is challenging. Driving simulator studies have shown that OSAS patients perform poorly (Hack *et al*, 2001) but most simulators are simple, not realistic and in particular lack face validity, for example, multiple off road events during a short run. The Institute for Transport Studies, University of Leeds, host the UK's most sophisticated driving simulator but had also developed a PC based simulator (MiniSim) which incorporates the same realistic graphics and is much closer to 'proper' driving than most existing systems. It thus has the potential to be used in everyday clinical practice. We have investigated whether two parameters, proportion of high frequency steering activity (HFS) and standard deviation of lane position (SDLP), previously shown to be impaired in drivers suffering from fatigue, might predict drivers' behaviour in safety-critical scenarios.

**Methods** After a practice run, 63 patients (age 53±10, ESS 11±3, ODI 39±19) completed 50 min motorway driving on the MiniSim. Two situations were programmed that required evasive action to avoid a crash. A 'fail' was determined by an outright crash or veering completely out of lane. We compared HFS and SDLP in subjects with 'pass' or 'fail' and with Oxygen Desaturation Index (ODI) and Epworth Sleepiness Score (ESS).

**Results** (Abstract S15 Table 1) 'Fail' was more likely with worse sleep disordered breathing, but was not affected by subjective sleepiness. Subjects who 'failed' had significantly worse HFS (0.27 vs 0.34, p=0.03) & SDLP (0.58 vs 0.41, p=0.002). Both HFS & SDLP worsened with time. There was also a strong correlation between HFS & SDLP (r=0.51, p<0.0001).

Abstract S15 Table 1 Comparison between patients passing & failing the simulator run (Mean HFS=mean for the proportion of high frequency steering activity in epochs 3,6,7 of the simulator run, Mean SDLP=mean for the standard deviation of lane position in epochs 3,6,7 of the simulator run)

| | ODI (Desaturations/h) | ESS | Mean HFS 3,6,7 | Mean SDLP 3,6,7 |
|---|---|---|---|---|
| 'Pass' | 34.97±3.47 | 12.13±1.02 | 0.26±0.012 | 0.41±0.02 |
| 'Fail' | 46.40±4.38 | 12.23±1.40 | 0.31±0.018 | 0.57±0.05 |
| p | 0.043 | 0.95 | 0.0406 | 0.0025 |

**Conclusion** These data show that HFS and SDLP have promise as objective markers of poor driving in OSAS patients. They relate to measures of disease severity and to an event which has face validity as an indicator of poor driving in the real world. The patient will not be aware that they are being measured and therefore they have potential for repeated use.

## S16 DETECTION OF SLEEP-DISORDERED BREATHING IN CHRONIC HEART FAILURE PATIENTS: UTILITY OF HEART RATE VARIABILITY VERSUS PULSE OXIMETRY?

doi:10.1136/thx.2010.150912.16

[1]N R Ward, [2]M R Cowie, [2]S D Rosen, [1]V R Roldao, [2]J Hooper, [2]T A McDonagh, [1]A K Simonds, [1]M J Morrell. *[1]Clinical and Academic Unit of Sleep and Breathing, Royal Brompton Hospital and National Heart and Lung Institute, Imperial College, London, UK; [2]Clinical Cardiology, Royal Brompton Hospital and National Heart and Lung Institute, Imperial College, London, UK*

**Introduction and Objectives** Sleep-disordered breathing (SDB) is a frequent comorbidity in chronic heart failure (CHF). Patients are often asymptomatic and sleep studies may be required for SDB diagnosis. Our department has previously reported that %VLFI component of Heart Rate Variability (HRV) is correlated with apnoea-hypopnoea index (AHI) in CHF (r=0.52). Thus, we tested the hypotheses that %VLFI component of HRV, or pulse oximetry, can be used to rule out SDB in patients with CHF.

**Methods** Stable CHF patients attending cardiology clinics were enrolled, irrespective of cause or severity of CHF. Patients were studied using polysomnography, simultaneous ambulatory electrocardiography and pulse oximetry. SDB was defined as AHI ≥15.0/h, measured by polysomnogram. Fourier analysis of the electrocardiogram was used to measure %VLFI component of HRV, with a cutoff ≥2.23% to indicate SDB. The oxygen desaturation index (ODI) ≥3% was measured by pulse oximeter, with a cutoff >7.5 desaturations/h to indicate SDB. Diagnostic performance of %VLFI and ODI≥3% were calculated, with the polysomnogram as reference standard for SDB diagnosis.

**Results** 180 CHF patients were studied, seven were excluded due to insufficient sleep (<200 min). In 173 CHF patients (mean (SD) age 66.9 (13.0) years; 86% male; Epworth Sleepiness Scale 7.6 (4.3); NYHA 2.1 (0.6); median (IQR) BNP 118 (55–239) pg/ml), SDB was present in 77 (45%) patients with mean AHI 32.4 (18.2)/h. %VLFI was measured in 77 (45%) patients: in CHF patients with SDB (n=36), mean %VLFI was 3.13% (2.4) compared to 3.25% (2.6) in patients without SDB (n=41). Cardiac pacing, atrial fibrillation and frequent ectopy prevented %VLFI measurement in the remainder. ODI ≥3% was measured in 171 patients: in CHF patients with SDB (n=76), mean ODI ≥3% was 29.2 (17.2)/h compared to 10.2 (6.4)/h in patients without SDB (n=95).

**Conclusion** The %VLFI component of HRV has no utility to screen for SDB in patients with CHF. Moreover, it could not be measured in more than half of this cohort of patients. In contrast, the high sensitivity and negative predictive value of the ODI ≥3% suggest pulse oximetry is a valuable tool to rule out SDB in CHF patients.

Abstract S16 Table 1 Diagnostic performance of %VLFI and ODI >3% for detection of SDB in CHF patients

| | %VLFI | ODI>3% |
|---|---|---|
| Sensitivity | 0.53 | 0.97 |
| Specificity | 0.44 | 0.32 |
| Positive predictive value | 0.45 | 0.53 |
| Negative predictive value | 0.51 | 0.94 |
| Positive likelihood ratio | 0.94 | 1.42 |
| Negative likelihood ratio | 1.08 | 0.08 |
| Area under receiver operating characteristic curve | 0.49 | 0.92 |

**Funding** This study was funded by the British Heart Foundation.

## S17 A PILOT STUDY OF THE PREVALENCE OF SLEEP DISORDERED BREATHING (SDB) AND NOCTURNAL HYPOXIA IN SYMPTOMATIC ADULTS WITH SICKLE CELL DISEASE (SCD) AND ITS RELATIONSHIP WITH DISEASE SEVERITY

doi:10.1136/thx.2010.150912.17

[1]P Murphy, [2]R Dillon, [3]A J Williams, [2]J Howard, [1]N Hart. *[1]Guy's & St Thomas' NHS Foundation Trust and Kings College London NIHR Biomedical Research Centre, London, UK; [2]Department of Haematology, Guy's & St Thomas' NHS Foundation Trust, London, UK; [3]Lane Fox Respiratory Unit, Guy's & St Thomas' NHS Foundation Trust, London, UK*

**Introduction** There are few effective therapies available for the long-term management of the cardiac and renal sequelae of SCD. Identifying reversible factors, which exacerbate disease severity, would facilitate development of new therapies or novel applications of established treatments. Nocturnal hypoxia (NH) merits investigation as a disease modulating factor as it is established that hypoxia promotes polymerisation of sickle haemoglobin and this is reversible with oxygen therapy (Noguchi *et al*, 1993). Although NH is common in children with SCD and is associated with poor outcome, similar data for adults with SCD are lacking. This is the first study to determine the prevalence of OSA and NH and quantify the severity of NH in adults with SCD. In addition, we investigated the correlation between the degree of NH and organ dysfunction.

**Method** Patients attending SCD clinic had an Epworth sleepiness score performed. Patients with either an ESS ≥10 or symptoms suggestive of SDB were offered nocturnal oximetry. Nocturnal oximetry findings were objectively scored and compared with the detailed clinical datasets collected at regular clinic attendances. OSA was defined as 4% oxygen desaturation index (4% ODI) of >10 events/h and NH was defined as >30% total sleep time (TST) with $SpO_2$ <90%.

**Results** 93 patients were screened. 34 had ESS ≥10 or clinical symptoms suggestive of SDB. 22 underwent nocturnal oximetry; mean ESS 12±4, clinic $SpO_2$ 96±4%, 4% ODI 8±6 events/h, nocturnal $SpO_2$ 91±4%, %TST $SpO_2$ <90% 43±41%. Prevalence of OSA and NH was 59%. The degree of nocturnal hypoxia was correlated with urine protein:creatinine (r=−0.35, p=0.02), elevated pulmonary artery systolic pressure (r=−0.71; p=0.0001) and prevalence of priapism (p=0.004). There was no difference detected in frequency of painful crises or hospital admission in patients with significant NH compared to those without NH.

**Conclusion** This small pilot study showed that OSA and NH had a prevalence of 59% in symptomatic adult SCD patients. These data have demonstrated a correlation between the severity of nocturnal hypoxia and pulmonary hypertension, renal impairment and priapism. These observations have not previously been reported. The strength of these correlations could suggest a causal relationship, although this needs to be confirmed in a larger prospective trial. Future studies should investigate the relationship between OSA, nocturnal hypoxia and organ dysfunction and need to be focussed on interventions such as nocturnal oxygen and continuous positive airway pressure.

# New assessments in cystic fibrosis

## S18 LONGITUDINAL ASSESSMENT OF BIOMARKERS FOR CLINICAL TRIALS OF NOVEL THERAPEUTIC AGENTS: THE RUN-IN STUDY

doi:10.1136/thx.2010.150912.18

[1]E W F W Alton, [2]C Boyd, [3]S Cunningham, [1]J C Davies, [4]S C Hyde, [2]J A Innes, [4]D R Gill, [2]A Greening, [1]U Griesenbach, [1]T Higgins, [2]D J Porteous. *[1]Department of Gene Therapy, Imperial College, London, UK; [2]Western General Hospital, Edinburgh, UK; [3]The Royal Hospital for Sick Children, Edinburgh, UK; [4]Gene Medicine Research Group, Oxford University, Oxford, UK*

We will be undertaking a phase IIB clinical trial of repeated application of liposome-based gene therapy over a one year period in approximately 100 CF patients (Multidose Trial). In preparation for this, we sought to address two key questions. Firstly, could we define the optimal set of patients in which the therapy could both be delivered (good access to the airways via nebulisation), and in whom any therapeutic effect was measurable (one or more abnormal measures of lung disease). Secondly, in this set of 'can deliver—can measure' patients, which biomarker(s) could be powered to be the primary outcome measure for the trial. To address both questions, we undertook a study (Run-in), cross-sectionally assessing 'can deliver' and longitudinally assessing a large set of candidate biomarkers for 'can measure'.192 patients from age 10 upwards, with $FEV_1$ >40% were enrolled at two clinical centres; 154 of these remained in the study after four visits spaced at approximately 4—5 month intervals. Biomarkers assessed cross-sectionally included radionucleotide deposition scans, CT and mucocilary clearance. Longitudinal biomarkers included a large series of serum, sputum and exhaled breath inflammatory markers, lung physiology, exercise-related assays and quality of life assessment. 12 patients were judged too severe for adequate delivery and were excluded. A shortlist of 4 biomarkers was generated based on a) showing a CF/non-CF difference, b) response to course of intravenous antibiotics, and c) coefficients of variation. These four were matched against the remaining 142 patients, and a further seven patients excluded in whom none of these short listed biomarkers was abnormal. 89 patients (3 or 4 biomarkers abnormal) have been definitely included to progress into the Multidose Trial, and a further 46 (1 or 2 biomarkers abnormal) are awaiting the final primary outcome selection. The Run-in study has, therefore, been able to a) select a cohort of 'optimal' patients in which to assess gene therapy and b) provide an indication of which may be the more useful biomarkers to use in phase IIB clinical trials of novel therapeutic agents.

## S19 REAL TIME PCR IN THE IDENTIFICATION AND MANAGEMENT OF *ASPERGILLUS* IN CF

doi:10.1136/thx.2010.150912.19

[1]C G Baxter, [2]A M Jones, [2]A K Webb, [1]D W Denning. *[1]University Hospital of South Manchester, Education and Research Department, Manchester, UK; [2]Manchester Adult CF Unit, Manchester, UK*

**Purpose** The reported prevalence of *Aspergillus fumigatus* in CF sputum varies widely from 12 to 57%. While patients with ABPA are routinely treated with antifungals, it is not know whether colonised