ORTHODEOXIA, AND POSTURAL ORTHOSTATIC TACHYCARDIA, IN 165 CONSECUTIVE, UNSELECTED PATIENTS WITH PULMONARY ARTERIOVENOUS MALFORMATIONS

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10.1136/thoraxjnl-2013-204457.51

**Background**

Patients with pulmonary arteriovenous malformations are often quoted as displaying orthodeoxia, that is, a fall in oxygen saturation on standing. It is unclear how common this phenomenon is, and how patients would compensate for any acute fall in SaO₂.

**Methods**

Postural changes in oxygen saturation and pulse were examined in a series of 165 prospectively-recruited patients with radiologically-proven PAVMs. Self-reported exercise at presentation was graded using a modified MRC dyspnoea scale. SaO₂ and pulse measurements were made in both erect and supine postures on 1–8 separate occasions throughout presentation to postembolisation follow up. These 522 sets of postural measurements displayed very high within-patient reproducibility.

**Results**

Age ranged from 17–87 (median 49) ys, 62 (37%) were male, and for 159 (96%) PAVMs were attributable to HHT. 18.9% were obese with a body mass index (BMI) >40. At presentation, the SaO₂ fell by at least 2% on standing in 51(33%) patients, including one with morbid obesity (BMI>40). At presentation, the SaO₂ fell by at least 2% on standing in 51(33%) patients, compared to the equivalent average supine reading. A smaller fall of 1–2% was present in a further 28 (17%) of patients. Patients with higher BMI had significantly higher supine SaO₂ for their erect SaO₂, and significantly lesser falls in SaO₂ on standing. A postural tachycardia consistently exceeded the increment required to sustain oxygen delivery at rest, across all SaO₂,12/163 (7.4%) of individuals met the pulse definition for postural orthostatic tachycardia syndrome with an increase on standing of more than 30 beats per minute. Once adjusted for baseline supine pulse and age, the erect pulse was lower in patients with higher BMI (adjusted regression coefficient 0.23 (95% confidence interval 0.026, 0.48), p = 0.011). Using the pre-specified 5 group grading system, exercise tolerance was worse in patients with lesser postural tachycardias (regression coefficient -2.19 (-3.74, -0.65) p = 0.006).

**Conclusions**

Orthodeoxia and postural tachycardia are common in PAVM patients. More pronounced postural tachycardias were associated with improved exercise tolerance. Further studies will be required to assess if this is because it is a surrogate of lower BMI, with obesity effectively limiting a further fall in SaO₂ on standing because of obesity-related lower supine SaO₂.

SPECIFIC VENTILATION INEQUALITY AND DEAD SPACE COMPONENTS OF LUNG CLEARANCE INDEX IN PATIENTS WITH ASTHMA AND CYSTIC FIBROSIS

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10.1136/thoraxjnl-2013-204457.52

**Background**

Lung clearance index (LCI) is a widely reported marker of gas mixing inefficiency within the airways that is derived using the multiple breath inert gas washout (MBW) technique. We developed two novel parameters, LCIvent and LCIds, to reflect the components of increased LCI due to (i) unequal convective ventilation between relatively large lung units, and (ii) increased respiratory dead space, respectively. We hypothesised that these parameters would be repeatable, would effectively discriminate between healthy controls and patients with asthma and cystic fibrosis (CF), and would distinguish between different sub-phenotypes of these diseases.

**Methods**

Washout data from sixty-six healthy control subjects, seventy-four patients with asthma, and forty-one patients with CF were fitted to a two-compartment model of gas mixing, and the parameters LCIvent and LCIds were calculated.

**Results**

LCIvent and LCIds were markedly elevated in patients with CF, and mildly elevated in patients with asthma, compared to controls, as illustrated in Figure 1. LCIvent and LCIds were weakly correlated in controls (R = 0.36, p = 0.01), moderately correlated in patients with asthma (R = 0.51, p = 0.0001), and strongly correlated in patients with CF (R = 0.89, p < 0.0001). LCIds was significantly raised in CF patients with chronic P. aeruginosa colonisation compared to those without chronic colonisation (1.49 vs 1.34, p = 0.004). LCI, LCIvent and LCIds were significantly raised in CF patients with a severe genotype compared to those with a mild genotype. No significant differences were observed between any of the asthma sub-phenotypes (severe vs non-severe, poorly-controlled vs not poorly controlled, exacerbator vs non-exacerbator, and eosinophilic vs non-eosinophilic) with respect to any MBW parameter. The intraclass correlation coefficients of LCIvent and LCIds exceeded 0.85 in the asthma and CF groups, and 0.60 in controls.

**Conclusion**

The novel parameters LCIvent and LCIds are repeatable and effectively discriminate between sub-phenotypes of CF, although their utility in asthma is currently unproven. Further studies are required to determine their utility in other airway diseases such as chronic obstructive pulmonary disease, to investigate their role as outcome measures in clinical trials, and to delineate their structural correlates.

Clinical studies in pulmonary vascular disease

OUTCOME AFTER PULMONARY ENDARTERECTOMY (PEA): LONG TERM FOLLOW-UP OF THE UK NATIONAL COHORT

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10.1136/thoraxjnl-2013-204457.53

**Introduction**

Chronic thromboembolic pulmonary hypertension (CTEPH) is a life threatening condition that historically has a poor outcome with supportive medical treatment. Pulmonary endarterectomy (PEA) is the treatment of choice and offers the...
EFFECT OF MACITENTAN ON HAEMODYNAMICS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION: RESULTS FROM THE LONG-TERM, RANDOMISED, PLACEBO-CONTROLLED SERAPHIN TRIAL

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Introduction and objectives Macitentan, a novel dual endothelin receptor antagonist (ERA), significantly reduced morbidity and mortality in pulmonary arterial hypertension (PAH) patients in the SERAPHIN trial (NCT00660179), the first event-driven outcomes trial in PAH. A substudy in SERAPHIN investigated the effect of macitentan on patients’ cardiac haemodynamics.

Methods 742 PAH patients were randomised to placebo, macitentan 3 mg, or macitentan 10 mg once-daily. Stable background PAH therapy, except injectable prostanooids and other ERAs, were allowed. At selected centres, patients underwent right heart catheterisation at randomisation and Month 6. Changes from baseline to Month 6 for mean right atrial pressure (mRAP), mean pulmonary arterial pressure (mPAP), pulmonary vascular resistance (PVR), cardiac index (CI) and mixed venous oxygen saturation (SvO2) were calculated for all patients and stratified in an exploratory analysis for background PAH therapy and baseline WHO functional class I/II vs III/IV. Median treatment effects (95% CI) between placebo and macitentan were statistically significant (P < 0.05) for PVR and CI for both subgroups, except for PVR in treatment naïve patients treated with macitentan 3mg (Table). Conclusions Macitentan significantly improved cardio-pulmonary haemodynamics in PAH patients. Improvements in PVR and CI were consistent irrespective of background PAH therapy and baseline WHO FC.

INEFFICIENT VENTRICULO-ARTERIAL COUPLING CONTRIBUTES TO REDUCED EXERCISE CAPACITY IN PULMONARY HYPERTENSION

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Introduction Venticulo-arterial (VA) coupling (Ees/Ea) in the right heart is defined by RV end-systolic elastance (Ees) and pulmonary arterial effective elastance (Ea) with Ees/Ea representing the mechanical efficiency of forward flow from the RV. Ees/Ea may influence exercise capacity in pulmonary hypertension (PH) because patients exhibit cardiac limitation at peak oxygen uptake (peak VO2) and suffer impaired exercise cardiac output adaptation. We hypothesised that Ees/Ea in the RV represents a
S46 Outcome after pulmonary endarterectomy (PEA): Long term follow-up of the UK national cohort

J Cannon, K Page, M Roots, A Ponnaabernam, C Tracy, D Taboada Buasso, K Sheares, C Ng, J Dunning, S Tsui, J Pepke-Zaba and D Jenkins

Thorax 2013 68: A25-A26
doi: 10.1136/thoraxjnI-2013-204457.53