APAH. Systemic inflammation also occurs in CHD-APAH but associated airway inflammation has not been investigated. This study investigates the relationship between inflammation, endothelin-1 and airway dysfunction in CHD-APAH patients.
Methods 58 patients were prospectively recruited: 20 CHD-APAH, 20 CHD and 18 healthy controls. Exclusion criteria were pre-existing lung disease, significant smoking history, scoliosis and Down's syndrome. Participants performed full lung function tests and provided serum and induced sputum samples at a single visit. Serum and sputum cytokines were measured by multiplex bead assay array and endothelin-1 levels measured by enzyme linked immunosorbent assay. Induced sputum was also assessed for total and differential cell counts.
Results Serum cytokines and endothlin-1 levels were significantly elevated in patients with CHD-APAH in comparison to CHD and healthy controls (See Table 1). There were no significant differences in sputum cytokine or endothelin-1 levels between the 3 groups, with no differences in total or differential cell counts. A significant correlation between serum endothelin-1 levels and FEF25–75 was found for CHD-APAH patients ($r = -0.6017$, $p = 0.0083$ Spearman). There were no significant correlations between measures of airway obstruction and serum cytokine levels.
Conclusions There is evidence of systemic inflammation in CHD-APAH patients but serum cytokines did not correlate with measures of airway dysfunction, and there was no evidence of airway inflammation. This suggests that inflammation does not play a role in airway obstruction in this patient group. Serum endothelin-1 is significantly elevated in CHD-APAH patients, and this did correlate with measures of airway obstruction. While elevated endothelin-1 in the pulmonary vessels may affect the adjacent airways, induced sputum endothelin-1 was not elevated. Whether serum endothelin-1 can cause bronchoconstriction without being associated with raised levels in the airways is unclear and requires further investigation.

P267 THE EFFECTS OF APELIN ON SERUM NT-PROBNP LEVELS IN PULMONARY HYPERTENSION PATIENTS VERSUS CONTROLS

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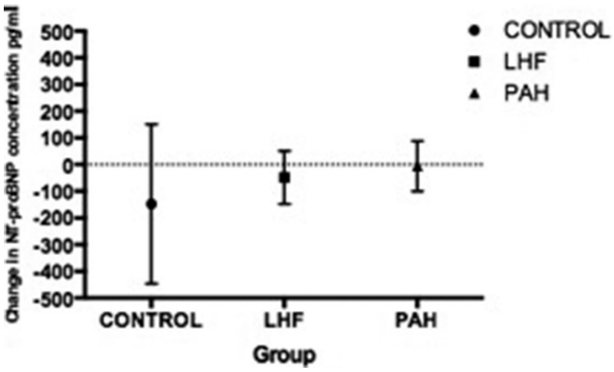
Background Pulmonary Hypertension has a poor prognosis and therapy is limited to symptomatic relief. Apelin, a new therapy, has the potential to address the underlying pathology whilst also providing relief of symptoms. NT-proBNP a marker of disease severity is commonly used to assess treatment effect.
Aims and objectives This study aimed to investigate, for the first time, the effects of apelin on serum NT-proBNP concentration in groups of pulmonary hypertension patients and controls. The hypothesis of the study was that apelin would cause a change in NT-proBNP.
Methods Serum samples from patients recruited for a haemodynamic investigation of apelin were used. The groups studied were controls, pulmonary arterial hypertension and pulmonary hypertension due to left heart failure. In the haemodynamic study each patient was given an apelin and placebo infusion separately over a period of several minutes. Serum samples were taken pre and post infusion. NT-proBNP concentration in the samples was determined using the ABNOVA ELISA kit.
Results There was no significant change in NT-proBNP levels due to apelin infusion across all groups ($P = 0.830$). On sub group analysis there was no significant change detected in any group as shown in Figure 1.



Abstract P267 Figure 1 Mean change in NT-proBNP levels post apelin infusion with 95% C.I. There was no significant change in NT-proBNP levels caused by apelin in any group

Conclusion NT-proBNP levels do not immediately change in response to several minutes of apelin infusion. This is consistent amongst control and pulmonary hypertension patients. Despite the lack of change in NT-proBNP levels seen in this study, the haemodynamic response pattern reported for apelin[1] has been associated with NT-proBNP changes in other drug studies. The main difference between these studies and this study was investigation of therapy effect over a longer time period. From our results we cannot conclude that apelin has no effect on NT-proBNP levels. Investigation of therapy over a longer time period is required.

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P268 THE ROLE OF GROWTH AND DIFFERENTIATION FACTOR 15 IN SMOOTH MUSCLE CELL PROLIFERATION IN PULMONARY HYPERTENSION

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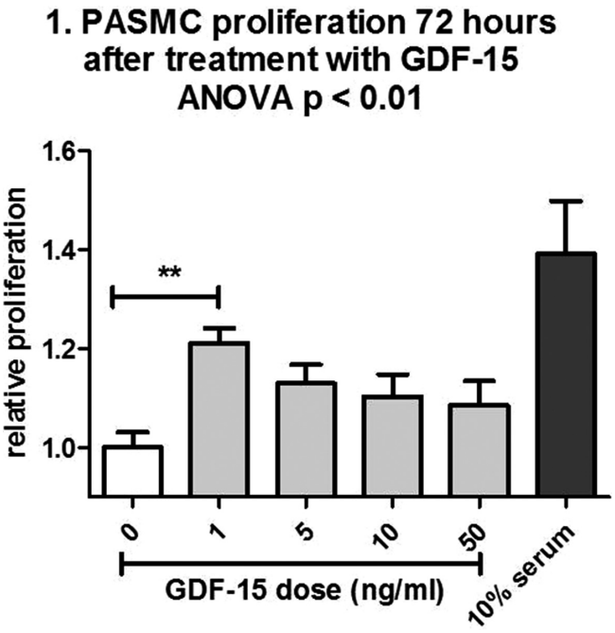
Introduction Growth and differentiation factor 15 (GDF-15) is a prognostic marker in pulmonary hypertension (PH). Its effects on endothelial cells have been documented, but its mechanism of action and role in the development of PH have not yet been fully investigated. We aimed to define the role and mechanism of action of GDF-15 in the development of PH.
Methods Rats were treated with moncrotaline (MCT) or vehicle control and euthanized after undergoing cardiovascular monitoring 4 weeks later. The expression of GDF-15 mRNA in the lung was measured by qPCR. Total GDF-15 protein levels in serum and lung were analysed by ELISA. The distribution of GDF-15 in the lung was analysed by immunohistochemistry. GDF-15 signalling in human pulmonary artery smooth muscle cells (HPASMCs) was analysed using western blot, and its role on HPASMC proliferation was measured using a cyquant assay.

Results GDF-15 mRNA and protein levels were raised in the lung homogenates of the MCT rat compared to controls ($p < 0.05$). Immunohistochemistry revealed GDF-15 was localised in the endothelial cells and to a lesser extent in the PASMCs of these animal. GDF-15 levels in the serum of the MCT treated rats was higher than that in those treated with vehicle control (771 ± 345 vs. 411 ± 305, $p < 0.05$). Serum GDF-15 was correlated with RV/LV+S weight in the MCT treated group (Pearson $r = 0.66$, $p < 0.05$). Immunohistochemistry also revealed an increase of phospho-TGFβ activated kinase 1 (TAK1) in PASMCs of the MCT rat. In HPASMCs GDF-15 (1 ng/ml) treatment resulted in an increase in proliferation over baseline at 72 h (Figure 1). GDF-15 was also able to induce phosphorylation of TAK1 in HPASMCs.



Abstract P268 Figure 1

Conclusions GDF-15 is over-expressed in the lung vasculature of MCT rats, mimicking human disease. GDF-15 was associated with the degree of right ventricular hypertrophy in these animals. GDF-15 downstream signalling molecule phosphorylated TAK-1 is present in increased levels in the vasculature of the MCT rat. *In vitro* GDF-15 treatment caused proliferation of HPASMCs and activation of TAK-1. Further investigation of this pathway is required to determine its relevance to human disease.

P269 PERIOPERATIVE OUTCOMES IN PATIENTS WITH PULMONARY HYPERTENSION UNDERGOING NON-CARDIAC NON-OBSTETRIC SURGERY IN A DESIGNATED UK PULMONARY HYPERTENSION CENTRE

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Introduction and objectives Patients with pulmonary hypertension (PH) represent an extremely high-risk surgical group, with previous reported mortality 7–18%, and predicting perioperative risk is difficult. The aim of this study was to characterise a current cohort of patients with pulmonary hypertension undergoing surgery in a National UK Designated PH centre and to determine predictors of adverse events.

Methods Consecutive patients with PH undergoing non-cardiac, non-obstetric surgery were identified by matching theatre and PH databases between 1st April 2008 and 1st April 2015. Demographics, recent echocardiogram, right heart catheterisation, B-natriuretic peptide (BNP), six-minute walk test (6MWT) and World Health Organisation functional class (WHO-FC) on last clinic visit was recorded. Anaesthetic and perioperative details; post-operative management, short-term morbidity and 28-day outcome were recorded. Data are mean±SD or median (range).

Results 37 procedures requiring anaesthesia were identified in 32 patients with PAH (7 idiopathic PAH, 1 PVOD, 24 CHD-PAH, 4 CTD-PAH) and 1 CTEPH. Average age was 44.4 ± 13 years, 27(84%) were female. Baseline preoperative WHO-FC was II (3, 9%), III (28, 88%), IV (1, 3%). Baseline 6MWT distance was 317 ± 68 m; BNP 200 (12–2027) ng/L; RV systolic pressure (RVSP) 85 ± 16 mmHg, tricuspid annular planar systolic excursion (TAPSE) 18 ± 7 mm. Cases including oesophagogastroscopy ($n = 4$), dental extraction ($n = 8$) under general anaesthesia (GA) were classified as minor; 6 (16%) including mastectomy, laparotomy and fasciotomy as major surgical procedures. Almost all (95%) were performed under GA; most were elective procedures and were monitored on the high dependency or intensive care unit post-operatively. Cardiovascular perioperative complications occurred in 6 cases (16%) including death in 2 patients (5.4%) in the days following surgery, in both cases related to PH crises, resulting in right ventricular (RV) failure. Baseline parameters of RV function including RVSP, TAPSE and the presence of a pericardial effusion were associated with adverse events.

Conclusion Perioperative mortality in patients with PH remains high, even in the current era. If surgery is deemed essential, PH centres with experts in cardiothoracic anaesthesia and ICU should be involved in preoperative planning with the PH multidisciplinary team guiding appropriate selection of patients, considering pulmonary haemodynamics and indices of RV function, as well as surgical factors.

P270 IDENTIFYING THE OPTIMAL D-DIMER CUT OFF VALUE FOR RULING OUT PES IN AN AMBULATORY CARE SETTING

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Introduction Patients attending the ambulatory pulmonary embolism (PE) clinic at the Glenfield Hospital are risk stratified into low, intermediate and high risk based on the BTS scoring.[1] Those with a low or intermediate pre-test probability go on to have a microlatex D-dimer assay and if this is greater than 0.5 ug/mL, imaging in the form of CTPA or VQ scan is carried out.

It has been suggested that using a higher cut off value of D-dimer may improve specificity without affecting sensitivity for a PE.

Methods Data was collected for 2139 consecutive patients who presented to the ambulatory PE clinic between June 2010 and Dec 2014. For each of these patients, age, BTS clinical probability, D-dimer results and final diagnosis was recorded.