157. Pulmonary circulation: clinical aspects of PAH, PTE and CTEPH

P1494

The development of pulmonary hypertension after first episode of acute pulmonary embolism and related risk factors

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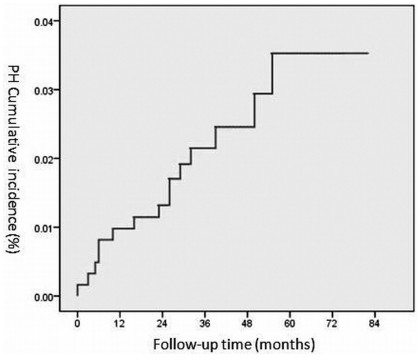
Background: Part of patients with acute pulmonary embolism(PE) will develop into pulmonary hypertension(PH) including chronic pulmonary thromboembolic hypertension(CTEPH). Related risk factors need to be addressed to guide clinical practice.

Objectives: To investigate the incidence of PH after PE and related risk factors.

Methods: Consecutive patients diagnosed as acute PE admitted to our institute from 2006 to 2010 were included. All the patients were followed till Dec 2011. During the follow-up, patients with PH showed in echocardiogram, defined as estimated systolic pulmonary artery pressure(sPAP) over 50mmHg, received right heart catheterization to confirm the diagnosis of CTEPH.

Results: 612 patients were included and the median follow-up period was 36 months. All-cause mortality was 17.3%. 15 patients developed into PH and 10 were diagnosed as CTEPH. The 1-, 2- and 5-year cumulative incidences of PH were 1.0%(95%CI 0.2%-1.8%), 1.3%(95%CI 0.3%-2.3%) and 3.5%(95%CI 1.5%-5.5%) respectively. Patients with varicose vein of lower limbs(HR 5.480,95%CI 1.058-28.385) and existence of PH at the beginning(HR 10.743,95%CI 2.315-49.852) had higher risk in developing into PH.



Conclusions: CTEPH is a serious complication in a significant number of PE cases. History of varicose vein of lower limbs and estimated sPAP over 50mmHg at the first episode of PE seem to predict the risk of CTEPH in long-term follow-up.

P1495

Measurement of gas transfer components using nitric oxide in post pulmonary endartectomy (PEA) chronic thromboembolic hypertension (CTEPH) patients

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Introduction: Reduced TLCO is frequently observed in CTEPH patients. Previous work has indicated the value of nitric oxide (NO) to differentiate the diffusing membrane capacity (Dm) and capillary blood volume (Vc); the components of TLCO. It has been suggested, that TLNO is a more accurate reflection of Dm, due to greater affinity for haemoglobin and independence from Vc. This study uses new technology to measure Dm and Vc, using NO, in a cohort of post PEA CTEPH patients. The aim of the study is to compare the relative contribution of Dm and Vc to the reduction in TLCO.
Methods: We studied 24 CTEPH patients (14male, 10female, mean age 56±15) post PEA. Full lung function were performed and TLNO and Dm were measured using single breath for NO and CO on a PFTpro system (Viasys). Vc was calculated using the equation 1/DLCO-1/DmCOxqCO=1/Vc. Patients with co-existing parenchymal lung disease were excluded from the study. Correlations between variables were looked at using Pearsons.
Results: Both Dm and Vc demonstrated a significant correlation with TLCO. Vc was reduced more than Dm (60%/89% respectively).
Conclusions: TLCO is still reduced post PEA, despite successful de-bulking of proximal obstructions and normal TLC and RV. The method used in this study is able to distinguish between the two components of gas transfer. Vc is more affected than the alveolar component Dm. The new technology offers a simple patient friendly procedure allowing measurements of Dm and Vc. This has the potential for improving our understanding of the different components of gas transfer. Further work is warranted in this area.

P1496

Circulating microRNA signature and its novel involvement in pathogenesis of chronic thromboembolic pulmonary hypertension

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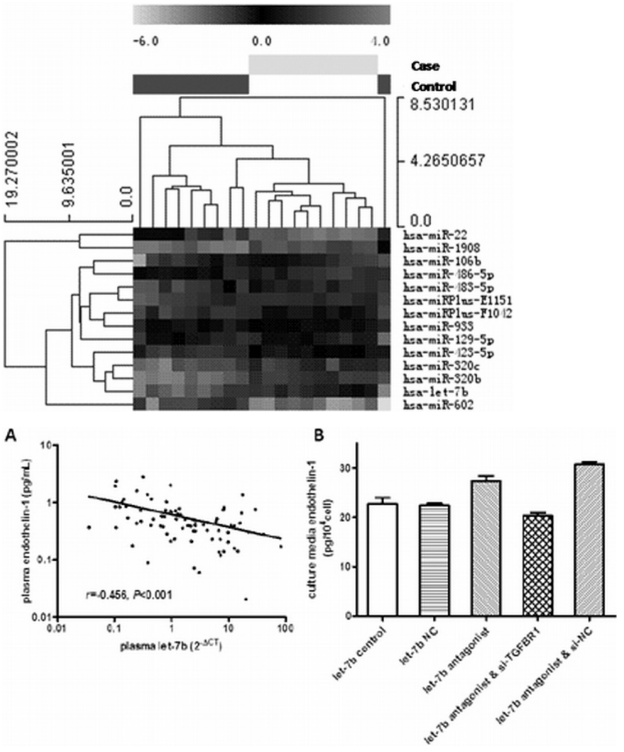
Chronic thromboembolic pulmonary hypertension (CTEPH) is a progressive disease characterized by multiple etiology and mechanism. Circulating miRNA is partially derived from cells affected by disease and therefore can serve as potential biomarker and reflect the pathogenesis of this disease. In present study, we compared miRNA expression in plasma from 10 CTEPH patients and 10 healthy control subjects by microarray, and fourteen miRNAs were indentified to be differentially expressed.
Selectively, five of the differentially expressed miRNAs were further validated in an independent 40 pairs of subjects by stem-loop qRT-PCR, among which let-7b and miR-22 were downregulated to about 25% in CTEPH patients. Endothelin-1



(ET-1) and transforming growth factor beta receptor 1 (TGFBR1) was the direct targets of let-7b by reporter assay, and plasma ET-1 level was reversely correlated to let-7b. TGFBR1 was further required for induction of ET-1 in endothelial cells.

P1497

Persistent lung perfusion defect is a risk factor for recurrent venous thromboembolism after pulmonary embolism

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Introduction: Up to 50% of patients with pulmonary embolism (PE) still have lung perfusion defects after 6 months of anticoagulant treatment, but little is known about the risk of recurrence in patients with persistent perfusion defect after an acute PE.
Aim of the study: To assess the risk of recurrent venous thromboembolism (VTE) in patients with persistent lung perfusion defects after a first episode of PE.
Patients and methods: Consecutive patients given at least 3 months of anticoagulant for an objectively proven first episode of acute PE were included. Ventilation/perfusion (V/Q) lung scan was performed 6 to 12 months after the diagnosis of PE. Objectively proven recurrent deep vein thrombosis (DVT) and PE were registered during follow-up. Persistent perfusion defects were defined as a pulmonary vascular obstruction > 10% on the V/Q lung scan.
Results: 318 patients (mean age 58±19 years) with an acute PE were included. 63 (19.8%, 95% CI, 15.4-24.2%) had persistent perfusion defects. During follow-up (median duration: 51 months [25th 75th percentiles: 27 - 73 months]), 71 patients (22%) had a recurrent episode of VTE. In multivariate analysis, persistent defect (HR 2.22; 95% CI, 1.3-3.75; p =0.0048), unprovoked PE (HR 3.48; 95% CI, 1.96-6.19; p<0.0001), persistent risk factor for VTE (HR 2.64; 95% CI, 1.08-6.48; p<0.0001) and age ([60 to 75] years; HR 1.88; 95% CI, 1.0-3.61; p=0.0112) were identified as independent risk factors for recurrent VTE whereas prolonged anticoagulation was a protecting factor (HR 0.19; 95% CI, 0.07-0.54; p=0.0001).
Conclusion: Persistent perfusion defect is an independent risk factor for recurrent VTE after a first episode of PE.

P1498

Involvement of the pulmonary micro-vasculature in chronic thromboembolic pulmonary hypertension (CTEPH)

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Introduction: Pulmonary endarterectomy (PEA) is the treatment of choice for patients with CTEPH. However, a limited subset of CTEPH patients present with persistent PH after PEA.
Aims: To assess microvascular lesions and clinical characteristics in CTPEH-patients with persistent PH after PEA.
Methods: We analyzed lung histology available from 8/10 patients with persistent PH after PEA and compared them with 10 randomly selected CTEPH-patients with successful PEA.
Results: Histopathology from 8 persistent PH patients revealed thrombotic lesions, intimal fibrosis and medial hypertrophy in peripheral small muscular pulmonary arteries of all analyzed lungs. 7/8 persistent PH patients displayed moderate pulmonary venous involvement, including intimal fibrosis of small pre-septal venules, foci of capillary multiplication, and hemosiderosis. All cases presented hypertrophy of bronchiolar systemic arteries. Hemodynamic data, exercise testing and medical history exhibited non-significant but by-trend discriminating values between the persistent PH and the successful PEA group for PVR (1199±154 dynes s cm^{-5} versus 825±98 dynes s cm^{-5}), DLCO (63±5% versus 75±4%), 6-minute-walk-distance (6MWD) (272±48m versus 415±31m), history of vascular implants (6/10 versus 0/10), and presence of subpleural septa on chest scanner (6/10 versus 2/10).
Conclusion: We report conspicuous remodeling of the pre- and post-capillary microvasculature in CTEPH-patients with persistent PH after PEA. Group-related discrepancies of PVR, DLCO, 6MWD, vascular implant-history, and one radiologic criterion were observed in CTEPH patients with persistent PH, as compared with CTEPH-patients with successfull PEA.

P1499

Inventive protocols of CT pulmonary angiography (CTPA) avoid artifacts in right pulmonary artery (rPA), improving detectability of pulmonary embolism (PE)

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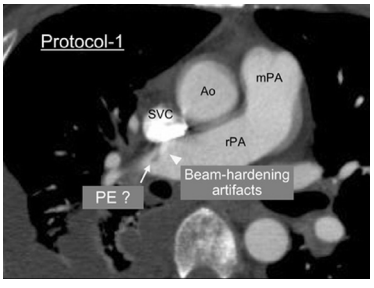
Purpose: A bolus injection of contrast medium (CM) in CTPA over-elevates the density in the veins. It makes too difficult to diagnose PE sometimes.
The purpose of this study is to evaluate three injection protocols for CTPA to improve the image quality of rPA.



Materials and methods: 24 consecutive patients suspected PE underwent CTPAs using a 64-detector MDCT. Each protocol was started with a 3.5ml/sec.-injection of 100ml of CM (300mgI/ml) via vein in upper limb. Three protocols followed the above CM injection, protocol-1 (P-1) with immediate exposure, protocol-2 (P-2) with exposure after 10 sec.-delayed, and protocol-3 (P-3) with exposure after injection of 30ml saline (3ml/sec.). We observed artifacts regarding rPA, subclavian veins, calcification, and motion. Then an artifact-observed score (AOS) was given 0 to 4 as artifact grade.
Results: Each average of AOS in rPA was 1.50 in P-1, 0.25 in P-2, and 0.13 in P-3. The AOS in P-1 was higher than the others, in P-2 (p=0.04) and in P-3 (p=0.001). Each average of AOS in subclavian veins and motion artifact did not differ from P-1 to P-3. The CM-density of all regions of interest in P-1 were higher than the others significantly.
Conclusion: Two inventive protocols are useful to reduce the artifacts in rPA. They may improve detectability of thrombi in rPA in CTPA.

P1500

Sleep-disordered breathing in acute pulmonary embolism: A dangerous comorbidity?

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Background: Sleep-disordered breathing (SDB) is a common comorbidity in patients with acute pulmonary embolism (PE) but its prognostic relevance is not clear. Therefore, we conducted a prospective cohort study to clarify if the presence of SDB is associated with an adverse outcome in acute PE.
Methods: 106 consecutive PE patients were prospectively evaluated by portable monitoring (PM). Nocturnal polysomnography was performed in all subjects who have been diagnosed by PM to have an apnoea-hypopnoea index (AHI) > 15/h or evidence of increased daytime sleepiness. All-cause mortality was registered after a mean observation period of 12 months.
Results: Neither central sleep apnoea nor periodic breathing were observed. Mild obstructive sleep apnoea (OSA) was diagnosed in 35.8% of patients. 12.3% of subjects suffered from moderate OSA. In 10.4% of the study population OSA was found to be severe. High-risk PE was significantly more frequent among study participants with an AHI > 15/h (p = 0.005). All-cause mortality was significantly higher in patients with moderate to severe OSA compared to subjects with an AHI > 15/h (8.3% vs. 2.4%, p = 0.003).
Conclusion: OSA is a common comorbidity to PE and might be associated with an increased mortality in survivors of acute PE.

P1501

Red cell distribution width (RDW): A new predictor for chronic thromboembolic pulmonary hypertension

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The most important long-term complication of pulmonary thromboembolism (PTE) is chronic thromboembolic pulmonary hypertension (CTEPH) associated with considerable morbidity and mortality.It is uncertain why some patients with acute pulmonary embolism develop CTEPH and others do not.Elevated red blood cell distribution width (RDW) has been associated with adverse outcomes of heart failure,pulmonary embolism and idiopathic pulmonary hypertension.Our aim is to investigate whether RDW might be a predictor of CTEPH in pulmonary embolism patients or not.This study is retrospective cohort study.A total of 203 consecutive patients with acute PE were included. Minimum follow-up period was 10 months.We collected each patient's baseline characteristics including RDW,Troponin-T and CRP.Receiver operating characteristic (ROC) analysis was performed to determine the optimal RDW cut-off levels to predict CTEPH. CTEPH frequency in PE patients(n=203) was 7.9% (n=16). RDW was higher in CTEPH patients than the patients without CTEPH (17.04±3.46; 14.64±1.82) (p=0.015). The optimal cutoff value of RDW for predicting CTEPH 14.65.The area under the curve of RDW for prediction of CTEPH was 0.735 (CI: 0.600-0.869). In cases with RDW levels >14.65, the specificity and sensitivity for CTEPH were 62% and 75%, respectively.Negative predictive value of RDW at cutoff 14.65 for CTEPH was 96.7%. At multivariate regression analysis,RDW, hazard ratio: 1.58 (95% confidence interval: 1.09-2.30) was predictor of CTEPH (p=0.016).High RDW levels was an independent predictor of CTEPH in PE patients.Therefore, RDW levels may provide a potential marker to predict CTEPH in PE patients.

P1502

The incidence of venous thromboembolism recurrence in patients after first episode acute pulmonary embolism and related risk factors

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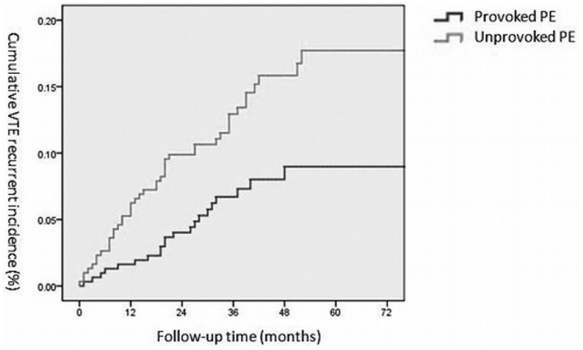
Background: Early identification of recurrent venous thromboembolism(VTE) in patients with first episode acute pulmonary embolism(PE) and related risk factors is important in clinical practice.
Objectives: To investigate the incidence of recurrence after PE, and identify clinical parameters associated with a higher likelihood of recurrence.
Methods: Consecutive patients with acute PE from 2006 to 2010 were enrolled. Baseline clinical data was collected and patients were followed up for years. The primary endpoint is symptomatic recurrent VTE and the second endpoint is death.
Results: 612 patients were included.The median follow-up period was 36 months and all-cause mortality was 17.3%. The 1-, 2- and 5-year cumulative recurrent incidences were 3.9%(95%CI 2.3%-5.5%), 6.9%(95%CI 4.9%-8.9%) and 13.5%(95%CI 10.2%-16.8%) respectively. Patients with unprovoked PE(HR 3.512,95%CI 1.810-6.814), concurrent deep venous thrombosis(DVT) (HR 5.390,95%CI 1.833-15.846) or varicose vein of lower limbs(HR 4.286,95%CI 2.210-8.313) had higher risk in recurrence. Conversely, patients with longer duration of anticoagulation(HR 0.971,95%CI 0.952-0.991) suffered less.
Conclusions: VTE recurrence is relatively common. Unprovoked PE, concurrent



DVT and history of varicose vein of lower limbs seem to increase the risk of recurrence. Longer duration of anticoagulation seems to protect patients from recurrent VTE.

P1503

Circulating endothelial cell levels decrease after vasodilator therapy and are a biomarker of clinical worsening in refractory pulmonary hypertension in children

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Background: Pulmonary vasodilators in general and prostacyclin therapy in particular have improved the outcome of patients with pulmonary arterial hypertension (PAH). Endothelial dysfunction is a key feature of PAH and we previously described that circulating endothelial cells (CECs) could be used as a biomarker of endothelial dysfunction in PAH. We now hypothesized that PAH-specific vasodilator therapy might decrease CEC numbers.
Methods: CECs were quantified by immunomagnetic separation with mAb CD146-coated beads in peripheral blood from children with idiopathic PAH (iPAH, n =30) or PAH secondary to congenital heart disease (PAH-CHD, n =30): before, after treatment and during follow up.
Results: Oral treatment with endothelin antagonists and/or PDE5 inhibitors significantly reduced CEC counts in children. In 10 children with refractory PAH despite oral combination therapy, subcutaneous (SC) treprostinil was added and we observed a significant decrease in CEC counts during the first month of such treatment. CECs were quantified during a 6 to 36 month-follow-up after initiation of SC treprostinil and we found that CEC counts changed over time, with rising counts always preceding clinical deterioration.
Conclusions: CECs might be useful as a biomarker during follow-up of PAH treatment in pediatric iPAH and PAH-CHD, to assess response to treatment and to anticipate clinical worsening.

P1504

Atrial natriuretic peptide as a serum marker of right atrial enlargement and function in pulmonary hypertension

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Background: Production of atrial natriuretic peptide (ANP) increases in response to right atrial (RA) expansion. However, association between serum ANP level and RA volume has been poorly investigated in pulmonary hypertension (PH). Also, no studies have examined the link between serum ANP levels and RA function.
Methods and results: A total of 51 PH patients were studied. The serum ANP level was 51.6 pg/ml [median, IQR: 31.7 – 121, normal range 0 - 43]. Volumetric analysis by cardiac magnetic resonance imaging (CMRI) showed greater RA volume in PH patients (58±23 ml/m^2) than in 22 controls (40±11 ml/m^2) ($p<0.001$). Analysis of RA function by CMRI indicated similar RA ejection fraction (RAEF) between the two groups; however, fractional emptying and reservoir volume were reduced in PH patients than in controls ($p<0.001$ for both). Correlation analysis showed significant association between serum ANP levels and RA volume ($r=0.45$, $p<0.001$). Serum ANP levels also correlated with CMRI indices of RA function [RAEF ($r=-0.66$, $p<0.001$), fractional emptying ($r=-0.75$, $p<0.001$) and RA reservoir volume ($r=-0.42$, $p=0.01$)].
Conclusions: Serum ANP level increases in response to RA enlargement. Importantly, the level is also a marker of reduced systolic and reservoir function of the right atrium in PH.

P1505

Atrial flutter and fibrillation in patients with chronic pulmonary hypertension

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Background: Atrial flutter and atrial fibrillation are frequently observed in patients with pulmonary hypertension but their clinical implications remain unclear.
Objectives: Aim of the study was to determine the prevalence and clinical impact of supraventricular tachyarrhythmias (SVTs) in patients with pulmonary hypertension.
Methods: In a 5-year, prospective study, we assessed the incidence of new-onset SVTs as well as risk factors, clinical consequences, management, and impact on survival in patients with pulmonary arterial hypertension (PAH, n=157) or inoperable chronic thromboembolic pulmonary hypertension (CTEPH, n=82).
Results: New onset SVTs were detected in 48/239 (20%) patients with a cumulative 5-year incidence of new-onset SVTs of 25.1% (95% confidence interval, 13.8-35.4%). Atrial flutter and atrial fibrillation were equally frequent. Stable sinus rhythm was re-established in 21/24 (88%) of patients initially presenting with atrial flutter and in 16/24 (67%) of patients with atrial fibrillation. Development of SVTs was associated with more severe hemodynamic impairment. New-onset SVTs were an independent risk factor of death ($p=0.04$, simple Cox regression analysis) with a significantly higher mortality in patients with persistent atrial fibrillation compared to patients in whom sinus rhythm was restored (estimated survival at 1, 2 and 3 years 64%, 55%, and 27% versus 97%, 80%, and 57%, respectively; $p=0.01$, log-rank analysis).
Conclusions: SVTs develop in a considerable number of patients with PAH or inoperable CTEPH and often cause clinical deterioration and right heart failure. Mortality is high when sinus rhythm cannot be restored.

P1506

The imPAHct of diagnosis delay in pulmonary arterial hypertension

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Introduction: With the availability of effective therapy, early diagnosis of pulmonary arterial hypertension is important; yet, early diagnosis remains difficult.
Aim: To investigate patients' experiences of the trajectory to receiving a diagnosis of pulmonary arterial hypertension (PAH).
Mixed-methods: UK national patient survey and in-depth interviews.
Results: 514 surveys analysed (most (83%) had been diagnosed with PAH from 2001 onwards. Interviews were conducted with 30 patients. Results are presented in 3 themes:
1) Symptom appraisal: 43% of survey respondents experienced symptoms (e.g. breathlessness) for more than one year before consulting a doctor. A process of appraising symptoms was apparent. As time progressed this period was punctuated by critical events that triggered seeking medical advice.
2) Process of elimination: Nearly half of the survey respondents (47%) were seen by four or more doctors before being diagnosed with PAH, a process taking on average more than 2 years. Once medical contact had been made patients described a period of 'elimination' and convoluted contact with the medical profession. Misdiagnosis was common until in young and older patients.
3) Being diagnosed: Receiving a diagnosis of PAH was described as 'a whirl of good and bad' and relief that it was 'not psychological'. Diagnosis disclosure often lacked empathy. Survey respondents noted quality of life and life expectancy as major concerns (60% and 55%, respectively).
Conclusion: The PAH diagnosis trajectory remains lengthy and burdensome. Our results emphasise the importance of an increasing awareness of this disease, to expedite the process of correct diagnosis and the referral of patients with PAH to specialised centres.

P1507

Exercise tests and anxiety independently reflect physical quality of life in patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension

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Background: Up to now, only few data existed evaluating quality of life in patients with PAH and/or CTEPH.

Question: To describe the association between anxiety, depression, cardiopulmonary hemodynamics, and exercise parameters with physical quality of life (QoL).
Methods: Patients with PAH and/or CTEPH performed a 6 minute walk test, cardiopulmonary exercise testing (CPET) and right heart catheterization and completed 3 QoL questionnaires (SF36, SRGQ and MacNew). Hospital Anxiety and Depression Scale (HADS) was used to assess psychological constructs like anxiety and depression.
Results: 63 PAH und 22 CTEPH patients were prospectively included. Peak oxygen uptake (VO2 peak) during CPET was 13±4 ml/min/kg and 6 minute walk distance (6MWD) was 325±127 m. After multivariate analysis anxiety showed an independent association with activity, impact, and total scores in SGRQ and with emotional, physical, social and total scores in MacNew and with mental score in SF36. There was an independent correlation between depression and physical, mental and symptom scores in SF-36. Peak VO2 showed an independent association with all above mentioned subscales in SGRQ and with physical and mental QoL in SF36, whereas 6MWD was associated with all above mentioned scores of the MacNew and the symptom score of SF36.
Conclusion: Peak VO2 and 6MWD reflect quality of life in patients with PAH and/or CTEPH. In addition, anxiety and depression showed a strong association with mental and physical QoL underlining the need for awareness of these disorders.

P1508

Prognostic risk factors of disease worsening in patients with functional class II pulmonary arterial hypertension

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Introduction: The open-label extension (OLE) phase of the EARLY trial provides a unique opportunity to analyse long-term data from WHO functional class II pulmonary arterial hypertension (PAH) patients. Here we investigated prognostic factors associated with PAH worsening.
Methods: PAH worsening was defined as initiation of parenteral prostanoids, atrial septostomy, lung transplantation or death. Data on these 4 parameters, collected annually until study end regardless of OLE participation or treatment discontinuation, for all 185 patients originally randomised to placebo or bosentan were included in this analysis. OLE continued until at least 50% of patients had the opportunity to be treated with bosentan for at least 5 years. Cox regression analyses, univariate (significance set at P<0.1 cut-off) and multivariate (backward selection set at P<0.1 cut-off, including all variables having a P-value <0.1 in the univariate analysis), were employed to determine prognostic factors of PAH worsening.
Results: In the univariate analysis, significant prognostic factors for a low risk of PAH worsening were time since PAH diagnosis >16 months, 6-minute walk distance >437.0 m and mixed venous oxygen saturation >68%. High values in NT-proBNP and PAH associated with connective tissue disease versus idiopathic, heritable or HIV-associated PAH were significant risk factors for PAH worsening. Apart from time since diagnosis, these factors were confirmed as significant in the multivariate analysis.
Conclusions: This analysis provides firm evidence of risk factors significantly associated with PAH worsening in patients at a functionally early stage of the disease.

P1509

Selection of the optimal nebulizer for further clinical development of inhaled nebulized nitrite (AIR001) in pulmonary arterial hypertension patients

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Introduction: Clinical trials utilizing nebulized inhaled Nitrite (AIR001), in patients with Pulmonary Arterial Hypertension (PAH) require a portable, highly efficient nebulizer capable of monitoring adherence and compliance.
Objectives: To evaluate the pharmacokinetics (PK), safety, and tolerability of AIR001 comparing the Philips I-neb AAD System (Philips Respironics, USA) with the Solo-Idehaler (nebulization head, Aeroneb® Solo (Aerogen, IR), aerosol-reservoir attachment, Idehaler™ (Diffusion Technique Francais, FR).
Methods: Utilizing a randomized, crossover, open-label design, 6 subjects received equivalent doses of AIR001 (based on standard in vitro characterization with AIR001 and the resulting % efficiency of each nebulizer to deliver drug). PK parameters for plasma nitrite and nitrate were determined. Supine and orthostatic hemodynamics were evaluated. Adverse events were monitored as was clinical chemistry, hematology, venous and percutaneous methemoglobin, and SaO_2.
Results: Nitrite PK differences were not statistically significant ($p < 0.05$) between devices.

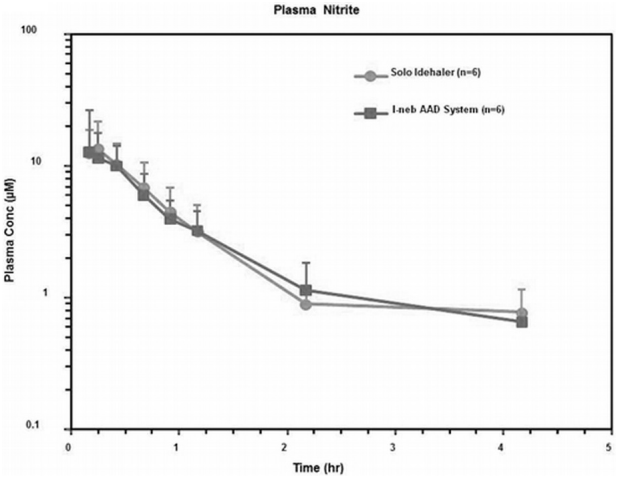

Figure 1

Efficiency was greater for the I-neb AAD System with no differences in safety or tolerability between devices.
Conclusions: Because of precise dosing, adaptive capacity, and its ability to monitor adherence and compliance, the I-neb AAD is optimal for further study of AIR001 in patients with PAH.

P1510

Potential pharmacological interactions between oral pulmonary arterial hypertension (PAH) therapies and new oral anticoagulants

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Background: Anticoagulation with vitamin-K antagonists is currently recommended in PAH. We aimed to search for potential pharmacological interactions between new oral anticoagulants (NOA) and oral PAH therapies.
Methods: We reviewed the potential pharmacokinetic and pharmacodynamics drug-drug interactions (DDI), in particularly regarding metabolism and drug transport, with bosentan (B), ambrisentan (A), sildenafil (S), tadalafil (T) and NOA (rivaroxaban, apixaban, dabigatran).
Results: B is metabolized mainly by hepatic cytochrome P450 (CYP) 3A4, A by uridine 5' diphosphate glucuronyltransferase and to a lesser extent, by CYP3A4 and CYP2C19. The organic anion transport proteins for B and P-glycoprotein for both are probably involved in the transports of these drugs. B, but not A, induces CYP3A4, which is involved in the metabolism of anti-Xa NOA rivaroxaban (30%) and apixaban (50%). Concomitant use of B may reduce their biological efficacy. S and T are also mainly metabolized by CYP3A4, but act as slight CYP3A4 inhibitors. The risk for clinically significant DDI seems low between S or T and anti-Xa NOA. However, in case of PAH-combination therapy, the risk for a decreased concentration might be amplified for anti-Xa NOA. Conversely, an increased risk of myocardial infarction recently evoked with dabigatran, an anti-IIa drug not metabolised by CYP, should preclude its use in PAH.
Conclusion: DDI may occur in PAH patients receiving NOA and PAH therapies, and potentially amplified in case of combination therapy. In the absence of robust clinical and pharmacological data, NOA are not recommended in PAH.

P1511

To study pulmonary hemodynamics and the prevalence of porto pulmonary hypertension (POPH) in cirrhotic patients

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Background: Pulmonary hypertension (PH) (mean pulmonary artery (MPA) pressure $\geq$ 25mm Hg at rest) associated with cirrhosis have variable etiologies and prognostic implications.

Aim: To study pulmonary hemodynamics and determine the prevalence of porto pulmonary hypertension (POPH) in cirrhotic patients.

Method: Retrospective study comprised 1492 patients with cirrhosis seen at a tertiary teaching hospital from July 2001 to March 2011 undergoing invasive haemodynamic measurements during hepatic venous pressure gradient (HVPG) study. The data on etiology of cirrhosis, medical history and Child-Pugh classification of liver disease also collected.

Result: 1492 patients(M:F,1177:315, Child A:B:C,378:360:754) mean age 45.4$\pm$13.2. 37(2.48%) had confirmed PH and 7 (0.47%) patients satisfied the criteria of POPH. Out of 37 PH patients, precapillary PH was present in 7 (POPH group) while postcapillary PH was present in 30 (2.0%) and was passive in 27 patients. Cardiac dysfunction (n=17), spirometric evidence of COPD (n=10 including 4 overlap with cardiac disease), unknown (n=4) and serological evidence of connective tissue disorders (n=3) were also present in postcapillary PH patients. Only 3 out of 30 patients had reactive postcapillary PH (Transpulmonary gradient (TPG) >12mm Hg). Higher MPA and TPG significantly associated with POPH

Conclusion: The prevalence of POPH in cirrhosis was 0.47%. Presence of PH in cirrhotic should alert the physician to search for more common causes other than POPH, may be more amenable to treatment, making them eligible and also reducing the risk associated with untreated PH, especially in patients being considered for liver transplantation.