265. Pulmonary hypertension in hypoxic lung disease

P2360

Late-breaking abstract: 5-HT mediates susceptibility of rats with low intrinsic aerobic capacity to hypoxia-induced pulmonary hypertension

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Introduction: Low aerobic exercise capacity has been linked with a higher probability of death. We have previously demonstrated that low exercise capacity rats have increased susceptibility to pulmonary arterial hypertension when subjected to chronic hypoxia. Here we investigate the role of 5-HT in conferring susceptibility.
Methods: We exposed high and low exercise capacity rats to a 10% O2 environment for 21 days, +/- daily treatment with a 5-HT inhibitor (pCPA). The animals, bred over 21 generations for high (HCR) or low (LCR) running capacity, differ by 500%. PAH biomarkers were determined in heart, lung and blood.
Results: LCR rats developed significantly greater PAH pathologies compared to HCR with regard to cardiac and pulmonary vessel remodeling, right ventricular (RV) pressure and echocardiographic measures. Cardiac histology demonstrated pCPA treatment ablated the RV hypertrophic response and myocyte apoptosis in both HCR and LCR animals. 5-HT levels in LCR animals were increased in response to hypoxia, yet unchanged in other groups, and levels in both strains were ablated by pCPA treatment. Although pCPA effected reduction in all PAH pathologies in all groups, subtractive analysis revealed no impact on the enhanced vessel remodeling and only a partial effect on RV pressure observed in LCR animals. RV mass and echocardiographic measures of RV function, however, were fully reversed.
Conclusion: These data support our hypothesis that intrinsically low aerobic capacity may predispose individuals to developing pulmonary arterial hypertension, and that the associated dysregulation of the 5-HT pathway principally impacts RV function rather than vessel remodeling.

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Spirometric corroboration of radiolographic changes suggestive of COPD and influence on ventilation-perfusion scanning

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Introduction: An abnormal chest radiograph (CXR) can affect the ventilation-perfusion (V/Q) scan interpretation in the investigation of suspected pulmonary embolism (PE). V/Q scans are not always preceded by a normal CXR and many CXRs are reported as showing changes "compatible with COPD".
We decided to ascertain whether radiological suspicion was supported by spirometric evidence of COPD and whether those with more severe COPD were more likely to have an intermediate probability V/Q scan.
Methods: All V/Q scans and CXR reports for the 12 months from February 2008 were analysed. The spirometry database was searched and results obtained.
Results: 68 patients had V/Q scans with CXRs reported as showing changes compatible with COPD. 44 (65%) had not had spirometry.
Of the 24 (35%) patients with spirometry, 3 reports were unavailable and 19 (90%) were consistent with COPD. The mean FEV1 was 60.2% predicted and the mean FEV1/FVC ratio was 50.7.
The V/Q scan reports are classified according to COPD severity in the table below.

Table 1

Spirometry	Number (%)	VQ scan report: Probability of PE		
		Low	Intermediate	High
No evidence COPD	2 (9%)	1	1	0
Mild	4 (19%)	2	0	2
Moderate	5 (24%)	4	0	1
Severe	6 (29%)	5	0	0
Very severe	4 (19%)	5	0	0

Conclusion: Of the 68 patients reported as having radiological "evidence" of COPD, only 24 (35%) had had spirometry. Of the 21 patients with spirometry reports available, 2 (9%) did not have COPD.
None of the patients with COPD had an intermediate probability VQ scan.
COPD is often "reported" on a chest radiograph but spirometric evidence is not always present and, if present, does not always confirm the radiological suspicion.

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Comparative effects of amlodipine and sildenafil on the NT-proBNP levels of patients with COPD-induced pulmonary hypertension

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Introduction: Pulmonary hypertension (PH) secondary to chronic obstructive pulmonary disease (COPD) is an important cause of death. N-terminal of pro brain natriuretic peptide (NT-proBNP) has been suggested as a noninvasive marker for the presence and severity of PH. The changes in NT-proBNP concentration correlated with clinical symptoms. Specific treatment of PH in the setting of COPD has not been adequately studied. We assessed oral vasodilators' (sildenafil and amlodipine) effect on NT- proBNP level in PH due to COPD.
Methods: Forty clinically-stable patients with the history of COPD who had a normal ejection fraction (EF), RV systolic pressure greater than 45 mmHg and baseline blood NT-proBNP levels above 100pg/ml were enrolled. They were divided into two groups. Patients in the first group received sildenafil 50 mg two times daily (group A) and the second group was given amlodipine 2.5-7.5 mg once daily (group B) for 2 weeks. NT-proBNP levels were measured before and after the 2 week drug administration.
Results: Drug therapy with oral vasodilators (both amlodipine or sildenafil) could significantly reduce NT-proBNP levels in COPD-induced PH patients. Also there were no significant differences between amlodipine and sildenafil on lowering NT-proBNP levels (effectiveness of therapies).
Conclusion: Drug therapy (oral vasodilators) in COPD-induced significantly decreased NT-proBNP levels in this study. Though, no significant difference between amlodipine and sildenafil in reducing NT-proBNP levels was observed. Changes in NT-proBNP levels could be used as an indicator to mirror the effectiveness of therapies.

P2363

Prevalence of pulmonary hypertension and right ventricular dysfunction in patients with mixed types of ILD

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Pulmonary hypertension (PH) defined by a mean pulmonary artery pressure (MPAP) > 25 mmHg worsens the prognosis of ILD and can compromise right ventricular function. This study investigates the prevalence of PH and right ventricular dysfunction in ILD patients.
Patients with a diagnosis of ILD based on HR-CT scan and lung function parameters were screened by echocardiography to detect signs of PH. A tricuspid pressure gradient (TI) ≥ 40 mmHg, dilatation or decreased tricuspid annular plane systolic excursion (TAPSE) indicated PH on echocardiography. If possible, right heart catheterisation (RHC) was performed in patients with PH on echocardiography to confirm the diagnosis. NT-proBNP was measured in all patients.
Results (mean±SEM): 206 ILD patients were included. These had a diagnosis of IPF (17%) NSIP (12%), DIP (5%), allergic alveolitis (6%), ILD associated to collagenosis (18%), sarcoidosis (8%) or other/unclassifiet ILD (33%). Mean Dlco and TLC was, respectively, 44±1% and 69±1% of expected. Mean NT-proBNP levels were 496±111 ng/l.
30 patients (14.5%) had signs of PH on echocardiography (TI = 59±3 mmHg, NT-proBNP 2209±657 ng/l). RHC data were obtained in 19 patients, and in 18, the diagnosis of PH was confirmed (MPAP = 39±2 mmHg). Nine patients (5%) had PH confirmed on RHC (MPAP = 42±3 mmHg) and had dilatation of the right ventricle, decreased TAPSE (mean 1.38±0.14 cm) and markedly increased values of NT-proBNP (mean 5599±1557 ng/l).
Conclusions: The estimated prevalence of PH in the present cohort of ILD patients was 15%. 5% of patients had verified severe pulmonary hypertension compromising right ventricular function.

P2364

Non-invasive evaluation in prediction of pulmonary hypertension in patients with idiopathic pulmonary fibrosis

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Pulmonary hypertension (PH) occurs rather frequently in patients with advanced idiopathic pulmonary fibrosis (IPF). However, no reliable non-invasive screening method of detection is available so far. Recently, new formula allowing to detect the patients with PH among patients with IPF and, also, to assess the mean pulmonary artery pressure (MPAP) in individual patients was published: $-11.9 + 0.272 \times SpO_2 + 0.0659 \times (100 - SpO_2)^2 + 3.06 \times FVC\%/TLCO\%$ [1]. The aim of our study was to confirm the usefulness of this formula in our group of IPF patients.
In a prospective study, lung function tests and right heart catheterization examinations were performed in a group of 27 patients with IPF. In total, pulmonary hypertension (MPAP > 20 mm Hg) was detected by catheterization in 17 patients (63%). Compared with the results of the formula, the significant correlation was not reached either for the PH defined according to the recent recommendation (MPAP > 20 mm Hg, r=0.135, p=0.502). or when the border level criterion for PH was heightened to 25 mm Hg, similar to the originally published data (r= -0.043, p=0.833). Also, the use of the tested formula to calculate the level of MPAP in individual patients was not helpful. We found only a non-significant correlation between the level of the mean cMPAP and the calculated MPAP in individual patients (r= -0.148, p=0.461).
In conclusion, our study did not confirm the possibility of using the published formula to predict with sufficient accuracy either the presence or the level of PH in patients with IPF.
Reference:
[1] Zisman DA et al. Prediction of pulmonary hypertension in idiopathic pulmonary fibrosis. *Respir Med* 2007;101(10):2153–2159.

P2365

Endothelial dysfunction in patients with chronic obstructive pulmonary disease

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Chronic obstructive pulmonary disease (COPD) is one of important problems of public healthcare. Structural and functional changes in the pulmonary arteries,

vascular remodeling has been observed in all COPD patients. Pathophysiologic findings of COPD could be explained by the effects of alveolar hypoxemia, endothelial dysfunction. Endothelin 1 (ET-1) is a vasoactive mediator that causes vasoconstriction and vascular wall proliferation.
The aim of the present study was to investigate systemic endothelial function and some parameters of pulmonary and central circulation in patients with stable moderate and severe COPD.
Methods: 20 COPD patients with 2 stage and 22 COPD patients with 3 stage were under consideration. Endothelial function was determined by Celermajer's test, plasma level of ET-1 was measured by enzyme-linked immunoassay.
Results: Reduction of endothelin-depending vascular reaction was determined in 28 patients (66%) with COPD: 18 patients were with severe and 10 patients were with moderate COPD. There was no difference in vasodilatation endothelin-depending function at 14 (34%) patients to compare with control ones. ET-1 level in plasma of COPD patients with 3 stage was higher ($p<0.05$) vs. 2 stages patients and healthy control ($p<0.01$). Linear regression analysis showed direct correlation between ET-1 level and pulmonary artery systolic pressure (r=0.68). These results mean that ET-1 dysfunction may contribute to increases in pulmonary arterial tone and pulmonary hypertension in COPD.
We conclude: endothelial dysfunction in patients with COPD become intensify from moderate to severe stage, that by-turn influence to increase on central and pulmonary haemodynamics damage.

P2366
The influence of right ventricular diastolic functions and pulmonary hypertension on exercise limitation and their relationship with serum NT-proBNP levels in COPD
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Introduction: During the course of the chronic obstructive pulmonary disease (COPD); pulmonary hypertension (PHT), right heart failure, exercise limitation develop due to elevated right ventricle afterload.
Method: In this study, 31 moderate-severe COPD patients, 20 healthy controls were included.Right ventricular diastolic parameters, serum NT-proBNP levels were studied. Exercise capacity was evaluated by cardiopulmonary exercise testing (CPET).
Results: Echocardiography revealed PHT in 13 of the COPD patients. NT-proBNP levels were found to be higher in the COPD group than in the control group,the difference between was statistically significant ($p<0.05$). NT-proBNP level had a relationship with PAP,there was no significant difference in NT-proBNP levels between COPD patients with and without PHT ($p>0.05$). COPD patients demonstrated statistically lower values than the control group with regard to anaerobic threshold oxygen consumption ($ATVO_2$) and carbondioxide production ($ATVCO_2$), and peak oxygen consumption (PVO_2) and peak carbondioxide production ($PVCO_2$) ($p<0.05$). There was a negative correlation between NT-proBNP levels, and AT, PVO_2 values determined by CPET.There was a difference between the COPD and control groups with regard to tricuspid annular plane systolic excursion (TAPSE) value,an echocardiographic parameter ($p<0.05$).
Conclusion: Our study demonstrates that NT-proBNP levels show a correlation with PAP and are raised in COPD patients.COPD may have a tendency for right ventricular diastolic dysfunction and that exercise limitation might be predicted by right ventricular functions and NT-proBNP levels.

P2367
Experience with pulmonary selective vasodilator treatment in COPD with severe pulmonary hypertension
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Background: Pulmonary hypertension (PH) in chronic obstructive pulmonary disease (COPD) is frequent and usually mild. However, some COPD patients present with severe dyspnea and marked PH. Whether pulmonary specific vasodilator therapy would be beneficial in this COPD subgroup is not known.
Methods: We analysed all patients with COPD $\geq$ GOLD II which were treated with either inhaled Iloprost (Ih), Bosentan (B) or Sildenafil (S) in our PH clinic.
Results: From 2000 to 2007 we identified 14 patients (age 65±9 years, 5 females, 13 ex-smokers, BMI 26±5 kg/m^2, mPAP 36±7 mmHg, SaO2 90±4%, FEV1 53±18%pred, TLCO 45±28%) treated with Ih (4), B (4), S (6). All patients were treated with inhaled beta-stimulators, anticholinergics and steroids according to their pulmonologists, all were orally anticoagulated and 10 were under supplemental oxygen. After 3 month, 5 patients improved their WHO/NYHA class (1 B, 4 S) and 10 their 6 minute walk distance (6MWD, 3 B, 2 Ih, 5 S, mean 67±54 m), the mean resting SaO2 remained stable (91±5%). After 6 month, WHO/NYHA class maintained improved in 5 patients (1 B, 1 Ih, 3 S) and 6MWD in 8 patients (3 B, 3 Ih, 2 S, mean 77±46m) with a preserved SaO2 91±5%. 9 patients are still alive 49±39 month after initiation of therapy.
Conclusions: In a highly selective COPD population with severe dyspnea and PH at rest, specific vasodilator therapy may be beneficial and well tolerated. Further studies in this field are highly warranted.

P2368
Evaluation of left ventricular function in patients with COPD – A mono centric retrospective study
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The functional abnormalities of right ventricle in long standing chronic obstructive pulmonary disease (COPD) have been well documented. Derangement of the left ventricular (LV) function in such patients, in the absence of other disorders affecting the LV, has not been clearly established.
This study has been designed to provide more definitive information concerning left ventricular function in patients with COPD primarily to ascertain the involvement of left ventricle in stable COPD patients in whom other sources of diastolic dysfunction has been systematically excluded which the previous studies had failed to do.
The aim of the study was to evaluate LV function in COPD patients.
To assess LV function in COPD patients, 30 patients with COPD without additional cardiac diseases and 30 age and sex-matched healthy subjects were enrolled into the study. We defined COPD by GOLD criteria. Well Investigated parameters of Left ventricular diastolic functions like E/A (peak velocity of early E wave (E)/peak velocity of early A wave (A) transmitral flow), IVRT (Isovolumetric relaxation time), MPI (Myocardial Performance Index) were used for the evaluation of LV diastolic function.
The study shows that 30% i.e. 9 out of the 30 patients admitted to the hospital with COPD had left ventricular diastolic dysfunction and that the risk of association with Left ventricular diastolic dysfunction is 6 times more in COPD patients than in a normal individual.
In COPD patients, LV diastolic function is significantly impaired and its magnitude is related with the severity of COPD as well as the increase in pulmonary artery pressure. This is in spite of preserved LV systolic function

P2369
Severe pulmonary hypertension in chronic lung disease. Long term effects on gas exchange of endothelin receptor antagonists or PDE5 inhibitors
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Drug therapy for pulmonary hypertension associated to chronic lung disease is currently discouraged for the negative effects on gas exchange.We retrospectively evaluated blood gases and 6MWT in patients with severe PH associated with IPF or COPD during 12 months of treatment with Bosentan or Sildenafil. 22 pts with diagnosis of severe pre-capillary PH at right heart catheterization were evaluated including 10 IPF and 12 pts with COPD. Haemodynamical and long term respiratory function data were available in 20 pts: 5 pts with COPD treated with Bosentan, 5pts COPD with Sildenafil, 5 pts IPF treated with ERA and 5 pts with PDE5-inh. Blood gases measuring paO2 and paCO2, PFTs and 6MWT were analyzed at baseline, T6 and T12 months. A-aO2 gradient was calculated using alveolar gas equation. Baseline there were not any difference between haemodinamics and gas exchange profile between IPF and COPD (PAPm = 40mmHg vs 47mmHg), PaO2 58 vs 56 mm Hg, PaCO2 36 vs 37 mm Hg. In 5 IPF pts treated with ETRA A-aO2 gradient increased by 28% and 30% at T6 and T12; in 5 IPF pts exposed to PDE5-inib by 4% and by 6% at the same time points. The distance at 6MWT decreased in IPF-ERA group (- 41 mt T12) and it increased (+90 mt T12) in IPF-PDE5-inhib. In 5 COPD treated with ERA A-aO2 gradient increased by 13% and 22% at T6 and T12 respectively while in 5 COPD pts exposed to PDE5-inib did non significantly change. At T12 the distance at 6MWT increased + 36 mt and + 88 mt in COPD-ERA treated and in COPD-PDE5inib treated respectively.Long term treatment with sildenafil is not associated to detrimental effect on gas exchange both in IPF or in COPD with severe PH.

P2370
Inhalation of a prostacyclin analog (iloprost) does not improve exercise capacity in COPD with disproportional pulmonary hypertension
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Background: Pulmonary hypertension (PH) is a common complication of COPD. Although it is likely that cardiovascular factors limit exercise capacity in patients with disproportional PH, most systemic pulmonary vasodilators failed to show any benefit in COPD. The objective of this trial was to investigate whether inhaled iloprost improves exercise capacity in COPD patients with disproportional PH.
Methods: We performed a randomized, controlled, double-blind, cross-over trial including 19 COPD patients with disproportional PH. Each patient was randomly allocated to nebulized placebo, iloprost 10ug and iloprost 20ug (Multisonic® Infracontrol) before performing a 6MWT at three different time-points. The primary endpoint was the change in walking distance, secondary end-points included exercise test variables. Data were analyzed using mixed-effect models.
Results: Patients had a mean age of 73.2 years±6.7 and FEV1% pred of 51.6%±30.0. The mPAP was 49.2 mmHg±9.3 during exercise. Three patients had severe side-effects, precluding study continuation. The walking distance was

not significantly affected by treatment (mean Δ [95% CI] -12.4m [-32.7 to -7.9],p=0.22). Neither the lowest SaO2 (-0.94% [-2.69 to - 0.82], p=0.28) nor the perceived exertion on BORG scale (0.12 [-0.58 to 0.82], p=0.73) differed among the groups. However, VO2 max (-76.9 mL/min [-122,1 to -31.6], p=0.002) and the maximal minute ventilation (-2.99 L/min [-4.5 to -1.5], p<0.001) were significantly lower in patients receiving iloprost as compared to placebo.
Conclusions: Iloprost inhalation does not improve exercise capacity in patients with COPD and disproportional pulmonary hypertension.

P2371
Pulmonary hypertension and exercise performance in advanced COPD
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Rationale: Pulmonary hypertension is a common occurrence in advanced COPD, but its effects on exercise performance remain uncleared.
Aim: To determine the effects of pulmonary hypertension in advanced COPD on exercise performance.
Methods: We conducted the exercise testing and the echocardiographic examination in 32 patients with advanced stable COPD. Mean pulmonary artery pressure (mPAP) was calculated from the acceleration time of pulmonary flow. Exercise capacity was evaluated by the distance walked in 6 min (6MWD) and by an incremental cardiopulmonary exercise test (CPET).
Results: The patients had a forced expiratory volume in 1 s (FEV1) of 1.15±0.34 L (40% predicted, range 35-50%), corresponding to GOLD stages III and IV, and a 6MWD of 310±62 m (mean ±SD). The CPET showed: a maximum workload of 50±22 W, a peak O2 uptake of 12.4±3.4 mL/kg/min, a peak heart rate of 125±23 bpm, a peak respiratory exchange ratio 1.03±0.7, a ventilation (VE)/CO2 production slope of 34±9, and a peak O2 pulse 7.1±1.3 mL. The peak VE was 40±13 L/min, and the calculated maximum voluntary VE 42±18 L/min. There was no significant difference in any of the CPET variables and 6MWD between the patients with a mPAP < 30 mm Hg (mPAP 24±5 mm Hg, n =17) and those with a mPAP> 30 mm Hg (mPAP 33±4 mm Hg, n=15). There was no correlation between PAP and any of the exercise measurements.
Conclusions: These results suggest that exercise performance in patients with advanced COPD and mild to moderate pulmonary hypertension is essentially limited by exhaustion of the ventilatory reserve.

P2372
Prevalence of established and exercise induced pulmonary hypertension in COPD
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Aim: To describe prevalence of pre-capillary pulmonary hypertension (PH) and exercise induced pulmonary hypertension (EIPH) in COPD without left sided heart diseases, and to relate PH to GOLD stages II- IV.
Methods: 98 patients, 64±7 yrs and 50% men, were recruited. Right heart catheterization with exercise was done. Pulmonary vascular resistance (PVR) was calculated. Pulmonary artery compliance (PAC) was defined as stroke volume/puls presssure. Pre-capillary PH was defined as mean pulmonary artery pressure (mPAP) ≥ 25 mmHg and pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg. Pre-capillary EIPH was defined as an increase in mPCWPexc ≤ 20 mmHg, and increase in mPAPexc, combined with abnormal exercise responses both in PVR (unchanged or increased from rest to exercise) and PAC (reduced from rest to exercise).
Results: Prevalence of pre-capillary PH was 27% with mPAP 29±4 mmHg. Categorized by GOLD stages, PH was found in 5% in GOLD II (mPAP 27±1), 28% in III (mPAP 28±4), and 52% in IV (mPAP 29±5). PCWP was normal at rest, 11±3 mmHg. During exercise 17% showed pathological increase in mPCWP (23±2mmHg). EIPH was found in 31%, mPAP rest and exercise 18±3 and 38±7mmHg, respectively. There were significant differences in mPAP for EIPH vs no EIPH, p<0.05. Categorized by Gold stages, EIPH was found in 39% in Gold II, 29% in III, and 10% in IV. Accumulated prevalence (PH and EIPH) was 58%.
Conclusion: PH and EIPH of pre-capillary type were a common finding in this COPD population. In lack of upper normal limit for mPAP during exercise, we suggest a combined evaluation of PAC and PVR during exercise to determine if increase in mPAP is a pathologic or an expected physiologic response to exercise.

P2373
Arterial blood gases during exercise in chronic obstructive pulmonary disease with and without pulmonary hypertension
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Aim: To evaluate blood gas responses during cardiopulmonary exercise test (CPET) when patients with chronic obstructive pulmonary disease (COPD) were categorized by GOLD stages and the presence of pulmonary hypertension (PH).
Methods: Right heart catheterization (RHC) and CPET to exhaustion with serial blood gas measurements were performed in 98 COPD patients in GOLD stages II-IV without left heart disease. Mean age±SD was 64±7 yrs and 50% were men. PH was defined as mean pulmonary artery pressure (mPAP) at rest ≥ 25mmHg.
Results: See table. PH was observed in 5, 28 and 52% in GOLD stages II, III and IV, respectively. At rest and at peak exercise PaO_2 decreased whereas $PaCO_2$ increased with advancing GOLD stages. At rest, only stage IV had lower (p<0.05) PaO_2 in patients with PH than in those without. At peak exercise, both stages III and IV had lower (p<0.05) PaO_2 in patients with PH than in those without. For $PaCO_2$ no significant differences were observed within each GOLD stage.

Table 1

mmHg	GOLD II		GOLD III		GOLD IV	
	mPAP <25	mPAP ≥25	mPAP <25	mPAP ≥25	mPAP <25	mPAP ≥25
n	36	2	21	8	15	16
PaO2 rest, kPa	10.2±1.0	10.3±0.9	10.1±1.1	9.2±1.1	8.5±0.9*	7.5±1.5*
PaO2 max, kPa	10.2±1.2	12.0±0.1	9.3±1.7¶	7.9±1.2¶	7.6±1.0§	6.4±1.1§

Values given as mean ± SD. *p=0.027; ¶p=0.036; §p=0.004.

Conclusion: PH was a common finding in advanced COPD. Arterial PaO_2 at rest and at peak exercise was inversely related to GOLD stages. Presence of PH within each stage was associated with lower PaO_2. Since RHC is not available to all COPD patients, CPET is useful in selecting candidates. Low resting PaO_2 and excessive decline in PaO_2 during exercise justify referral to further PH investigation.

P2374
Experimental hypoxia-induced pulmonary hypertension is prevented by moderate exercise training in mice
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Pulmonary hypertension (PH), a progressive disease of multifactorial etiology, has a poor prognosis and results in right heart dysfunction. PH is characterized by pulmonary vasoconstriction and abnormal vascular remodeling processes. Current medication does not cure the disease; at best disease progression can be mitigated. Main symptoms of PH are fatigue and shortness of breath. Thus, exercise training has been considered as counterproductive in the past. In our study, moderate exercise training prevented pulmonary vascular disease in a mouse model of hypoxia-induced pulmonary hypertension. During 21 days of exposure to hypoxia mice were trained on a treadmill, daily, for five days a week. Readouts were maximum walking distance, maximum oxygen uptake (VO_2 max), right ventricular systolic pressure (RVSP), measured continuously by telemetry, right ventricular mass in relation to the left ventricle and septum, and small vessel muscularization. Treatment with sildenafil in combination with training improved the maximum walking distance compared to non-trained control mice. Placebo-treated trained mice in hypoxia showed a significant increase of VO_2 max, the effect being similar to the effect of sildenafil. RVSP was reduced to a healthy level in placebo-treated trained mice; small vessel muscularization was reduced to a similar degree as with sildenafil-treatment only. Chronic hypoxia induced a significant hypoxia-induced upregulation of PDE5 in whole-lung homogenate, which was absent in trained mice. Overall, our data demonstrate the efficacy of exercise training for prevention of hypoxia-induced pulmonary hypertension, which might be mediated by inhibition of PDE5 upregulation.

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Biomarkers for pulmonary hypertension in interstitial lung disease
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Pulmonary hypertension (PH) is defined by a mean pulmonary artery pressure (MPAP)>25 mmHg. New patients with ILD are screened by echocardiography to detect signs of PH. This study evaluates NT-proBNP, D-dimer, uric acid and exhaled NO as biomarkers in diagnosis of PH in patients with ILD.
206 patients with ILD were screened for PH by echocardiography. A tricuspid pressure gradient (TI) ≥ 40 mmHg, dilatation or decreased tricuspid annular plane systolic excursion (TAPSE) indicated PH on echocardiography. If possible, right heart catheterisation (RHC) was performed in patients with PH on echocardiography to confirm the diagnosis. Levels of biomarkers in patients with and without PH on echocardiography, were measured and sensitivity, specificity, negative (NPV) and positive predictive values (PPV) for detection of PH were calculated.
Results (mean±SEM): 30 patients had PH based on echocardiography (TI = 59±3

mmHg). In 19 patients, RHC data were obtained, and in 18, the diagnosis of PH was confirmed (MPAP = 39±2 mmHg). There was a statistical significant relationship between high values of NT-proBNP and the presence of PH, with an area under the ROC curve of 0.85. With a cut-off value of 110 ng/l, higher values of NT-proBNP had a sensitivity of 93%, a specificity of 55%, a NPV = 98% and PPV = 27% for detecting PH on echo. 47% of the patients had NT-proBNP values below 110 ng/l. There was no statistical significant relationship between the levels of uric acid, fibrin D-dimer and exhaled NO and the presence of PH.
Conclusion: A value of NT-pro-BNP below 110 ng/l may be used to rule out the presence of PH, and to reduce the need for echocardiographic screening for PH in ILD patients.

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Pulmonary hypertension in obesity-hypoventilation-syndrome
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Introduction: In Obesity-Hypoventilation-Syndrome (OHS), pulmonary hypertension (PH) is considered a common feature.
Aims: To determine frequency and severity of PH in OHS patients treated with non-invasive pressure ventilation (NPPV).
Methods: Prospective cross-sectional study of consecutive patients admitted for follow-up of NPPV (initiated ≥3 months before). OHS was defined by BMI≥30kg/m^2, capillary carbondioxid tension ($PaCO_2$)≥45mmHg prior NPPV initiation without other causes for hypoventilation. Right-heart catheterization (RHC) was performed at rest without oxygen supplementation, daytime sleepiness measured by Epworth Sleepiness Scale (ESS).
Results: 177 patients considered to have OHS were screened. Among 64 patients who met the diagnosis criteria for OHS, 21 patients (10f, 11m; median age 62.2 [53.9;71.7] years, BMI 45 [40;53] kg/m^2, $PaCO_2$ 39.6 [37.8;45.5] mmHg) gave consent for RHC. Only 4 (19%) patients had normal mean pulmonary artery pressure (mPAP<20mmHg), mPAP 18 [15;18.5] mmHg and pulmonary vascular resistance index (PVRI) 224 [148;305] dyn*sec*m^2/cm^5; 8 patients (38.1%) presented with "Borderline"-PH (mPAP 20-24mmHg), mPAP 22 [22.5;23] mmHg and PVRI 392 [287;485] and 9 patients (42.9%) had a manifest PH (mPAP≥25mmHg), mPAP 33 [29;34] mmHg and PVRI 440 [384;728]. In 3 patients with PH, pulmonary capillary wedge pressure was >15mmHg; 2 of them presented with transpulmonary pressure gradient >12mmHg. In patients with PH, ESS (7 [6;11]) was significantly higher than in those without PH (3 [0.5;5.5], p=0.03) or Borderline-PH (3.5 [2.5;6.5], p=0.03).
Conclusion: Mild to moderate PH is quite frequent in OHS, even after initiation of NPPV. Its impact on survival and quality of life has to be studied in future trials.

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Left ventricle diastolic dysfuntion in severe COPD and exercise tolerance
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COPD patients with similar airflow obstruction could have different degree of dyspnea and exercise tolerance. Actually it is unknown why this happens. The aim of our study was to evaluate the prevalence of left ventricle diastolic dysfunction (LVDD) in stable severe COPD patients, analyzing its implication in exercise tolerance and the relationship with specific functional and analytical parameters.
Methods: We evaluated 75 consecutive outpatients with FEV_1 between 30-50%. Twenty five (33%) were excluded because of previous heart disease, atrial fibrillation or Charlson score > 5. Pulmonary function test, 6-minute walking test (6MWT), arterial gases, NTproBNP, inflammatory markers (CRP, leukocytes) and echocardiographic DD parameters were performed in all patients.
Results: Patients were 67±6 y/o, 92% men, tobacco consumption 58±24 p/y. Prevalence of risk factors was: hypertension 44%, DM 26% and dyslipidemia 32%. The functional data showed: FEV_1 39±5%, FVC 76±16%, TLC 129±24%, RV 228±87%, PaO_2 67±10, BMI 28±5, dyspnea MRC scale I-II (72%) and III (28%), 6MWT distance 367±87 m, BODE between 2-7.
LVDD prevalence was 98% (type I 85%, type II 15%). No relationship was found between 6MWT distance or dyspnea and DD parameters (E/A ratio, pulmonary vein flow, E/E' ratio), hyperinflation or laboratory tests. LVDD did not correlate to hyperinflation, inflammation or right ventricle overload.
Conclusions: Prevalence of LVDD in severe COPD patients is very high however it does not seem this condition determines their exercise tolerance. In our study, high prevalence of LVDD is not related to air trapping, inflammation or interventricular dependence so other factors should be studied.
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