356. COPD monitoring in stable disease and during exacerbation

P3214

Symptom/risk assessment in alpha-1-antitrypsin deficiency (AATD) using the 2011 GOLD algorithm

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Background: The 2011 GOLD guidelines on COPD diagnosis, management & prevention recommend use of validated questionnaires like CAT (COPD Assessment Test) or mMRC (modified Medical Research Council) breathlessness scale to assess symptoms against "risk" determined by GOLD staging or exacerbation frequency.
Aim: To determine concordance between CAT & mMRC scale in risk assessment in patients with AATD.
Methods: 309 consecutive patients on the AATD registry (PiZZ) were grouped into 4 GOLD categories (A,B,C,D) based on their CAT/mMRC scores and GOLD stage/exacerbation frequency. We then compared patient distribution in the 4 categories using each method.
Results: Using CAT score as the symptom grade (<10 and >10) and GOLD grade (1/2 or 3/4), 6.1% of patients were placed in group A (low symptoms/low risk); 39.2% in group B (high symptoms/low risk); 2.3% in group C (low symptoms/high risk) & 52.4% in group D (high symptoms/high risk). Data distribution was similar using CAT & exacerbation history (<2/yr or >2/yr) to determine risk. However using mMRC to determine symptoms & GOLD stage for risk produced a significantly different distribution (A=20.3%; B=24.7%; C=5.0% and D=50.0%: p<0.0001).
Data using mMRC score & exacerbation frequency was similar to that using GOLD stage and different to that using CAT with exacerbation frequency (p<0.0001).
Conclusions: Using either mMRC or CAT scores to determine symptoms results in a significant difference in the proportion of patients being categorised into the risk categories which will affect risk assessment and hence therapeutic choice. Longitudinal follow up and monitoring will enable the best method and threshold to be determined for patient management.

P3215

Reproducibility of non-invasive measures of arterial stiffness in mild to severe stable COPD using a new cuff-based operator independent device

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Introduction: COPD is associated with significant cardiovascular morbidity and mortality. Recent evidence suggests that treating COPD may improve arterial stiffness, a key determinant of cardiac risk. Endpoints with high reproducibility are desirable when assessing the impact of an intervention. A new cuff-based operator-independent device (Vicorder) has been developed for measuring arterial stiffness.
Aims: To assess pulse wave velocity (PWV) and augmentation index (AI) reproducibility, using the Vicorder device, in clinically stable COPD patients.
Methods: Between 27/11/12-15/2/12 repeat measurements of PWV and AI were made on 23 consecutive mild to severe stable COPD patients (12 males, 11 Females; Mean age 66±8 years; Mean predicted FEV1 50±19%), recruited from an inner-city teaching hospital out-patients.
Results: PWV mean = 8.9±1.2 m/s, mean difference = 0.035 m/s, Co-efficient of variation (COV) = 4% and limits of agreement (LOA) = -0.68 - +0.76m/s.

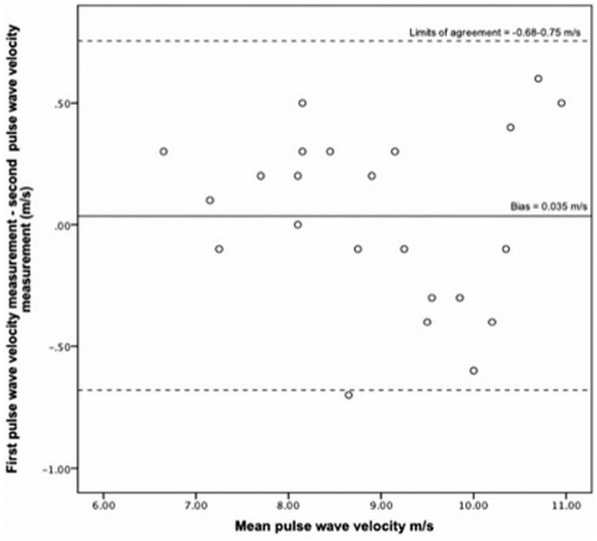

Figure1: Bland-Altman plot comparing repeated pulse wave velocity measurements using a Vicorder device in stable COPD patients with mild to severe disease

AI mean = 17.8±6.7 mmHg, mean difference = -0.7 mmHg, COV = 27.9% and LOA = -10.4 - +9.02 mmHg. Based on the above data, a sample size of 30 pairs would detect a change in PWV of 0.27 m/s with a power of 80%.
Conclusion: Vicorder measurements of PWV, but not AI, in stable COPD patients are highly reproducible and ideal for use in screening programmes and COPD research due to its operator independent non-invasive nature.

P3216

An analysis of patient acceptability of receiving a 72 hour phone call post discharge following a COPD exacerbation

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Introduction: A British Lung Foundation survey revealed that COPD patients would appreciate more support on discharge from hospital.To improve patient experience Imperial NHS Trust created a new service consisting of a hospital COPD nurse telephoning patients 72 hour's post discharge.
Objectives: A pilot study to assess the patients' acceptability of receiving a phone call following a COPD exacerbation. The views of COPD nurses conducting the calls were also sought.
Method: 125 semi- scripted calls were performed over a 9 month period of 2011. At the end of each call, the patient was asked to rate the helpfulness of the call (1

= not helpful at all. 5 = very helpful) and if they would like a call in future. Each COPD nurse completed an anonymous questionnaire focussing on how useful they felt the call has been for patients and themselves.
Results: 110/125 calls were completed in total with an average duration of 9-10 minutes each. 81% of patients rated the call a 3 (quite helpful) or above. The greatest proportion (58%) gave a helpfulness score of 4. 5% of patients gave a score of 1/5. 43% of patients were keen to have a similar call in future.
Questionnaire results indicated that 2 of 3 nurses felt the calls were very useful to their job and to their patients, with the remaining nurse rating the calls as quite useful. One nurse felt the calls helped identify patients at risk of readmission, therefore giving her opportunity to intervene. All three nurses wanted this service to continue.
Conclusion: This pilot study indicates that a phone call post discharge is acceptable to patients and nurses and that benefit can be gleaned from this service. It is being continued.

P3217
Nighttime symptoms and reduced quality of life among COPD patients
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Introduction: Little is known about the impact of COPD symptoms at night on patients' quality of life.
Methods: In a 12-week, Phase III trial of twice-daily aclidinium (ACCORD I), COPD patients completed an electronic diary each morning for 2 weeks before baseline. Diaries included questions on presence and severity of nighttime symptoms and sleep quality. Health status and dyspnea were assessed via SGRQ and BDI. Post hoc analyses were performed to study the relationship between nighttime COPD symptoms and other symptomatic and health status measures. Nighttime symptoms were defined 2 ways: 1) ≥3 nights sleep disturbance during baseline week and 2) ≥3 nights coughing, wheezing, and/or breathlessness during baseline week. Data from the week before baseline for patients with >3 days of diary entries were analyzed via T-test and Chi-square.
Results: The analyses included 535 of 561 randomized patients. Patients with nighttime symptoms had significantly worse health status, as seen in SGRQ Total and domain scores, vs patients without ($p<0.0001$ for all, both definitions). A significantly higher percentage of patients with nighttime symptoms reported sleep disturbance on SGRQ vs those without ($p<0.0001$ both definitions). Patients with nighttime symptoms were more breathless (BDI domains, focal scores $p<0.002$, both definitions), had longer time to sleep onset, lower sleep quality, more awakenings, difficulty falling back to sleep, less total sleep, and were less rested in the AM (all $p<0.02$, both definitions) vs those with no symptoms.
Conclusions: COPD nighttime symptoms are associated with impaired health status, breathlessness, and poor sleep. Clinicians should consider COPD nighttime symptoms when prescribing treatment.

P3218
The journey to severe obstructive lung disease – Retrospective study of FEV1 decline
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Aims: To assess the rate of decline of FEVI over time in patients with GOLD stage 3- 4 COPD and compare the rate of decline in non smokers and smokers.
Methods: The primary outcome was the rate of decline of FEV1/year in current smokers versus non smokers; secondary outcomes included the rate of decline in FEV1 at different stages of airflow obstruction.
In a retrospective case series, we included patients with a primary diagnosis of COPD, GOLD stage 3- 4 under regular review with 3 years spirometry data performed in the respiratory clinic using standard methods. The sample was divided into non- smokers, persistent smokers, and intermittent quitters.
Results: Data was available for 95 patients range 3-23 years.
The rate of decline in smokers was significantly higher than non-smokers. The mean (SD) decline in FEV1 (ml/yr) was faster in earlier stages in GOLD2 53.2 (16.7); GOLD3 32.0 (29.7) and GOLD4 5.9 (7.2). In the overall sample the line of best fit of FEV1 over time was exponential.
The rates of decline (mean (SD)) in non-smokers GOLD3 was 33.9 (35.3) and GOLD4 17.3 (51.3) and for smokers GOLD3 = 42.7 (34.5) and GOLD4 = 25.3 (N/A).

Rate if decline in FEV1 in ml/year

	Number	Mean	SD
Smoker	25	91.1	74.6
Intermittent quitters	25	61.1	47.2
Non-smokers	45	37.8	45.7
Total	95	58.0	58.8

Conclusion: Even in late stages the decline in FEV1 is faster in smokers than intermittent quitters who declined faster than non smokers. Unlike the Fletcher Peto diagram we found that the decline in FEV1 was faster in earlier than later stages. The benefits of quitting diminish as the disease progresses. To minimise lung damage it is essential identify people in early stages and for them to stop smoking immediately.

P3219
Comparison of quality of life scores with modified Medical Research Council (mMRC) dyspnoea scale using data from the European health-related quality of life study
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The 2011 Global Initiative for chronic obstructive lung disease (GOLD) guidelines recommend a combined assessment for measuring the impact of COPD which considers current symptoms and future exacerbation risk. Two symptom cut-points are proposed using the COPD Assessment Test (CAT) score ≥10 and modified Medical Research Council (mMRC) dyspnoea score ≥2. There are currently no published data comparing CAT scores by different mMRC grades.
This analysis examined health status scores for CAT, St George's Respiratory Questionnaire (SGRQ) and short form health survey (SF-12) Physical Component (PC) split by mMRC grade in a primary care population using data from the Health-Related Quality of Life in European COPD Study.
Data from 1817 patients (mean [SD] FEV_1 1.6 [0.6] L; age 64.9 [9.6] years; males 72%) were used. The CAT, SGRQ and SF-12 PC scores are tabulated.

	CAT		SGRQ		SF-12 PC	
mMRC	N	mean±SD	N	mean±SD	N	mean±SD
0	343	11.7±6.8	313	28.5±15.1	338	44.5±8.1
1	691	15.7±7.0	610	39.4±15.5	681	39.8±7.7
2	424	20.5±7.5	388	50.5± 15.8	415	35.0±7.4
3	271	23.5±7.4	243	61.1±13.8	264	30.5±7.2
4	79	27.3±8.3	73	73.3±14.5	75	28.1±7.5

The mMRC showed a clear relationship with scores from the comprehensive generic and disease-specific measures. mMRC Grade 1 was associated with very significant levels of health status impairment. Even the patients with mMRC Grade 0 had modestly elevated CAT and SGRQ scores, which means that mMRC Grade 0 does not mean the absence of symptoms.

P3220
The effect of reducing breath holding time to assess diffusion capacity
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The single breath method to measure diffusion capacity requires a subject to inspire a gas mixture followed by a 10±2 second breath hold. However, dyspnoea may preclude measurement in patients with advanced pulmonary disease. We sought to determine if breath hold time reduction had a significant effect on measured D_LCO values.
Forced spirometry and CO-diffusion by the single breath method were performed in duplicate with breath-holding for 10±2 seconds, 8±2 seconds and 6±2 seconds in 30 controls (FEV_1 107±12.04% predicted), 30 severe COPD patients (FEV_1 37.2±7.92% predicted), and 30 patients with interstitial lung disease (ILD) (FEV_1 69.5±17.61% predicted).
There was no significant difference between DL_{CO}(SB) and DL_{CO}(VA) measured at 10, 8 and 6 seconds in the control (p=0.4431) and ILD groups (p=0.5915). However, there was a significant difference between DL_{CO}(SB) (p=0.0003) and DL_{CO}(VA) (p=0.0183) measured at 10, 8 and 6 seconds in the COPD group.
In the presence of severe airway obstruction the DL_{CO} decreases with breath hold time reduction. However, in healthy controls and patients with ILD, there was no significant change in the DL_{CO} when breath hold time is reduced from 10 to 6 seconds. This could allow for a reduction in breath hold time when measuring the DL_{CO} in patients with advanced ILD who are unable to breath hold for 10 seconds.

P3221
Reference values for respiratory system resistance in adults
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The degree of airway disease is usually determined in spirometry using maneu-

vers that require quite some effort. i.e. FEV1 and FVC. Bodyplethysmography can assess airway obstruction during tidal breathing by determination of airway resistance. Reference values for resistance are, however, scarce.
Within the emphysema versus airway disease (EvA) study we therefore have determined airway resistance in a population of 261 apparently healthy Caucasian subjects aged 45 to 75 with 163 males and 98 females. These were ex-smokers for more than a year or never smokers (27%) with no evidence of acute or chronic lung disease. We determined total resistance (Rt), inspiratory resistance (Rin), expiratory resistance (Rex) and specific resistance (sR).
Rex for the entire group was 0.22±0.11 kPaxsec/L (95 Percentile = 0.45) for males it was 0.20±0.12 kPaxsec/L and for females it was 0.26±0.12 kPaxsec/L. Rin for the entire group was 0.162±0.07 kPaxsec/L (95 Percentile = 0.29) for males it was 0.15±0.07 kPaxsec/L and for females it was 0.18±0.08 kPaxsec/L.
Rt for the entire group was 0.19±0.09 kPaxsec/L (95 Percentile = 0.34).
The resistance values for the females as compared to males were significantly higher for all 4 types of parameters ($p<0.001$ each). As expected resistance parameters Rt, Rin and Rex showed a strong inverse correlation with FEV1 (mL). There was no impact of age or packyears. The data obtained can form the basis for the evaluation of airway resistance in obstructive lung diseases like COPD.
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P3222
The longitudinal determinants of decline in COPD and asthma-COPD overlap in an Australian population
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Longitudinal examination of the characteristics of COPD and asthma-COPD overlap will improve our understanding of these conditions and help identify the role of systemic inflammation (SI). We hypothesised that overlap and SI are associated with the greatest decline in FEV_1 and health status.
Aim: To determine the association between the decline of FEV_1 and other clinical outcomes over time.
Methods: A prospective cohort study with 4 year follow up. Participants with COPD and asthma-COPD overlap, underwent an assessment of spirometry, health status, and biomarkers of CRP and sputum cell counts at baseline and 4 years.
Results: 84 (84%) of the original cohort were contactable, 41(41%) were re-assessed, and there were 15 deaths. The mean (SD) age at follow up was 72.2 (6.8) years. COPD and overlap diagnosis was 57.5% and 42.5% respectively. The mean difference in FEV_1 was -.08mls (0.3). 6MWD decreased by 42 (44)m and there was a 2.2 (11.4) unit decrement in SGRQ. Changes did not differ by diagnosis. Those with SI (CRP >3mg/l) at baseline had the greatest decline in SGRQ [diff 5.7 (2.4) versus -2.2 (2.5); p=0.03], but there was no difference in FEV_1 decline. Mean (SD) baseline FEV_1% pred (41.6 (12.3) V 59.5 (18); p=0.0007), 6MWD (319 (100) V 440 (97); p=0.0001) and SGRQ (55 (16) V 42 (17.7); p=0.009) was worse in the group that died compared to survivors.
Conclusions: Overlap asthma-COPD is not associated with increased functional decline. SI is associated with declining health status, suggesting a need to target treatment to low grade SI. Overall there was only slight health status and functional decline over 4 years, however the 15% that died had the greatest baseline impairment.

P3223
Association between COPD and other co-morbid conditions: Results from a 1-day, point-prevalence study in 2,04,912 patients from 860 cities and towns in India
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COPD is known to be associated with various systemic manifestations. We aimed to study the association between COPD and cardiovascular disease, diabetes and anemia in a cohort of patients from 22 states and 5 union territories in India.
Methodology: 13,225 general practitioners (GPs) and general physicians (Gen Ps) from 860 cities and towns were randomly selected and invited to participate in this 1-day point-prevalence, cross-sectional study. On 1st February 2011 all participating doctors captured details of age, gender, presenting symptoms and diagnosis of all patients who visited them. Clean data was transferred into the EPI INFO software and associations between COPD and other co-morbid conditions were analyzed using chi-square test.
Results: 7,400 doctors consented and provided clean data of 2,04,912 patients (M: 54.1%; F: 45.9%) who visited their clinic/hospital. Out of these 6118 (3.0%) patients had COPD. Presence of doctor-diagnosed COPD was strongly associated with co-presence of ischemic heart disease (IHD) [OR: 2.66 (2.3, 3.0);p<0.0001], Hypertension (HT) [OR:2.19 (2.0, 2.4);p<0.0001], Congestive Heart Failure [OR:4.55 (3.8, 5.3);p<0.0001], Diabetes [OR: 1.71 (1.6, 1.9); p<0.0001], Stroke [OR:2.17 (1.6, 2.9);p<0.0001], Arthritis [OR:1.34 (1.2, 1.6);p<0.0001] and Anaemia [OR:1.27 (1.1, 1.4);p<0.0001]. These associations remained even after adjustment for confounding factors.
Conclusion: COPD is strongly associated with the presence of IHD, HT, CHF, Diabetes, Arthritis and Anaemia in an Indian population.

P3224
Anaemia and survival in COPD patients with acute hypercapnic respiratory failure
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Background: Previous studies have shown a relationship between anaemia and survival in COPD but the aetiology and natural history remains unclear.
Aim: To determine the temporal relationship between anaemia, nutritional status, co-morbidity and survival in severe COPD.
Methods: Patients with COPD and acute hypercapnic respiratory failure treated with non-invasive ventilation were included in the study. Data collected: Charlson co-morbidity index (CCI), GOLD stage, BMI, albumin, haemoglobin (Hb) at intervals up to 2 years prior to and after index admission, haematinics, and CRP. The temporal change in prevalence of anaemia and relationship with other factors was determined. Impact on survival was assessed by Cox's regression analysis.
Results: 65 patients mean (SD) age 71 (10.5) years, GOLD stage: IV 63%, III 21%, II 19%. During interval of 6-24 months prior to admission mean (SD) Hb fell from 13.3 (1.7) g/dl to 12.6 (2.0) g/dl; p=0.03. The fall in Hb was greatest in those who died: 0.88 (1.19) v 0.18 (0.88) g/dl p=0.013. Anaemia prevalence increased from 20% to 43% OR 3.0 (95% CI 1.29-7.14), and was greatest in GOLD stage IV disease: 59% v 17.4% OR 6.8 (1.72-29.4) and if age-adjusted CCI ≥4: 53.8% v 27% OR 3.1 (1.08-9.2). There was no association between anaemia and BMI, albumin or CRP. In-patient death was associated with a lower Hb (11.5 (1.73) v 13.30 (1.97) p<0.001) and haematocrit (37.1(5.0) v 41.6 (6.0) p<0.005). Survival was worse if anaemic: median (IQ range) 12 (1-674) v 475 (63-720) days, HR 3.15 (1.65-6.0) p=0.0002.
Conclusion: Anaemia is common in severe COPD, often unrecognised and rarely investigated. Anaemia increases with disease progression and is associated with shortened life expectancy.

P3225
Inflammasome activity in acute exacerbations of chronic obstructive pulmonary disease
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Inflammasome is a multi-protein complex that mediates activation of caspase-1 which promotes the secretion of the proinflammatory cytokines IL-1β and IL-18 via Toll-like receptors (TLRs), which detect the presence of pathogens through pathogen associated molecular patterns (PAMPs). Aim of the study was to examine the changes occurring in inflammasome linked components during bacterial acute COPD exacerbations (AECOPD).
We examined 26 patients with COPD hospitalized for infectious AECOPD according to Anthonisen's criteria and 20 patients with stable COPD. Bacterial infection was documented by PCR. IL-18, IL-1β, caspase-1, and TLR-2 levels were measured in induced sputum and serum at baseline and after the AECOPD treatment using ELISA, as well as in control subjects.
IL-1β, TLR-2 and caspase-1 (p=0.013) levels were increased in AECOPD. In contrast, IL-18 levels were found significantly lower in sputum of AECOPD compared to stable state (p=0.05), while right after treatment increased to the stable state levels. An inverse correlation was found between IL-18 levels and sputum macrophages in AECOPD (r=-630, p=0.028). Positive staining of IL-18 was observed in macrophages in immunocytochemistry. Serum IL-18 levels were elevated in exacerbations (p>0.05) compared to stable state, and decreased after treatment to stable disease levels (p>0.05).
Our data indicate that there is a dysregulated inflammasome activity in bacterial AECOPD that might contribute to the susceptibility of COPD patients in repeated bacterial exacerbations. Understanding the inflammasome pathways may provide insights into disease pathogenesis that might serve as potential targets for therapeutic intervention.

P3226
Peripheral neutrophil stiffness is increased in COPD severe exacerbations
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Introduction: Stable COPD patients increase peripheral neutrophils stiffness (E). We hypothesized that during exacerbations the increase in E can be enhanced.
Objective: To determine peripheral neutrophils E in patients with COPD severe exacerbations during hospitalisation and at convalescence (12 wks after discharge).
Methods: 25 COPD patients (70± [SD] 9 yrs; all smokers) were assessed during the follow-up period, of whom 11 recurred (median, 7±4 wk). E was measured

using atomic force microscopy. Both, CAT questionnaire and ADO index were also assessed. Ten smokers with normal lung function were used as controls.
Results: On admission, E in COPD patients (956±422 Pa) is increased compared to controls (439±216 Pa) ($p<0.05$). Compared to admission, the 14 patients who completed the study improved lung function (FEV1 and PaO2), CAT score (from 23±6 to 13±6), C-RP values and number of leukocytes at convalescence; however, E remained unchanged (1,008±474 vs 903±448 Pa). In the 11 patients who recurred, no differences were observed between admission and recurrence (907±376 vs 801±359 Pa). A significant association between ADO index and E at admission in COPD patients (n, 25) (Rho 0.60, $p<0.05$) was observed.
Conclusions: Neutrophils E is increased in patients with COPD severe exacerbations but did not vary at convalescence despite clinical, functional and biochemical improvement. These findings suggest that the rheological properties of neutrophils may be driven by a different underlying inflammatory response.
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P3227
Phenotyping of patients with COPD from exhaled air by ion mobility spectrometry
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Background: COPD is a heterogeneous disease including several comorbidities. Different phenotypes have been proposed, among them patients with frequent exacerbations. We investigated whether an electronic nose is sensitive in the detection of such characteristics.
Methods: Thirty stable COPD patients and 26 control subjects breathed at rest into a special 6.5L tube via a valve. Analysis for VOCs was done online by ion-mobility spectrometry (IMS, Sionex). It turned out that data could be condensed into 23 voltage bins (columns) and 693 reading points (rows) of retention time yielding a matrix of 23x693 signals. For each matrix element values were compared between groups or within COPD patients by Mann-Whitney-U-test at p=0.005. Columns with at least 10 significant row differences were considered as different. This handling of multiple testing of correlated data was based on bootstrap results indicating <2 differences occurring by chance at p=0.005.
Results: Ten columns differed between COPD patients and controls, 2 between COPD I/II versus III, and 2 between patients with (n=14) and without at least one exacerbation during the last year, while the distribution of COPD stages (FEV_1) was similar in the latter patients. In single columns the number of significant rows much exceeded the threshold of 10. The analysis of comorbidities also suggested differences in IMS signals.
Conclusion: Breath profiles from a highly sensitive electronic nose correlated with COPD disease severity and characteristics. This might help in the non-invasive differentiation between COPD phenotypes.
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P3228
Sputum VEGF level increases with treatment of COPD acute exacerbation
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Introduction: The role of vascular endothelial growth factor (VEGF) in COPD pathogenesis has been studied widely; however the change in blood and airway VEGF levels during the treatment of an acute exacerbation has not been investigated. In this study we aimed to evaluate the changes in plasma and sputum VEGF levels during COPD exacerbation.
Methods: 14 subjects (64±10 years) with established COPD participated in the study. Spontaneous sputa and EDTA-plasma samples were collected for VEGF measurement at admission to hospital due to an acute exacerbation of COPD (Anthonisen type I-II) and also at discharge from hospital. During hospitalization (8±1 days) patients were treated with systemic corticosteroids (n=12) and/or with antibiotics (n=7). VEGF concentration was measured by ELISA. Data are shown as mean±SD and analyzed with parametric tests.
Results: Sputum VEGF levels positively correlated with FEV1 percent predicted (r=0.61, p=0.02) and FEV1/FVC (r=0.55, p=0.04) at baseline, while no relationship was observed between plasma VEGF level and clinical parameters. There was no correlation between sputum and plasma VEGF concentrations (p=0.65). Sputum level of VEGF increased significantly (6670±6252 pg/ml vs. 9735±6909 pg/ml, before vs. after treatment, p=0.04) following treatment, while there was no change in plasma VEGF levels (179±98 pg/ml vs. 173±93 pg/ml, before vs. after treatment p=0.73).
Conclusion: Recovery from COPD exacerbation might be associated with increased airway VEGF level. Analysis of sputum but not plasma may reflect the changes in VEGF levels in COPD patients during exacerbation.
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P3229
Interaction of relevant domains in the heterogeneity of severe COPD exacerbations: The exacerbome network
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Different factors may play a role in the pathogenesis of COPD exacerbations (ECOPD). The Exacerbations of COPD in Spain (ECOS) is a multi-center longitudinal study aimed to improve our understanding of the pathobiology and heterogeneity of ECOPD. We aimed to explore the weight and interaction of the different domains that are involved in the heterogeneity of the disease by building a network that link and relate all of them (exacerbome). In the ECOS study we included 99 patients in whom we obtained a battery of tests during hospitalization because of ECOPD, when clinically stable and after discharge. A selection of variables from the demographic, symptoms, lung function, biology, microbiology and imaging domains were analyzed and used to construct the exacerbome, where each node correspond to each of these variables, node size was proportional to the percentage of abnormal values of that particular variable and nodes were linked if there was a statistically significant correlation between the two variables being explored. Dyspnea, presence of bacteria in sputum by polimerase chain reaction, leukocytosis, active smoking, pulmonary hypertension on echocardiography, PaCO2, inspiratory capacity to total lung capacity (IC/TLC) and fibrinogen were the most important and interconected nodes of the exacerbome on admission whereas age, dyspnea, presence of bacteria in sputum, presence of emphysema, diffusing capacity and blood eosinophils higher than 2% were the most important nodes on stability. These results show that network analysis is a novel approach to help understanding the heterogeneity of severe ECOPD.
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Association of gastro-esophageal reflux disease symptoms with COPD severity and acute exacerbations of COPD
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Background: Gastroesophageal reflux disease (GERD) is common in COPD patients but there is little prospective data on the impact of GERD on COPD exacerbations.
Objectives: To evaluate the association of GERD and GERD-related therapy with disease severity and exacerbation frequency in COPD patients.
Methods: 1087 COPD patients and 392 controls were included. GERD symptoms were evaluated with GERD-Q questionnaire and treatment with proton pump inhibitors (PPIs) was recorded. All patients were contacted monthly and acute exacerbations of COPD (AECOPD) and hospitalizations for COPD exacerbations were recorded.
Results: The presence of significant GERD symptoms was more common in COPD patients compared to controls (25.4 vs. 9.0%, $p<0.001$) and was associated with more severe disease. Frequency of AECOPD and hospitalizations in 1 year was associated with GERD score (r=0.703, $p<0.001$ and r=0.723, $p<0.001$, respectively). COPD patients with GERD symptoms experienced more AECOPD and hospitalizations compared to patients without GERD symptoms (4.18±1.66 vs. 0.99±0.96, $p<0.001$ and 2.63±1.63 vs. 0.36±0.59, $p<0.001$, respectively). COPD patients receiving PPIs experienced less AECOPD and hospitalizations than COPD patients who did not receive PPIs, both in the presence of GERD symptoms (1.60±0.69 vs. 4.27±1.60 AECOPD, $p<0.001$ and 0.90±0.56 vs. 2.69±1.61 hospitalizations, $p<0.001$) and in the absence of GERD symptoms (0.88±0.79 vs. 1.25±1.22 AECOPD, $p<0.001$, and 0.28±0.47 vs. 0.52±0.75 hospitalizations, $p<0.001$).
Conclusions: GERD symptoms are significantly associated with COPD exacerbations and hospitalizations and treatment with PPIs is related to less exacerbations and hospitalizations.

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Antibiotic use for hospitalized chronic obstructive pulmonary disease exacerbations: A propensity adjusted analysis

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Background: Antibiotics are frequently used in the treatment of chronic obstructive pulmonary disease (COPD) exacerbations. However, international guidelines suggest their use should be restricted to specific sub-groups based on the Anthonisen Criteria. The aim of this study was to assess the impact of antibiotic therapy on outcome in COPD.

Methods: We conducted a multi-centre prospective observational study assessing patients hospitalized with COPD exacerbation. Multivariable logistic regression was used to compare outcomes in patients treated with and without antibiotic therapy, including adjustment using a propensity score and adjustment for recognised predictors of 30-day mortality. The outcomes of interest were 30-day mortality and length of hospital stay.

Results: 1031 patients were included in the study. Median age was 74 years (interquartile range 63-75) and 48.7% were female. Mean FEV1 was 46% (standard deviation 19%). 30-day mortality was 5.4%. 818 patients (79.3%) received antibiotic therapy on admission (23.5% combination therapy, 76.5% monotherapy). Antibiotic prescribing according to Anthonisen criteria was: Type 1 - 84% patients received antibiotics, Type 2 - 78.6% and Type 3 - 70.3%. After adjustment for propensity to receive antibiotic therapy and recognized predictors of mortality, there was no association between antibiotic use and 30 day mortality (OR 0.96 (0.37-2.48), p=0.9) or length of hospital stay (p=0.8).

Conclusion: Antibiotic treatment is frequently used in hospitalised acute exacerbations of COPD. This study did not find any evidence of benefit in terms of mortality or length of hospital stay.