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Asthma & COPD: converging or diverging chronicity?

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ABSTRACT BOOK



P01. [117] Diagnostic value of CT pulmonary artery diameter to evaluate pulmonary hypertension in patients with end stage COPD

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Introduction

Pulmonary hypertension (PH) in end-stage COPD is associated with a higher mortality and an increased risk on exacerbations. We retrospectively evaluated the diagnostic value of the pulmonary artery (PA) to aorta (A) diameter ratio on chest computed tomography (CT) for PH in end-stage COPD patients.

Methods

Patients with end-stage COPD evaluated for eligibility for lung transplantation between 2004 and 2014 were retrospectively analyzed. Clinical characteristics, chest CT scans, spirometry and right-sided heartcatheterizations (RHC) were studied. Diameters of the pulmonary artery (PA) and ascending aorta were measured on CT. Multiple linear regression was used to examine the relationship between PA diameter, PA:A ratio and mean PA pressure (meanPAP). Specificity and sensitivity numbers and area under the curve (AUC) of different cut-offs of PA diameter and PA:A ratio in diagnosing PH were calculated.

Results

In total 92 patients, with mean age of 55.1 years were evaluated. A number of 30 patients (32.6%) had pulmonary hypertension at RHC (meanPAP > 25 mm Hg). PA:A ratio and PA diameter were significantly correlated with meanPAP, $r = 0.498$ and $r = 0.489$, respectively ($p < 0.001$). A PA:A ratio of >1 had a 50% sensitivity and a 85% specificity for identifying patients with pulmonary hypertension (AUC 0.70 (95 % CI 0.58- 0.83; $p < 0.001$).

Conclusion

PA diameter and PA:A ratio are significantly associated with meanPAP. A PA:A ratio of >1 has a high specificity for pulmonary hypertension. Therefore in subjects with a PA:A ratio > 1 there is a high degree of certainty that they actually have PH. However, PA:A ratio of less than 1 does not rule out presence of PH.

P02. [44] Examining climatic influence on the respiratory health of Qatar residents: A comparative analysis between winter and summer months

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Inhalation of air particulates may result in serious health problems, most notably with the respiratory system. Due to a variety of factors (traffic, construction, weather patterns), the air in Doha is of poor quality and is significantly over targets for PM_{2.5} and PM₁₀ (WHO, 2014 rankings). We examined the levels of particulate matter to determine if there was a daily or weekly pattern. We then compared the number of air particulates in the summer and winter and attempted to determine if small (0.5 – 2.5 mg/l) or large (>2.5 mg) particulate matter was related to weather patterns and resulted in increased use of the nebulizer at a local clinic. We found that particle number (both small and large) was highest around 6 am and lowest around 12 pm, a pattern that didn't change between months. The number of large and small particles was generally lower on Friday when human activity was lowest. The temperature decreased in winter while humidity increased; wind speed remained relatively constant. Data suggest that nebulizer use was higher in the winter and lower in the summer although the reasons for this are speculative. There was no relationship found between the number of people using the nebulizer and the number of air particles.

Critchley, K.A, PhD, RN, Teather, K., PhD, Alamgir, A., Dsouza, N. & Jabonete, L.

P03. [90] The Microbiomes of COPD and Bronchiectasis: Converging or Diverging?

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Background

There is overlap between COPD and bronchiectasis both in their clinical features and in their microbiology as determined by traditional sputum culture. 16S metagenomics sequencing offers a non-culture based alternative that can more accurately characterise the diseases' microbiome. We compared microbiome profiles of two cohorts of patients, one with stable COPD and the other with bronchiectasis, and analysed their relationship with disease severity.

Methods

97 COPD patients recruited into a longitudinal study and 133 bronchiectasis patients participating in a longitudinal study provided sputum samples when clinically stable. The bacteria present in sputum was analysed by 16S rRNA metagenomics sequencing on the Illumina MiSeq platform followed by sequence analysis in Qiime. Profiles were compared between the two diseases, and also within each individual disease, to correlate markers of disease severity such as frequency of exacerbation, GOLD or bronchiectasis severity index score with markers of inflammation such as Resistin, IL-1 β , IL-8 and TNF- α .

Results

The two diseases showed distinct but overlapping microbiome profiles with a high degree of heterogeneity. A number of patients with either condition had a microbiome dominated by genera such as *Haemophilus* whilst other patients had a diverse microbiome dominated by *Veillonella*, *Prevotella* and *Leptotrichia*. More *Pseudomonas* was identified in bronchiectasis patients compared to COPD. In both COPD and bronchiectasis patients, a lower microbiome alpha diversity was associated with a higher disease severity index ($P < 0.01$) and more frequent exacerbations ($P < 0.01$). Airway inflammatory profiles in both diseases were dominated by neutrophilic inflammation, however the diseases could not be distinguished based on the inflammatory profiles.

Conclusions

The stable microbiome in both COPD and bronchiectasis is broadly similar despite the aetiology of the diseases being different. Microbiome profiling in both diseases can identify patients at higher risk of exacerbations and disease progression.

P03a. [111] Clinical features of patients with pulmonary embolism (PE)

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Aim

To analyze the incidence, co-morbidity, risk factors, relapses and mortality in patients with PE.

Patients and methods

We performed a retrospective study of 415 patients with pulmonary embolism (mean age 63.5 ±14.3 years) and cases of relapses, hospitalized in the clinic of pulmonary diseases at UMHAT "St. Marina" Varna for a 5 year period (2010-2014).

Results

Females with PE were with higher mean age than males ($p < 0.001$). Co-morbidity scored with Charlson index was 1.55. The incidence of massive PE for the 5 year period was 30.4% and the incidence of relapses was 32.2%. There was no significant difference between the two groups ($\chi^2 = 6.5$; $p = 0.164$). The risk of massive PE is twice higher in the presence of immobilization for more than four days ($p > 0.05$). The risk of lethal outcome in patients with massive PE is 3 times higher than those with non massive forms. (OR=3.15; CI 95% 1.71-582). The mortality was significantly higher in females ($\chi^2 = 9.69$; $p = 0.04$). The mortality in the group without relapse is 12.4% versus 8.5 % in the relapse group without reaching significance ($p = 0.23$). The use of fibrinolytic therapy reduces the mortality in massive forms of PE with 35% (OR=0.65; 95%CI 0.25-1.42; $p = 0.24$). The incidence of relapses does not differ during the investigated 5 year period ($\chi^2 = 2.39$; $p = 0.66$). 67.8% of patients with relapse of PE have been treated with oral anticoagulants. At the time of the relapse 49.15 % of them are on current treatment with oral anticoagulants.

Conclusion

Pulmonary embolism is a common cause of death. The risk is higher in patients with prolonged immobilization and increased co-morbidity score. The mortality is higher in females and the use of fibrinolysis reduces the death rate. Appropriate oral anticoagulant treatment and follow up can prevent the onset of relapse.

P03b. [58] Comparison of Comfortability and Effectiveness of Total Face Mask and Oronasal Mask in Non-invasive Positive Pressure Ventilation in Patients with Acute Respiratory Failure

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Background

There is a growing controversy on using oronasal masks (ONM) as the choice in acute and critical cases by authorities while total face mask (TFM) has been developed to bring patients' compliance higher. Yet, there is no prove for clinical superiority of TFM in spite of its higher admission by patients. So, this trial was designed to compare TFM and ONM during NPPV in patients with acute respiratory problems.

Methods

Through a randomized controlled trial, referrals to a reference hospital for respiratory failure in Tehran from February to November 2014 were recruited considering inclusion and exclusion criteria. Epidemiologic, clinical and paraclinical information were recorded 60 minutes and then 6 and 24 hours after NPPV started. Supportive level of ventilator was evaluated by IPAP and EPAP beside O₂ total consumption. Patients' comfort was assessed using Visual Analog Score system (VAS) when they used masks.

Results

VBG trend showed no difference between the groups. However TFM was much successful after 6 hours when patients passed the acute phase of attack ventilation, especially in PCO₂ and HCO₃. Concerning patients' comfort and acceptance, except pain in cheeks, other parameters were statistically similar in both groups. However, total VAS score showed equality of acceptance in two groups. Likely, total time of NIV was similar. Intubation was needed in 2 of ONM and 1 of TFM users and each group reported one death.

Conclusion

The present study advises to make both TFM and ONM on the table to give perfect per case choices to be selected by both physician and patient in the case of any disadvantages or lack of tolerance for one of the two masks since there were no many basic statistically significance in this regard.

P03c. [59] Evaluation of the validity and reliability of the CAT (COPD Assessment Test) questionnaire among COPD patients attending Masih Daneshvari Hospital

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Background

For COPD patients, influence of disease on quality of life is measured via questionnaires. In this study, the goal was to evaluate the validity and reliability of the short and easily translated COPD Assessment Test (CAT), Persian translation.

Materials and Methods

This was a cross sectional pilot study with completion of the Persian translation of the CAT questionnaire by COPD patients attending the emergency room Masih Daneshvari Hospital during the time period between winter of 2012 and summer of 2012. The results of the questionnaire were compared with the Saint George Respiratory Questionnaire, number of respiratory medications and frequency of visits to the emergency room.

Results

In total, 32 patients participated in this study with mean age of 60±13 years and 98% of the patients were men and 7% were women. The Cronbach's alpha coefficient for the CAT questionnaire was calculated to be 0.732. There was statistically significant correlation between the scores from the CAT questionnaire and the total scores from the SGRQ (Pearson correlation coefficient=0.590, P=0.010).

Discussion

This pilot study showed that the CAT questionnaire was well accepted by the patients with almost all questions being answered. The reliability of the questionnaire using Cronbach's alpha coefficient was acceptable and the questionnaire score correlated with the total score on the SGRQ questionnaire.

P03d. [57] Noninvasive Positive Pressure Ventilation: a cross-sectional descriptive study of our first experience

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Background

Non-invasive positive pressure (NIPPV), in which endotracheal intubation is not required and can afford the same effectiveness compared to invasive ventilators, can be used for selected patients. Studies are going on to improve the rules in case selection and NIPPV indications. Based on our search, no survey has been performed in this topic in our country where this method is not conventional. This study is to evaluate the efficiency of a separate specialized ward which has been established to take NIPPV and respiratory rehabilitation in our hospital since January 2011 with staff.

Methods

Up to March 2012, 326 patients who were admitted in different units with several causes had been taken NIPPV. Diagnosis, age, gender, ward and indication of admission were assessed in this cross-sectional retrospective study.

Result

The mean age was 61.99 years. In several combined diseases, Hypertension was the most common with a 40.5% proportion. Chronic Obstructive Pulmonary Disease (COPD) with 52.92% and Sleep Apnea (9.54%) were the most common diagnoses. There was 4.6% mortality between clients. NIPPV was utilized in pulmonary wards (66.26%), emergency room (21.47%), ICU and CCU respectively.

Conclusion

According to the study, Patients with COPD and Sleep apnea were the most NIPPV users who took the service in different areas even out of intensive care units (ICU). So this method can be more cost effective and beneficial. We recommend engagement of trained nurses under a pulmonologist's guide for easier and safer utilization out of ICUs and more educational courses for related specialists such as anesthetists, internists and physiotherapists.

P04. [104] Anemia and iron deficiency in patients with Chronic Obstructive Pulmonary Disease – association with disease severity?

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Background

Chronic obstructive pulmonary disease (COPD) is a complex disease entity including disturbances of metabolic functions. Over the last decade there has been a focus on comorbidities in COPD. This includes anemia, since anemia and iron depletion decrease physical activity and cause multiple other symptoms. The aim of this study is to investigate the prevalence of anemia and iron deficiency in patients with COPD and its association with disease severity.

Methods

Data was collected retrospectively from 162 patients with possible COPD referred to a pulmonary outpatient clinic. A spirometry was performed, and COPD was diagnosed or excluded based on the GOLD criteria; 96 patients had COPD. Information about oxygen saturation, MRC and CAT scores, BMI and medical history was obtained. Blood samples were analyzed for hemoglobin (Hgb) and erythrocyte (Ery) values, iron and vitamin B12, C-reactive protein (CRP) and vitamin D status. Comorbidities were registered based on information in patient hospital records.

Results

The COPD patients were distributed according to the GOLD criteria into groups A (n=35), B (n=20), C (n=14) and D (n=29). There was an equal distribution into group A vs. groups B+C+D in COPD patients both with and without anemia. Anemic and non-anemic patients were also comparable in terms of gender, CRP and vitamin D levels and lung function, but significantly different in terms of age, MRC score and number of comorbidities. A significantly higher proportion of patients with kidney and/or heart disease was found in COPD patients with coexisting anemia compared to those without. 13.5 percent of the COPD patients (13/96) had anemia; one had iron deficiency anemia. There were no significant Hgb and Ery value differences between patients with and without COPD.

Conclusion

A limited number of COPD patients had anemia, including iron deficiency anemia. However, results indicate that patients with coexisting COPD and anemia experience a greater disease burden.

Disclosure: The authors have disclosed no conflict of interest.

P05. [35] The clinical and economic impact of the combined interventions of telehealth, specialist respiratory nursing care and health coaching interventions for COPD admissions in an urban setting

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Aims

To demonstrate the scale of impact of telehealth using the Clinitouch system when combined in parallel with health coaching and specialist nurse interventions triggered by biometric data in a redesigned service for COPD patients with a history of over two prior admissions in the previous 12 months.

Method

Data for admissions from the acute trusts and interventions from Leicester Partnership Trust , Spirit Healthcare and Totally Health were received from Leicester City CCG over a twelve month period in a cohort of patients with a mean admissions rate of 3.13 historic admissions in the previous 12 months. Data were analysed for the impact on admissions and overall resource use.

Results

The mean monthly admission rate in the historical control group was 13.9 and the mean monthly admission rate in the intervention group was 4.6. The mean number of patients enrolled in the intervention was 54. The admissions were reduced from 222 to 74. The relative reduction in unscheduled admissions was 67%. The number of admissions decreased at a statistically significant rate from 3.13 admissions per patient to 1.02 over the 12 month period ($p=0.0000003$).

Conclusions

The Leicester City CCG pilot intervention was successful in reducing expenditure on people with COPD by reducing admissions to hospital, despite relatively small numbers of patients in the intervention. The savings delivered to the CCG were also sizeable, despite these small numbers. The intervention merits upscaling to numbers that would make cost savings a feasible concept.

P06. [101] Integrated management of allergic respiratory diseases

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Background

Allergen immunotherapy (AIT) has shown efficacy and safety in big clinical trials, involving patients with different sensitization profiles. Sublingual immunotherapy (SLIT) is a safe and effective modality of administration of AIT. In the last few years, important milestones for treatment of both allergic rhinitis (AR) and allergic asthma (AA) have been achieved by a large clinical development programme with SQ[®]HDM SLIT-tablet, a house dust mite (HDM) tablet SLIT product.

Methods

Results of clinical studies (MT-02, MT-04, MT-06) on SQ[®]HDM SLIT tablet have been revised, focusing the analysis on main outcomes for asthmatics.

Results

Patients with house dust mite (HDM) respiratory allergy, including patients with allergic rhinitis (AR), allergic asthma (AA), and co-existing AA and AR have been successfully treated for both conditions. Allergy immunotherapy has been shown to be effective and safe in AA and AR patients. It has been demonstrated that AIT with SQ[®]HDM SLIT-tablet can reduce the daily dose of inhaled corticosteroids (ICS) necessary to achieve a satisfactory asthma control and the probability of experiencing asthma exacerbations following ICS step-down.

Conclusions

AIT with SQ[®]HDM SLIT-tablet is safe and effective in asthmatic patients, and it should be considered an important therapeutical option for HDM-allergic asthmatics. These findings are in line with the concept of “one airway-one disease” which empathize that AR and AA are components of a single and complex inflammatory disease involving both upper and lower airways. Unfortunately, there is still an unjustified scepticism on AIT among clinicians, particularly in chest physicians. These results, together to the huge amount of scientific literature on AIT, should be convincing, also for clinicians other than allergists, that it is a valid therapeutical option both in AR and AA.

CONFLICT OF INTEREST STATEMENT: Enrico Heffler does not have any conflict of interest to declare.



P06a. [73] Bronchodilator response as a marker of poor asthma control

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Background

Asthma guidelines emphasise the importance of monitoring disease control in managing asthma. The relationship between asthma control and lung function is still debated.

Objective

The aim of this study was to evaluate the relationship between lung function, including bronchodilator response in terms of improving in FEV₁ after administration of salbutamol, and asthma control.

Methods

246 patients with known asthma and in regular chronic treatment according to international guidelines were consecutively enrolled in a 12 month-period. All patients were evaluated by asthma control test (ACT), spirometry and bronchodilator test with salbutamol 400 mcg. The study was approved by our Institutional Ethic Committee and patients signed an informed consent to take part to the study.

Results

Mean ACT value was 18.8. Patients with significant bronchial reversibility had lower ACT mean values. This finding was confirmed in both patients with airway obstruction and in those with normal spirometry. There was a significant correlation between ACT values and bronchodilator response.

Conclusions

The persistence of a significant degree of bronchodilator response despite regular treatment according to guidelines was a marker of worse asthma control.

No external funds for this study.

No conflict of interest to declare.

P07. [83] Socioeconomic and ethnic inequalities in COPD medicine use: a register-based study in Copenhagen, Denmark

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Background

Social inequalities in health is increasing in Denmark. With around 430,000 patients in Denmark, Chronic Obstructive Pulmonary Disease (COPD) is the disease that contributes most to social inequalities in health. Long-acting bronchodilators (LABD), [including long-acting beta-2-adrenoceptor agonists (LABAs), long-acting muscarinic antagonists (LAMAs), and fixed dose combination of inhaled corticosteroid (ICS) and LABA (LABA-ICS)], are recommended as first-line maintenance therapy for COPD patients. However, more than 40% patients who need pharmacotherapy in Copenhagen are not using any inhaled medication. This study aims at examining the association between COPD medication use, and ethnic background and indicators of socioeconomic position (SEP) among incident COPD patients diagnosed in 2003-2007 in Copenhagen.

Methods

This is a register-based cohort study with two main outcomes of interest: persistence with maintenance therapy and therapy reinitiation. Data on hospital contacts and prescriptions, as well as socio-demographic variables were retrieved from Danish national registers. Patients were divided into three therapy groups: monotherapy, two-drug therapy and combination therapy. Descriptive analyses were performed, and the Cox proportional hazards model was used in each therapy group to look at relationship between the outcomes and social factors, i.e. ethnic background, education, income and employment.

Results

1129 incident patients had at least one prescription of maintenance therapy. The median time for continuous LABD use was 67 days since diagnosis (95%CI not available). Among the 921 patients who terminated their therapy episode during follow-up, more than half (n=533, 57.9%) restarted a therapy episode after a pause, of which the median was 34 days. Patients with other ethnic background were less persistent (HR=1.40, 95%CI=1.03-1.90 for two-drug therapy). Unemployed subjects were more persistent than those who were employed or retired (HR=0.49, 95%CI=0.28-0.86 for monotherapy). Income and education were found insignificant for persistence. Neither SEP nor ethnic background had a significant association with therapy reinitiation.

Conclusion

Ethnic minorities, compared with ethnic Danes, are less persistent with maintenance therapies. Retirement is a risk factor for patient persistence.

P08. [40] Severe airflow limitation with some reversibility - asthma or chronic obstructive pulmonary disease, how to detect?

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Often patients older than 40 years with a smoking history of 10 pack-years have airflow limitation with some reversibility and the presence of a post bronchodilator FEV₁/FVC < 0.70. So it is difficult to detect is there asthma (A) or chronic obstructive pulmonary disease (COPD) using only spirometry. The mechanism of airflow limitation in patients with A and COPD is different. Using different lung functional methods can help to detect main cause of airways disorders.

Aims

To determine the usefulness of using the combination of different methods of an airways assessment to detect functional features in patients with A and COPD.

Methods

We selected patients with severe airways disorders (FEV₁ < 40% pred.) and some reversibility and known history of diseases. All patients were performed spirometry, bodyplethysmography, impulse oscillometry (IO) and investigation of lung elasticity (LE).

Results

There was no considerable difference between parameters spirometry and lung volumes in both groups. Patients with COPD (n=31) and A (n=18) had differed in LE and resistance by IO. Coefficient of retraction (CR) was 0.18±0.06 kPa/l in patients with COPD vs 0.32±0.08 in patients with A (p<0.001). Resistance at 5Hz was 194±31% pred. in patients with COPD vs 355±39 in patients with A (p<0.001). Resistance at 20Hz (R20) was 119±12% pred. in patients with COPD vs 226±25 in patients with A (p<0.001). Shunting of R20 increases with increase of lung parenchyma destruction. The relation Raw/R20 showed significant difference between patients with normal and decreased CR (1.04±0.31 and 2.11±0.37 accordingly, p<0.001).

Conclusions

All patients with A had severe airways disorders by spirometry and IO.

Patients with COPD had severe disorders by spirometry but less changes of resistance by IO.

Raw/R20 was about 1 or less in patients with normal LE and about 2 or more in patients with loss of lung elastic recoil.

Combination of spirometry, IO and bodyplethysmography may be useful to detect airways disorders connected with lung parenchyma destruction.

P09. [84] Exploration of High Dimensional Data and Validation of Metabolic Syndrome Biomarkers of Particulate Induced Lung Injury in World Trade Center Exposed Firefighters

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Introduction/ Rationale

We have previously shown that biomarkers of Metabolic Syndrome (MetSyn) can predict future World Trade Center lung injury (WTC-LI), defined as FEV₁ less than the lower limit of normal (LLN) after exposure to particulates during the events of 9/11. In a nested case-cohort control study, lipids, heart rate, and glucose were predictive. We now validate these findings in the cohort with available lipid and lung function measurements.

Methods

Biomarker expression was explored using hierarchical clustering and principal component on a subset of the larger cohort that had serum biomarkers available. Partial Least Squares Discriminant analysis of 21 biomarkers was further used to demonstrate segregation into WTC-LI cases and controls. We then examined all pulmonary function tests (PFT) until March 2015 of N=9648 World Trade Center rescue and recovery workers. We included firefighters with FEV₁≥LLN prior to 9/11. Of the remaining N=7711, N=787 developed WTC-LI and N=6813 had FEV₁≥LLN. We modeled the ability of biomarkers at the first post-9/11 exam to predict FEV falling below LLN at the most recent PFT with binary logistic regression.

Results

High-dimensional clustering showed clusters of multiple pathways involved with WTC-LI, including lipid-inflammatory, protease/antiprotease, and metabolic syndrome, Figure 1A, B, and C. Binary logistic regression shows that MetSyn biomarkers are significant predictors after adjusting for age, exposure intensity, and smoking, Table 1. Of interest, odds of developing WTC-LI were similar among smokers, fasting glucose>110, and dyslipidemia (1.37, 1.40, and 1.39 respectively).

Conclusion

Clustering analysis shows that metabolic derangement is associated with WTC-LI. We have validated the utility of the biomarkers traditionally used for metabolic syndrome to predict future lung injury in a larger population of exposed individuals. These biomarkers are associated with dyslipidemia, insulin resistance, and cardiovascular disease, and suggest that systemic inflammation can contribute to future lung function loss.

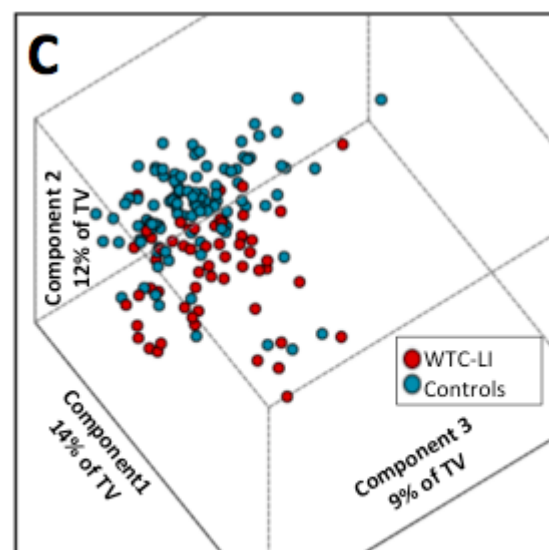
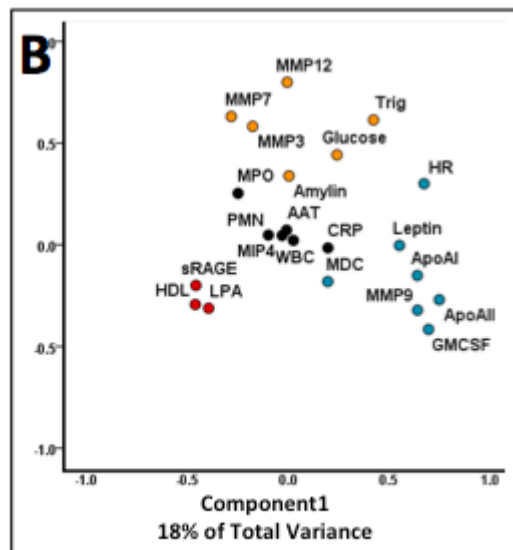
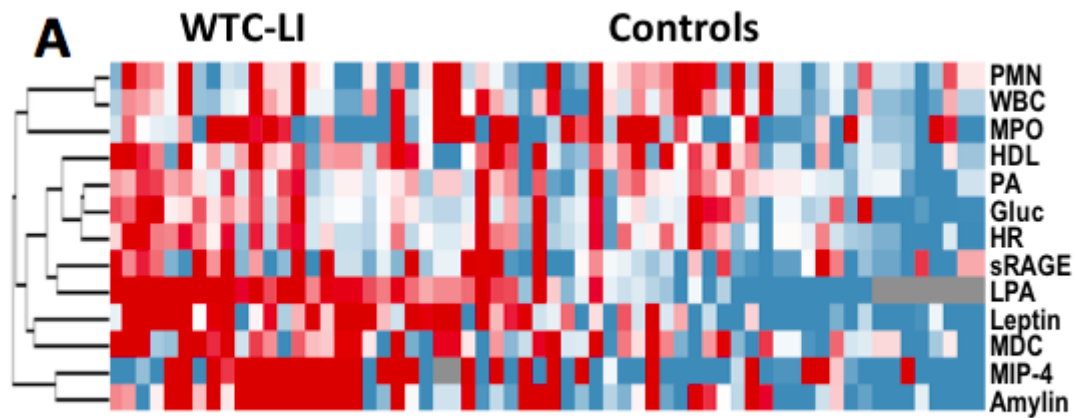


Table 1. Biomarkers of World Trade Center Lung Injury

Biomarker	OR	95% CI
SBP \geq 135mmHg	1.28	1.01-1.63
HDL<40, Trig>150	1.39	1.17-1.65
Glucose>110mg/dL	1.40	1.07-1.84
Smoker	1.37	1.18-1.59

Adjusted for exposure group and race.

-2 log likelihood = 5027.77; Hosmer Lemeshow p=0.748

P10. [109] Non-invasive Ventilation for Motor Neurone Disease with Bulbar Onset and Severe Bulbar Dysfunction

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Introduction

Motor neurone disease(MND)is a rapidly fatal neuromuscular disease.Respiratory failure(RF)remains the most common cause of death due to progressive respiratory muscle weakness.Although non-invasive ventilation(NIV)has been shown to improve survival in patients with preserved bulbar function,there is uncertainty about the role of NIV in those with bulbar onset and severe bulbar dysfunction.

Aim

To evaluate our current practice and assess the effect of domiciliary NIV on survival in MND patients with impaired bulbar function.

Method

Data from sequential MND patients referred to a Sydney tertiary University teaching hospital respiratory failure clinic was collected.Age,sex,forced vital capacity percentage predicted(FVC%)at initial consultation,length of survival from diagnosis were analysed for patients using domiciliary NIV between 2011&2014.

Results

During this period,35MND patients with RF(20 male,mean age 67years and FVC%81)were assessed. 19patients(54%)elected for domiciliary NIV and 2 were intolerant to treatment.17patients were successfully established on NIV in spontaneous/timed mode(89% success rate).Age and FVC%(mean±SD)of the NIV group were 65±17 and 77±28 vs. 69±13 and 85±28 in the non-NIV group.The number of patients established on NIV had increased(8 patients in 2014 vs. 3 patients in 2011).The majority of the NIV group(12 patients,71%) had impaired bulbar function.Seven MND patients had bulbar onset and severe bulbar dysfunction(age 66±11 and FVC%75±23).Mean survival was 309 days(95%CI 211-408) vs. 265 days(95%CI 89-443)in those without NIV(3 patients,age 79±9,FVC% 92±11).Mean survival in the NIV group with preserved bulbar function(10 patients,age 61±20,FVC% 78±32) was 543 days(95%CI 536-551) vs. 511 days(95%CI 469-554) in those without NIV(15 patients,age 69±12,FVC% 88±28).

Conclusion

There has been a progressive increase in NIV use for MND patients with RF from 2011-2014.The majority were successfully established on NIV after specialist respiratory assessment.MND patients with bulbar dysfunction is a challenging group.Although clinicians are rightly concerned about commencing NIV in those with bulbar impairment due to potential complications,this does not seem to be apparent in our data.Domiciliary NIV has favourable effects on survival in patients with preserved bulbar function while similar benefit is also conferred in those with bulbar onset and severe bulbar dysfunction.

P11. [118] Long term domiciliary nocturnal non-invasive ventilation (NIV) experience in a Sydney tertiary referral hospital between 2010 and 2014

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Background

Respiratory failure patients are increasingly using domiciliary non-invasive ventilation (NIV). Many have chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome (OHS), obstructive sleep apnoea (OSA) or multiple comorbidities. However, indications for NIV have not been well defined.

Objectives

To determine the primary indication for commencing nocturnal domiciliary NIV and to examine changes in prescription patterns over 5 years.

Methods

A retrospective analysis was conducted on data from a Sydney tertiary referral sleep & respiratory failure centre. NIV titration studies between 1st January 2010 and 31st December 2014 were analysed to assess the indications for NIV.

Results

218 patients used nocturnal NIV (138 males, 64%) with mean age of 66 +/- 17 years. Indications for commencing NIV are listed in Table 1.

Table 1. Indications for commencing nocturnal NIV

Primary Indication	2010	2011	2012	2013	2014	Total	Percentage (%)
COPD	10	4	4	3	7	28	13
Overlap syndrome (COPD +OSA)	8	4	11	8	7	38	17
OSA	20	13	7	26	26	92	42
OSA/OHS	7	3	5	4	11	30	14
OHS	1	0	3	0	5	9	4
Neuromuscular disease	5	3	2	2	6	18	8
Other (Palliation)	1	0	1	1	0	3	1
	52	27	33	44	62	218	

Conclusion

The use of long-term domiciliary NIV has increased over the last five years by 17%. OSA and OHS have increased by 20% and 14% respectively which is consistent with the growing obesity epidemic. OSA was the commonest indication, although most had other comorbidities (e.g. heart failure) necessitating NIV. The overlap syndrome was the second commonest indication and OHS was the fastest growing. These findings highlight the indications for and changes in NIV usage which will assist in prioritising resources for local NIV services.

Key Words: NIV, COPD, OSA, OHS, Indications

Conflict of Interest: None

P12. [41] Asthma, a risk factor for lower limit of normal FEV1/FVC among non-smoking Korean

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Backgrounds

Except for tobacco, risk factors for impaired lung function have not been researched. Due to the culultural difference, the risk factors for lung function impairment is different (i.e. indoor air pollution in Mongolia, coal and/or bio-mass smoke in China, and etc.). Although, for management of lung function impairment, it is important to know the etiology, however, there is few literatures for risk factors in Korean general population. Therefore, the risk factors for lung function impairment among the general non-smoking Korean population by sex stratification.

Methods

From the Korean National Health and Nutritional surveys IV and V, those with spirometry data (n=8164) were included in the present study. After the sex stratification, multiple survey logistic regression analyses were preformed to evaluate the assoication between potential risk factors and impaired lung function. The lower limit of normal in FEV1/FVC was used for outcome.

Results

For males and females, the proportion of lower limit of normal FEV1/FVC was 11.94% and 13.9%, respectively. After adjustment for age, residence, education status, household incomes, second-hand smoke, BMI, occupation, and comorbid (acute coronary syndrome, angina, old tuberculosis history), the asthma was significantly associated with lower limit of normal in FEV1/FVC (for males, OR=3.81, 95%CI=1.26-11.51; for females, OR=4.28, 95%CI=3.09-5.94).

Conclusion

The asthma was associated the impairment of lung function among non-smoking Korean population. To prevent further lung function impairment, a careful control system for asthma should be established at the health policy setting.



P13. [119] study of the correlations between exhaled nitric oxide and atopy status, FCER2 mutation, and asthma control in children

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Introduction

Fractional exhaled nitric oxide (FENO) is actually used as a biomarker of airway inflammation in asthma. The measurement of FENO is a feasibility test for diagnosis and treatment of children with asthma, especially for who are treated with inhaled corticosteroids (ICS).

Objectives

The aims of this study were to evaluate the correlations between FENO and atopy status, blood eosinophil levels, FCER2 mutation, and asthma control.

Subjects and Methods

It was a prospective and descriptive study. All children with uncontrolled asthma, presented at Consultation Department of National Paediatric Hospital (Hanoi, Vietnam), were included after IRB approval. They were followed up during 3 months to evaluate clinical status and asthma control.

Result

42 children with uncontrolled asthma with mean age of 9.7 ± 2.6 years (6 - 17 years) were induced in the present study. The male/female ratio was 2.5/1. The mean FENO levels were 25.7 ± 25.9 ppb. It was higher in patients with positive skin test for respiratory allergens ($p < 0.05$). FENO was significantly correlated with eosinophil levels in peripheral blood ($r = 0.5217$, $p = 0.0004$). There were 4/42 patients (9.5%) having mutation of FCER-2 gene (rest 28364072 SNP). In this group, the levels of FENO were also higher ($p < 0.05$). The levels of FENO were decreased after 3 months of treatment (16.7 ± 8.3 ppb; $p < 0.05$) with a negative correlation between FENO levels and inhaled corticosteroid (ICS) doses ($r = -0.3834$; $p < 0.01$). The levels of FENO were higher in partial controlled and controlled asthma children.

Conclusion

The measurement of FENO is a useful tool to predict clinical and genetic characteristics and asthma control levels in Vietnamese children. However, its role in long term follow-up of children with asthma in developing countries should be evaluated in the future.

P14. [106] Is there a relationship between Uric Acid, Uric Acid to Creatinine Ratio and Severity of AECOPD?

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Introduction

Acute exacerbation in chronic obstructive pulmonary disease (COPD) may result in a lot of systemic consequences due to hypoxemia and systemic inflammation.

Aim

We aimed to investigate uric acid levels and uric acid to creatinine ratio in COPD patients developing acute exacerbation.

Methods

We included 25 patients who had been admitted with acute exacerbation of COPD according to the GOLD diagnosis and treatment guidelines between May and December 2011. Uric acid and creatinine levels were recorded from blood samples of the patients.

Results

Average uric acid and uric acid to creatinine ratio values were 5.7 ± 2.09 mg/dl and 7.32 ± 3.0 in patients with mild hypoxemia, 6.4 ± 2.1 mg/dl and 7.01 ± 2.9 in those with moderate hypoxemia, and 6.7 ± 2.0 mg/dl and 9.1 ± 1.8 in those with severe hypoxemia, respectively. While no statistically significant correlation was found between uric acid levels and uric acid to creatinine ratio in the three groups ($p=0.97$, $p=0.76$, respectively), these values were found to increase along with increasing severity of hypoxemia.

Conclusion

Uric acid levels and the ratio of uric acid to creatinine remained unchanged while severity of hypoxemia increased during acute exacerbations of COPD, however, these values were found to increase with increasing severity of hypoxemia.



P15. [91] Impact of the delivery site of antibody fragments within the lung on their local residence time

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Aim

Pulmonary delivery of PEGylated monoclonal antibody (mAb) against cytokines offers a targeted therapy, thereby enhancing the efficacy of asthma treatment. However, the site of delivery within the lung may influence the clearance of mAbs from the lung. Therefore, in this study, we examine the residence time of PEGylated anti-IL17-Fab' in the lung after delivery to the deep lung or to central airways and evaluated the effect of polyethylene glycol (PEG) size on the residence time.

Methods

Site-specific PEGylation of anti-IL17-Fab' was carried out using linear 20 kDa PEG or two-armed 40 kDa PEG. Transport of the mAb through the respiratory epithelium was analyzed Calu-3 cells cultured at an air-interface. For residence time studies, mAb were delivered to the deep lung or central airways. At different time points post-delivery, samples were collected to determine the presence of mAb. In a second experiment, inflammation was induced in mice by intratracheal instillation of LPS and clearance of mAb in the inflamed lung was evaluated after delivery to the deep lung.

Results

We found a more prolonged residence of PEGylated Fab' on the apical side of Calu-3 cells than that of Fab' alone. Similarly, residence time studies in mice highlighted that Fab' was cleared more rapidly compared to PEGylated Fab' after deep lung or central airway delivery. mAb resided longer in the lung following delivery to the deep lung than after delivery to central airways. However, PEG size had minimal effect on residence time. In addition, PEG-Fab'- residence in the lung was not affected by the enhanced mucus that is produced during inflammation.

Conclusions

PEGylation of mAb greatly enhances the residence of mAb in the lungs, which is not affected by inflammation and enhanced mucus in the lung. Delivery site in the lung alters the residence time of mAb in the lungs. To conclude, PEGylation of mAb might help to enhance the efficacy of antibody therapy in asthma and other respiratory diseases.

P16. [75] Multi-dimensional response to out-patient pulmonary rehabilitation in COPD and COPD-Asthma Overlap syndrome: Retrospective Study

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Background/Aim

Pulmonary rehabilitation (PR) is an endorsed therapy for COPD. Recently there is increasing awareness on COPD-Asthma overlap syndrome, yet their response to PR is unknown. This study aimed to outline the multidimensional response to out-patient PR in patients with a primary diagnosis of COPD (Group A) and COPD-Asthma overlap syndrome (Group B) who completed the same PR program.

Method

A retrospective review was conducted on 40 patients (COPD n=26; COPD-Asthma overlap syndrome n=14) who had completed an 8 weeks of out –patient PR and 12 months review. The outcome measures were 6-minute walk distance (6MWD), CAT Score, Chronic Respiratory Disease Questionnaire (CRQ), Body Mass Index (BMI), ground walking duration per day and days per week.

Results

Both groups demonstrated significant improvements in 6MWD, CAT Score, CRQS total score, ground walking duration per day and days per week immediately following PR. At 12 months, these improvements remained significantly higher than baseline only in CAT score, ground walking duration per day and days per week in both groups. Interestingly, a significant difference in CRQ was observed only in Group B ($p<0.05$) compared to Group A ($p>0.05$).

Conclusion

This study supports the need to consider the multidimensional response to evaluate the efficacy of out-patient PR, as response is differential in patients with COPD and COPD-Asthma overlap syndrome. Further prospective RCTs are warranted to validate these findings.

P16a. [76] Longitudinal Changes in FEV1,Hyperinflation,and 6-Minute Walk Distance in Patients with Frequent Exacerbations of Chronic Obstructive Pulmonary Disease and Their Impact to the Hospitalisation and ICU Admission Rate.

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Background

In chronic obstructive pulmonary disease (COPD), a decreased inspiratory capacity to total lung capacity ratio (IC/TLC) is associated with dynamic hyperinflation and poor exercise capacity. The relationship among hyperinflation, FEV1, and 6-minute walk distance in patients with advanced COPD with frequent exacerbations (>2 per one year) has not been previously described. We hypothesized that frequent exacerbations of advanced COPD (CIII and DIV GOLD stages) affects IC/TLC ratio and exercise capacity (6MWD).

Objective

The aim of our study was to assess the impact of exacerbation rate to dynamic hyperinflation and exercise capacity and through assessment these to assess the hospitalisation and ICU admission in patients with advanced COPD.

Methods

We prospectively measured lung function and 6MWD in 56 patients with advanced COPD, one year apart. The patients were classified according to frequency of exacerbation: 29 patients with frequent exacerbation (>2 per one year) and 27 patients with non-frequent exacerbation (<2 per one year).

Results

Patients with frequent exacerbation had reduced lung function, static hyperinflation (IC/TLC < 25%) and reduced 6MWD compared with the non-frequent exacerbation COPD subjects on all three evaluations ($p < 0.01$). There was a statistically significant deterioration in IC/TLC and 6MWD after 1-year follow-up in the frequent exacerbation COPD compared with non-frequent exacerbation COPD ($p < 0.001$). More hyperinflation (IC/TLC < 0.25) was associated with lower FEV1 and 6MWD ($p < 0.001$). More hyperinflation and lower 6MWD were associated with more frequent hospitalisation and ICU admission ($p < 0.01$). Multivariate analysis determined that the frequent exacerbation is a significant factor associated with a more higher level of dynamic hyperinflation and a more lower level of 6MWD.

Conclusions

FEV1, and 6MWD are reduced in patients with COPD with frequent exacerbations and a more significant reduction of these data was noted in hyperinflation. The evidence of longitudinal deterioration was not seen in non-frequent exacerbation COPD subjects. More significant hyperinflation, more lower lung function and more lower 6MWD were associated with more frequent hospitalisation and ICU admission of patients. These findings suggest that in patients with advanced COPD with frequent exacerbations, by reducing the exacerbation rate of the disease, the decline of lung function, decreased dynamic hyperinflation and improved 6MWD might be decreased.

P17. [53] Activin-A is over-expressed in severe asthma and is implicated in angiogenic processes

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Background/Aims

Activin-A is a pleiotropic cytokine involved in the regulation of allergic inflammation. Its role in the regulation of angiogenesis, a key feature of airway remodelling in asthma, remains unexplored. The aim of this study was to examine the expression of activin-A in asthmatics of varying severity, exploring possible associations with airway angiogenesis especially in severe asthma, and further investigate the effects of activin-A on angiogenesis *in vitro*.

Methods

Expression of activin-A and its protein receptors, ALK-4 and Act-R1IA, was measured in the serum, bronchoalveolar lavage fluid (BALF) and endobronchial biopsies from 16 healthy controls, 19 mild/moderate and 22 severe asthmatics by means of ELISA, immunohistochemistry and immunofluorescence, and associated with pulmonary function and markers of airway remodelling, including angiogenesis. The effects of activin-A on baseline and vascular endothelial growth factor (VEGF)-induced human pulmonary (HPMEC) and umbilical vein (HUVEC) endothelial cell responses were examined by proliferation assays and an *in vitro* angiogenesis model. VEGF signalling (VEGFR1/VEGFR2/soluble (s)VEGFR1), as well as pro- and anti-angiogenic cytokine release (IL-17, IL-18, IL-32) were investigated, by means of real-time PCR and ELISA, in the presence/absence of activin-A, VEGF, IL-13 and activin-A neutralising antibody. Cytokine release was compared with BALF concentrations of these cytokines *in vivo*.

Results

Activin-A expression was significantly elevated in the serum, BALF and bronchial tissue of the asthmatics, while expression of its protein receptors was reduced. Endothelial expression of ALK-4/Act-R1IA was also reduced in the presence of IL-13 *in vitro*. Activin-A suppressed VEGF-induced endothelial cell proliferation and angiogenesis, inducing autocrine production of anti-angiogenic soluble (s)VEGFR1 and IL-18, while reducing production of pro-angiogenic VEGFR2 and IL-17. In parallel, BALF concentrations of sVEGFR1 and IL-18 were significantly reduced in severe asthmatics *in vivo* and inversely correlated with angiogenesis.

Conclusions

Activin-A is over-expressed and has anti-angiogenic effects *in vitro* that are not propagated *in vivo*, where reduced basal expression of its receptors is observed especially in severe asthma.

P18. [102] Educational diagnosis and Chronic Obstructive Pulmonary disease (COPD): first stage of rehabilitation.

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The management of COPD is complex .It combines medication for respiratory rehabilitation. The latter combines several components such as: education, nutrition, exercise

The educational diagnosis is the key step in the therapeutic education of patients with COPD ; because it allows the planning of an educational program tailored to support population

The aim of our study was to evaluate the knowledge ; attitudes and practices of COPD patients recruited pulmonology consultation level .

Population: 33 male patients , average age 58 years (51 - 75 years) 75% ex -smokers .A questionnaire exploring their knowledge, attitudes and practices regarding the disease has been developed .It was administered to patients indirectly in their language.

Results

82% did not use the term COPD or Chronic Obstructive Pulmonary designer for the affection they suffered. Only 12% knew the meaning of the acronym COPD. As a cause of this condition : 57 % of subjects identify tobacco, 63 % mentioned a hereditary factor and 9 % believe that COPD is a contagious disease. 76 % identified the lung as the organ reached during this condition.

If 15% of patients surveyed believe that we can cure this disease , 63% describe it as a serious disease for various reasons. Confinement to bed is the priority element connected to gravity. About 40% of exacerbations management are not able to recognize worsening and 40 % do not know properly use the inhaler device .

Use of physician:36 % use only in emergencies. In case of worsening of their symptoms 24% expect the appointment with the doctor.

From a therapeutic point of view , only drugs are mentioned , exercise such as walking is not mentioned. But 51 % use traditional means.

The information gathered will allow us to develop a therapeutic education program adapted to our population, choice of language, development of objectives , choice of content and educational techniques.

P18a. [107] Levels of antioxidant enzymes and CRP in patients with COPD and metabolic syndrome (MS) and their association with obesity

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Introduction

Patients with metabolic syndrome (MS) have been recently recognized as a distinct phenotype in the COPD population. Antioxidant enzymes and CRP play key role in the pathogenesis of both COPD and MS.

Aim

The aim of the present study was to investigate the levels of CRP and antioxidant enzymes superoxide-dismutase (SOD) and glutathione-peroxidase (GPx) in patients with COPD and MS, compared to those without the syndrome and their association with the indices of overall and abdominal obesity.

Patients and Methods

A cross-sectional study was performed among 183 COPD patients (mean age 65.6±7.3) and 103 subjects without respiratory diseases served as a control group (mean age 52.97±6.3). The presence of MS was identified by the IDF criteria. BMI and waist circumference were calculated and the levels of SOD, GPx and CRP were measured.

Results

The prevalence of MS was 48.1% in COPD cohort vs. 39% in the control group. COPD patients had significantly higher BMI and WC compared to the control group ($p<0.001$). The levels of antioxidant enzymes were significantly lower in COPD patients presenting MS (GPx 37.1±6.1 U/gHb; SOD 1203.3±149.5 U/gHb), compared to those without the syndrome (GPx 38.5±7.8 U/gHb; SOD 1220.2±175.5 U/gHb) and the control group (GPx 40.4 ± 38 U/gHb; SOD 1264.5 ± 120.5) ($p<0.05$). In obese patients (BMI >35) the levels of SOD and GPx were significantly lower compared to overweight patients and those with normal BMI ($p<0.05$). The levels of CRP were significantly higher in patients with COPD and MS, compared to COPD patients without the syndrome and the control group ($p<0.05$). Linear regression analysis showed significant negative association between antioxidant enzymes and waist circumference (WC) ($\beta=-0.243, p<0.001$ for SOD; $\beta=-0.191, p=0.002$ for GPx) and BMI ($\beta=-0.143, p=0.016$ for SOD; $\beta=-0.149, p=0.012$ for GPx).

Conclusion

The present study demonstrates decreased antioxidant defense and increased inflammation in patients with COPD and MS and association between antioxidant enzymes and the indices of overall and abdominal obesity.

P19. [105] Clinical, Functional Characteristics and Exercise Capacity of the Frequent Exacerbator COPD Phenotype

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Introduction

Exacerbator phenotype is one of the described COPD phenotypes and frequent exacerbators are characterised by the presence of at least two exacerbations or one hospitalized exacerbation in the previous year.

Aim

We aimed to describe the clinical, functional characteristics and exercise capacity of frequent (FE) and infrequent exacerbator (IE) COPD patients.

Methods

We conducted a case-control study. Based on their frequency status in the previous year, COPD patients were classified as FE(≥ 2 events) or IE(< 2 events). Modified Medical Research Council (mMRC) Dyspnea Scale, CAT, spirometry and six-minute walking test (6MWT) were performed. Co-morbidities were quantified by the Charlson Comorbidity Index (CCI). BODE indices of the study subjects were calculated.

Results

Sixty COPD patients and 26 healthy controls with a ≥ 10 pack-years of smoking history were consecutively enrolled. COPD patients were subgrouped as FE-COPD (n=33) and IE-COPD (n=27). Postbronchodilator FEV₁/FVC and postbronchodilator FEV₁% were significantly reduced in FE-COPD. Based on the GOLD criteria 90% of the IE-COPD group comprised of moderate and severe COPD patients, while 75% of the FE-COPD group included severe and very severe COPD patients (p=0.013). The mMRC and CAT scores were significantly higher in FE-COPD group as compared with IE-COPD. BODE indices were significantly higher in FE-COPD group than the IE-COPD patients (5[3-8]vs.2[1-3], p=0.0001). 6MWD was lower in FE-COPD group than the IE-COPD patients (195[120-360] vs. 400[359-420], p=0.0001). The number of exacerbations were significantly correlated with CAT score (r=0.67, p=0.0001), mMRC score (r=0.59, p=0.0001), BODE index (r=0.59, p=0.0001), 6MWD (r=-0.49, p=0.001), FEV₁% and FEV₁/FVC (r= -0.42, p=0.001 and r= -0.36, p=0.007).

Conclusion

In the present study FE-COPD patients had more severe airway obstruction, higher symptom scores, lower exercise capacity, higher BODE indices supporting to be evaluated in a distinct phenotype. Significant correlations were observed among the number of exacerbations, higher symptom scores, higher BODE indices and lower exercise capacity. BODE index known as a good predictor of survival could anticipate a frequent exacerbator phenotype in COPD.

P19a. [110] Effects of the inhibition of RhoA signaling pathway on TGF β 1-induced myofibroblastic differentiation of bronchial fibroblasts derived from asthmatic patients

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Background

Fibroblast to myfibroblast transition (FMT) plays an important role in bronchial wall remodeling, which is crucial for asthma development. Chronic inflammation of the airways is the major inducer of airway tract remodeling, because it causes overproduction of pro-inflammatory cytokines and growth factors. These include TGF- β ₁ which is the most important FMT stimulator. Our previous studies revealed the differences in the cytoskeleton architecture of unstimulated human bronchial fibroblasts (HBFs) derived from asthmatic (AS) and non-asthmatic (NA) patients. In comparison to NA HBFs, AS HBFs formed thicker and more aligned 'ventral' stress fibers, attached to mature focal adhesions [1]. These differences correlated with a higher elastic modulus of AS HBFs and their increased predilection to TGF- β ₁-induced FMT [2]. Because RhoA-dependent pathway(s) regulate actin cytoskeleton rearrangements and stress fibers formation, RhoA activity may account for the differences between AS and NA HBFs [3]. However, the involvement of RhoA in FMT remains unaddressed.

Experimental Model and Methods

HBFs, isolated from bronchial biopsies derived from asthmatic and non-asthmatic patients, were cultured in DMEM supplemented with 10% FBS. For endpoint experiments, the cells between 5th-15th passage were used. HBFs were plated in serum-free conditions, pre-treated with RhoA-pathway inhibitors (rhosin, Y-27632, SMIFH2) and stimulated with TGF- β ₁ to induce myofibroblastic differentiation. FMT efficiency (relative number of α -SMA+ cells) was estimated with immunofluorescence, whereas PCR and Western blot were used for the analyses of FMT-related gene expression and protein levels.

Results and Conclusions

Chemical inhibition of RhoA and/or its effectors attenuated TGF- β ₁-induced FMT in HBFs populations derived from asthmatic patients. It indicates that the cross-talk between RhoA- and canonical TGF β /Smad-dependent pathway regulates α -SMA expression in 'asthmatic' HBFs and determines the efficiency of their myofibroblastic differentiation.

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P19b. [112] Effects of the sulforaphane on TGFβ₁-induced fibroblast-to-myofibroblast transition in bronchial fibroblasts derived from asthmatic patients

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Background

D,L-sulforaphane [SFN] is a natural isothiocyanate produced by enzyme-myrosinase-during the mechanical damage of fresh plant tissue from cruciferous vegetables such as broccoli. Many studies indicate multi-targeted sulforaphane properties like anti-inflammatory, anti-fibrosis and anti-bacterial activity and potential cancer prevention [1,2]. Bronchial asthma is characterized by persistent airway inflammation and airway wall remodeling in which fibroblasts-to-myofibroblasts transition [FMT] takes part [3]. Previous *in vitro* studies show that human bronchial fibroblasts [HBFs] derived from asthmatic patients demonstrate enhanced differentiation into myofibroblasts after TGFβ₁ treatment [4]. Activation of TGFβ₁/Smad signaling pathway leads to up-regulation of profibrotic proteins, including α-smooth muscle actin [α-SMA] - the major marker of FMT. Furthermore, the cross-talk between TGFβ₁/Smad signaling and Nrf2-dependent pathway participate in regulation of crucial determinants of fibrotic diseases [1].

Experimental Model and Methods

In vitro cell cultures of primary human fibroblasts from bronchial 'asthmatic' biopsies were treated with SFN (1-15μM) and stimulated with TGFβ₁ to induce myofibroblast differentiation. Cell viability and proliferation were determined and non-toxicity concentration of SFN was selected to further studies. Relative number of α-SMA positive cells (FMT efficiency) and phospho-Smad translocation into the cell nucleus were estimated with immunofluorescence. Moreover, immunoblotting was used for the determining expression of FMT-related protein and phospho-protein levels.

Results and Conclusions

Our research demonstrate that SFN (up to 5 μM concentration) has no influence on 'asthmatic' HBFs viability and proliferation. Nevertheless, SFN attenuates FMT by the inhibition of α-SMA expression. Surprisingly it is not directly associated to TGFβ₁-induced Smad2/3 phosphorylation but probably related to TGFβ₁/Smad and Nrf2-dependent pathway cross-talk. Our data suggested the possible application of SFN to prevent the bronchial wall remodeling in asthma.

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