6th INTERNATIONAL WORKSHOP ON LUNG HEALTH
New approaches to respiratory diseases

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Abstract Leaflet

Organising Associations

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Background
Chronic obstructive pulmonary disease (COPD) is currently one of five diseases that are characterized by the highest death rate. Cardiovascular events constitute an important reason thereof. The aim of our study was to assess the total CVR in patients with COPD of severe course for predicting the development of cardiovascular accidents, as well as the ways to justify the correction of total CVR for each patient.

Materials and methods
We examined 29 men with severe course of COPD in stable phase of pathological process (average age - 65.4 ± 2.6 years). In relation to smoking, patients were distributed as follows: 28 (96.6%) of them were "active smokers" in the past or at present, duration of smoking was 36.4 ± 3.9 years, the index "pack / year" - 38.8 ± 2.5; one (3.4%) patient had never smoked.
General clinical methods of physical examination were conducted with mandatory measurement of blood pressure (BP). The criteria for inclusion of patients in the study were: verified COPD (FEV1 <80% of the appropriate volume, FEV1/FVC <0.7). To determine the degree of total CVR, demographic indicators (age, gender), attitude to smoking (smoker / non-smoker), systolic blood pressure and total cholesterol in the blood serum (mmol / l) were determined for each patient.

Results and discussion
All examined patient had rather severe bronchial obstruction, FEV1 level in post-test was 45.9 ± 2.19% of appropriate volume, ratio of FEV1/ FVC - 0.47 ± 0.12.
Depending individually on the cumulative value of CVR calculated by SCORE, the examined patients were attributed to one of the categories (Table 1).

Table 1

<table>
<thead>
<tr>
<th>No.</th>
<th>CVR degree</th>
<th>Number of patients, abs. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Very high</td>
<td>20 (69.0)</td>
</tr>
<tr>
<td>2.</td>
<td>High</td>
<td>9 (31.0)</td>
</tr>
<tr>
<td>3.</td>
<td>Moderate</td>
<td>–</td>
</tr>
<tr>
<td>4.</td>
<td>Low</td>
<td>–</td>
</tr>
</tbody>
</table>

Conclusions
1) COPD patients with severe course in general are attributed to people with relatively high risk of adverse cardiovascular events;
2) in patients with COPD with severe course, the very high overall CVR is nearly 70%, high - 30%; which suggests that moderate and low overall CVR in these patients is extremely rare;
3) management of patients with COPD of severe course requires actions aimed at correcting the RF, which can still be modified, weight loss, smoking cessation, increased physical activity, blood pressure control and lipidogram indicators.
Using of combination of inhaled medicines, which include inhaled corticosteroids and long-acting beta-2-agonist in the treatment of patients with severe chronic obstructive pulmonary disease (COPD) is promising.

**Aim**
That is why the aim of our study was to evaluate the clinical efficacy and safety of the new combined medicine Bufomix (ORION, Finland), which includes budesonide and long-acting beta-2-agonist formoterol during the 8-week course of treatment of the patients with severe COPD.

**Material and methods**
28 patients with severe COPD were included to the study. The Effectiveness of treatment was assessed before and after 4 and 8 weeks since inclusion patients in the study. The assessment was based on clinical symptoms, and dynamic of the lung function. The safety of the drug was evaluated by the occurrence of side effects in patients.

**Results**
After 4 weeks of treatment in patients with COPD was generally noted positive dynamics of clinical parameters (tabl.1), although changes in functional parameters (FEV1, FVC) were unreliable. After 8 weeks of treatment, individual performance or kept on the reached level or even slightly increased (tabl.2).

**Conclusion**
It was shown that the Bufomix well tolerated and can be recommended as a drug of choice for treatment of the patients with severe COPD.

### Dynamic of the cough and dyspnea in COPD patients

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Steps of the study</th>
<th>before the inclusion</th>
<th>in 4 weeks</th>
<th>in 8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough, score</td>
<td>1,69±0,12</td>
<td>0,69±0,10*</td>
<td>0,25±0,09*</td>
<td></td>
</tr>
<tr>
<td>Dyspnea, score</td>
<td>2,52±0,41</td>
<td>1,60±0,23*</td>
<td>1,02±0,11*</td>
<td></td>
</tr>
<tr>
<td>* – p&lt;0,05</td>
<td> </td>
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<td></td>
</tr>
</tbody>
</table>

### Dynamic of the lung function in patients with COPD in the post-test

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Steps of the study</th>
<th>before the inclusion</th>
<th>in 4 weeks</th>
<th>in 8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1, %</td>
<td>41,4±2,77</td>
<td>45,9±3,21</td>
<td>48,3±3,28</td>
<td></td>
</tr>
<tr>
<td>FVC, %</td>
<td>92,2±4,17</td>
<td>93,4±3,85*</td>
<td>94,9±4,26*</td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>0,45±0,12</td>
<td>0,49±0,11</td>
<td>0,51±0,14</td>
<td></td>
</tr>
<tr>
<td>* – p&lt;0,05</td>
<td> </td>
<td> </td>
<td> </td>
<td></td>
</tr>
</tbody>
</table>
Background
most often on the clinical outcomes of elderly patients with COPD affected to a greater extent of cardiovascular and metabolic pathology, than to the bronchial obstruction.

The aim of the work - to study the frequency and severity of comorbidity as a ischemic heart disease, arterial hypertension, atherosclerosis, obesity and diabetes mellitus in COPD patients.

Materials and methods
we examined 44 patients with COPD - 34 men, average age - 62,7 ± 5,57, history of the COPD - 17,7 ± 4,11, smoking history - 31,4 ± 5,71. All patients were clinically examined, and the main CVD factors were assessed: blood pressure, total cholesterol (TC), blood glucose (G), body mass index (BMI).

Results
12 (27.3%) patients had a history of coronary artery disease; in 7 (15.9%) - type II of diabetes mellitus, hypertension - in 21 cases (47,7%) persons. Excess body weight had 11 (25%) patients (average BMI - 47,7 ± 6,21), and obesity of the 1-st degree - 9 (20.5%) patients (average BMI - 33,7 ± 4,92). Hypercholesterolemia identified in 15 (54.1%) patients ( TC average - 6,7 ± 1,32), hyperglucosemia - in 5 (11.4%) patients (average level of glucose - 7,2 ± 1,1), in 10 (22.7%) patients were identified violations of cardiac conduction in the form of AV block of 1 degree or bundle branch block.

Conclusions
the majority of the observed COPD-patients had cardiovascular or comorbidity. This group of patients require lifestyle modification, carrying out of the medical therapy aimed to correcting dyslipidemia, hyperglucosemia and to achievement of the target blood pressure values, according to the adopted recommendations. These measures should help to reduce the severity of the manifestations of the cardiovascular problems in this category of COPD patients that undoubtedly will influence on the course of COPD.
Background
Solid organ transplantation provides life saving treatment for many patients with end stage organ disease. These patients are at constant risk for opportunistic infections, drug related pulmonary toxicities and malignancies due to their chronic state of immunosuppression. A transplant recipient’s susceptibility to pulmonary complications is multifactorial. Nosocomial, donor and recipient exposures occurring at predictable intervals after organ transplantation contributes to the occurrence of pulmonary complications.

Aim
To evaluate the spectrum and period of occurrence of pulmonary complications in renal transplant recipients (RTR) under tacrolimus based triple immunosuppression (TBI).

Method
A prospective observational study was carried out in the RTR under TBI admitted with respiratory complaints from June 2016 to April 2018. Institutional ethical clearance was obtained for carrying out the study. Informed consent was obtained from all the patients included in the study. Data pertaining to the study such as transplant parameters, clinical profile, associated risk factors, radiological findings, blood parameters, sputum/BAL culture reports, response to appropriate treatment were obtained and analyzed.

Observation
The total number of renal transplants done in our centre till the time of study was 1384. TBI was started from 2010 in our centre. During the period of study 42 incidents of pulmonary complications occurred in 37 RTR under TBI. Pulmonary complications were categorized as 0-1 month, 1-6 months and >6 months post transplantation. In the category 0-1 month post transplantation 12 incidents (29%) were recorded and among them bacterial pneumonia (8 cases-67%) was the most common complication. In 1-6 months post transplantation 11 incidents (26%) occurred. And this group was dominated by bacterial pneumonia (3 cases-27%). In the >6 months post transplantation category 19 incidents (45%) occurred and polymicrobial infection (4 cases- 21%) was the most common. The pulmonary complications due to infective cause comprised around 36 cases (86%). Only 6 cases (14%) were recorded to be non-infectious. The reported non-infectious pulmonary complication was acute pulmonary edema due to graft dysfunction (5 cases- 83%) and acute cellular rejection (1 case-17%). The infectious pulmonary complications comprises of 12 bacterial pneumonia (33%), 4 fungal pneumonia (11%), 5 mycobacterial lung infections (14%), 7 polymicrobial(19%) infections. No growth in sputum/BAL culture was observed in 8 cases(22%). Mycobacterial infection was most common in the >6months post transplantation category. Most of the patients responded to appropriate antibiotic therapy. 6 patients (16%) expired due to pulmonary complications.

Conclusion
Pulmonary complications are important causes of morbidity and mortality in renal transplant recipients. Effective immunosuppression has led to increase in infectious complications in renal transplant recipients. In our study, bacterial pneumonia was the most common pulmonary complication in RTR and its incidence was highest during the first month of immunosuppression, followed by polymicrobial infection. Infectious pulmonary complications were the most common cause of death in the study group.
P05. [232] New formulation approach for dry powder inhalers to improve CF/COPD inhalation therapy

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Background
The chronic bacterial infection and/or acute bacterial exacerbations leads to serious complications in the case of cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD). Inhaled formulations, through the pulmonary entry gate, allow local treatment of these diseases, in fact have a number of benefits over oral medications. The production of inhalation forms is an important task of pharmaceutical technology developments. Currently, two antibiotic agents are commercially available on the market, inhaled tobramycin and aztreonam. Ciprofloxacin could be found in a clinical phase III status in this respect. Recently, the spread of dry powder inhaler (DPI) products is most noticeable, compared to the pressurized aerosols since their use is more advantageous in many ways. According to the formulation approaches of DPIs basically, a traditional, carrier-based; and carrier-free systems can be separated. However, both formulations have advantages and disadvantages also.

Aim
Preparation and investigation of a new ciprofloxacin hydrochloride (CIP) containing DPI formulation, which combines the advantageous properties of the two above-mentioned DPI types to more effective, targeted lung therapy.

Methods
By DPI development, the selection of the appropriate excipients and the elaboration of a technology protocol have paramount importance. Then, following the production of the samples, investigation of their physicochemical characteristics and determination of the aerodynamic behavior by *in vitro* lung model as a pharmaceutical technological task will be the next steps. These are supplemented by the *in silico* lung modeling, which is already working specifically with patient-specific parameters. Optimized products for *in vivo* studies may also perform. During the present work, CIP containing DPI compositions were prepared and investigated. We have created as a reference products a traditional, carrier-based DPI, - which is formulated to be the same as the most of the commercial products - and a carrier-free sample, which contained sodium stearate as an excipient. By combining the advantages of the two above-mentioned DPI types, we have produced a novel formulated sample - spray-dried drug on a surface-modified carrier -. The physicochemical properties were characterized, and the aerodynamic values of the samples were examined based on the Andersen Cascade Impactor *in vitro* lung model, furthermore, we investigated the *in silico* behavior of the samples, too.

Results
The results of the pharmaceutical form will be highlighted which are consistent with the results of physicochemical examinations. Based on the results of the *in vitro* lung model, the novel formulated DPI has the best lung deposition results (approximately three times better than a traditional, carrier-based product), it is related to the fact that the mass median aerodynamic diameter of this product is the smallest, and this sample is well got out during inhalation from the capsule/device. By the *in silico* model, a high lung deposition was detected, too, which is consistent with the *in vitro* measurement results.

Conclusion
The novel combined formulated DPI of CIP can increase the effectiveness and targeting of the lung antibiotic therapy.

Acknowledgment
This work was acknowledged by the Ministry of Human Capacities, Hungary grant 20391-3/2018/FEKUSTRAT and supported by the EFOP-3.6.3-VEKOP-16-2017-00009 project.
**P06. [47] Significance of cardiovascular evaluation in patients with moderate Chronic Obstructive Pulmonary Disease (COPD)**

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This article declare all commercial interests

**Introduction**

Chronic obstructive pulmonary disease (COPD) with prevalence 5-13% is a major cause of morbidity and mortality in the world and fourth leading cause after myocardial infarction, malignant diseases and cerebrovascular incidents. The main cause of morbidity and mortality in COPD patients are cardiovascular diseases. COPD is an independent cardiovascular risk factor even in mild and moderate stage of the disease, due to persistent low-grade systemic inflammation. Early diagnosis and treatment of cardiovascular morbidity in COPD patients is important for improving life quality and prognosis.

**Aim**

To evaluate cardiovascular morbidity in patients with moderate COPD.

**Material and methods**

Cross-sectional study. Investigated group: 63 patients (40 male, 23 female) with diagnosed moderate COPD (forced expiratory volume in 1st second - FEV1 50-80%) according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria and according to ABCD classification: 60% (B), 40%(A). Control group - 30 subjects with normal spirometry (without COPD) as controls. Inclusion criteria for both groups: age 40-75, cigarette smoking history >=10 pack/years, signed consent for participation and clinically stable condition at least 6 weeks prior enrolment. Exclusion criteria: other chronic or acute pulmonary disease, diabetes mellitus, valvular heart disease, left ventricular hypertrophy, body mass index>35 kg/m², liver or renal failure, anaemia, muscle disorders, patients who do not want to participate. All patients underwent pulmonary function tests (spirometry and gas analysis), chest-X ray in two directions (postero-anterior and latero-lateral position), resting electrocardiogram (ECG), 24 hour-ECG-Holter monitoring, two-dimensional (2D)Doppler echocardiography, Doppler-ultrasound of lower limb and carotid arteries.

**Results**

The COPD group showed significantly higher prevalence of right ventricular (RV) abnormalities. RV systolic dysfunction was present in 47,61%, pulmonary hypertension (PH) in 23,8%, tricuspid regurgitation as most frequent valvular abnormality in 14,28%, left ventricular (LV) systolic dysfunction in 14,28%. Electrocardiography results obtained premature ventricular (PVCs) contractions in 6,34%, p-pulmonale in 7,93%, right bundle branch block (RBBB) in 4,76%. There was significant difference between normal ECG findings in patients with moderate COPD 8,33% versus 76,67% in control group. 24-hour-ECG-Holter monitoring allowed detection of arrhythmias in asymptomatic patients, and detected abnormalities were significantly higher compared to resting ECG. 24h-ECG-Holter monitoring revealed premature supraventricular (PSCs) contractions in 38,1%, sinus tachycardia in 33,3%, PVCs in 47,6%, PVCs pairs in 14,3%, PVCs couplets in 9,5%, un-sustained ventricular tachycardia in 4,8%. Carotid plaques without stenosis were detected in 33,3%, with stenosis less than 40% of the arterial lumen in 9,5%, with stenosis 40-60% of the lumen in 4,76% and intima-media thickness (IMT) > 0,5mm in 28,6%. According to this, in the control group 10 patients (33,33%) had normal finding, 12 (40%) had thickened IMT and 8 patients (26,67%) non-stenotic atherosclerotic plaques. Frequency of peripheral artery disease in COPD patients based on Doppler ultrasonography of lower limb arteries was significantly higher in COPD 61,93% versus 43.33% in the control group.
Conclusion
Cardiovascular evaluation in patients with moderate COPD is very important because of the increased risk of cardiovascular incidents in the early stage of the disease. Integrated-care approach for COPD patients is significant for early detection of unrecognized coexisting cardiac disorders.

Keywords
COPD, echocardiography, pulmonary hypertension, arrhythmias, electrocardiogram
P07. [106] CHANGING PHASES OF THE LUNG DURING WHOLE LUNG LAVAGE ON LUNG ULTRASOUND - A NOVEL MONITORING APPROACH

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Introduction
Lung ultrasound (LUS) has been proven to yield valuable information for lung and pleural pathology. It is well validated for assessing extravascular lung water in fluid overload conditions like chronic renal failure and congestive cardiac failure. Pulmonary alveolar proteinosis (PAP) is a condition characterized by the accumulation of abnormal surfactant in the alveoli which hampers gas exchange and leads to hypoxia. Whole-lung lavage (WLL) is the treatment of choice. It can also be used to monitor stages of controlled lung de-aeration in WLL and can also help decide the point of termination of lung flooding.

Case report
A 55 year old lady with biopsy proven PAP presented with respiratory failure. WLL was planned. LUS was used to study the stages of lung flooding as previously described for ARDS model. 6 areas screened based on six areas that are normally examined like upper zone, mid zone and lower zone showed alveolar interstitial pattern. The probe was insinuated as lateral as possible under the chest wall to look at the lateral areas. One lung ventilation (OLV) was done and isolation of lavage lung was confirmed which was seen as lung collapse (lung pulse) on LUS. Saline infusion resulted in increase in B lines followed by tissue like pattern with fluid bronchogram on LUS(alveolar flooding) in all the areas. All six areas screened which showed the following patterns from baseline till the termination of WLL:

• Stage 1: Alveolar interstitial pattern in supine position (basic pattern of PAP) [Figure 1]
• Stage 2: Postintubation, the isolated lung for lavage underwent collapse revealing the presence of lung pulse [Figure 2]
• Stage 3: Saline infusion resulted in increase in the appearance of B lines [Figure 3]
• Stage 4: B lines increased in number [Figure 4a] and became confluent till the appearance of fluid bronchograms with tissue pattern [Figure 4b]

During the lavage of the second lung, appearance of alveolar flooding pattern resulted in termination of saline infusion rather than wait till fluid flooded into the endotracheal tube. Chest radiograph showed clearing of the parenchymal shadows and LUS pattern of normal A profile (Stage 5) in all the lung fields.

Conclusion
To the best of our knowledge, this is the first time LUS was used for this indication. LUS, a non-invasive surface imaging technique can quantitate lung water content and thus can be used to guide stages of lung flooding during lavage and ensuing aeration following drainage of fluid during WLL. Apart from indicating termination of lung flooding, LUS can also help in reducing complications such as spillage into ventilated lung, overdistension of alveoli and systemic absorption of saline. Further prospective studies are required to validate this tool and set guidelines for its use in WLL in patients with PAP.

Key words
Alveolar proteinosis, lung ultrasound, whole-lung lavage
Background
Chronic Obstructive Pulmonary Disease (COPD) is one of the most common chronic diseases and a major cause of morbidity and mortality. The etiology of this disease is multifactorial. Systemic inflammation and oxidative stress seems to play an important role in the pathogenesis of the disease. Recently several potential biomarkers had been evaluated in COPD, regarding a better understanding of the disease, a better approach to the diagnosis and providing the developing of new therapeutic strategies.
The aim of the present study was to evaluate blood biomarkers of inflammation, oxidative stress and correlated with eosinophils counts in blood samples of COPD patients.

Methods
We studied patients (n=20) with stable COPD (mean age 71.30 ± 7.68 years). Lung function was assessed with body plethysmography (mean FEV₁ 59.130 ± 5.035 % predicted). The C-reactive protein (CRP) levels, a marker of systemic inflammation, were evaluated using a chemiluminescent immunoassay. The levels of malondialdehyde (MDA), a marker of oxidative stress, was determined using a spectrophotometric assay. Blood eosinophils counts were evaluated in plasma of COPD patients. The study was conducted according to the rules of the declaration of Helsinki. All participants were informed about the nature and purpose of the study and gave their consent.

Results
The biomarker of oxidative stress was found to be significantly (p≤ 0,05) higher in COPD patients with eosinophils levels > 2% (MDA 10,652±1,700 nmol/mL) when compared with COPD patients with eosinophils levels ≤2% (MDA 6,446±1,578 nmol/mL). This increase is significantly (p≤ 0,05) more evident in the COPD patients with CRP levels ≥ 3 mg/L.

Conclusions
The blood biomarkers studied seems to be promising systemic markers of the disease. More studies are needed in order to validate blood biomarkers in COPD and phenotypes subgroups.
P09. [195] SERUM VITAMIN D LEVELS IN CHILDHOOD ASTHMA: A MATCHED CASE CONTROL STUDY FROM EASTERN INDIA

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Background
Studies mainly from western countries and few from India have studied the association between childhood asthma and vitamin D level. We aim to study the relationship between serum vitamin D level and childhood asthma in children from Eastern India.

Methods
This matched case-control study was conducted in tertiary care hospital over a period of 1 year. Children with asthma and healthy controls aged 6-14 years were included. Those, who have received vitamin D in the preceding year, associated co-morbidity, severe malnutrition, and clinical rickets were excluded. Asthma severity was classified as per the GINA guideline 2015. Blood samples were taken for the measurement of serum vitamin D, calcium, phosphate, alkaline phosphatase, and total IgE level. Pulmonary function test was done by spirometry. Vitamin D deficiency, insufficiency, and sufficiency was classified as per the standard guideline. The study was approved by the Institute Ethics Committee, and written informed consent was obtained prior to patient enrollment. Statistical analyses were performed using the statistical soft-ware: Epi info 7, and SPSS (v20).

Results
A total of 132 children were included (cases = 66; controls = 66). The vitamin D levels were as follows: Among cases, 34(51.51%) were deficient and 24(36.36%) were insufficient; among controls, 15(22.72%) were deficient and 37(56.06%) were insufficient. The mean (SD) serum vitamin D level in case was 19.23 (7.12) ng/mL, and in control was 26.37 (5.97) ng/mL [t (114.54) =-2.83, p=0.002]. Vitamin D deficiency was significantly associated with occurrence of asthma (OR= 3.65; 95 % CI=1.71 to 7.77) as compared to control, but not the vitamin D insufficiency (OR= 1.95; 95 % CI= 0.75 to 5.04). There was a significant difference in mean (SD) serum vitamin D level in different asthma severity [F (4, 123) =22.32, p=0.002], which means as the severity of asthma increase the level of vitamin D decrease.

Conclusions
Vitamin D deficiency (not insufficiency) is found to be associated with childhood asthma occurrence and its level of control in children from Eastern India.

Funding
None

Conflicts of interest
None
RSV LOWER RESPIRATORY TRACT INFECTION IN UNDER-FIVE CHILDREN: A STUDY FROM EASTERN INDIA

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Background
Respiratory syncytial virus (RSV) is a common cause of acute respiratory infection in children under-five in developing countries. It can cause severe disease in children leading to hospitalization. The severe RSV disease is common in children with underlying co-morbidity. We aim to study the clinical profile and outcome of children hospitalized with RSV infection.

Methods
This observational study was conducted over two-year period in a tertiary care teaching hospital of Eastern India. Under-five children with acute lower respiratory tract infection (ALRTI) requiring hospitalization were screened for suspected viral etiology. Nasal and throat swabs were collected and transported to the laboratory at 2°C–8°C in viral transport media. RT-PCR was performed using a SuperScript II one-step RT-PCR Platinum Taq kit (two multiplex nested RT-PCRs used). All products underwent electrophoresis in 2% agarose gel, and typing was performed according to PCR product size. The demographic, clinical, and outcome details were recorded in pre-designed Performa. The study was approved by Institute Ethics Committee. Written, informed consent was obtained prior to enrolment of patients into the study.

Results
A total of 206 children aged 2-60 months hospitalized with acute viral lower respiratory tract infection (ALRTI) were included after meeting the eligibility criteria. The age groups affected were as follows: 2-6 month = 15.3%; >6-12 month =13.7%; >12-60 month = 8.4%), and sex ratio (M:F) was 1.64:1. RSV only was isolated in 63 (30.6%) cases, and in co-infection with other viruses and bacteria in 14 (9.8%) cases. RSV-B dominated over RSV-A. Of 77 cases, 19 children died (case fatality rate of 24.7%). The children who died commonly have some underlying co-morbid condition (prematurity being the most common), and have co-infection with other respiratory viruses. Most cases occurred in the month of January, March, July, August, and November.

Conclusion
RSV constitutes a significant viral cause of ALRTI in children under-five in Eastern India requiring hospitalization. The case fatality rate was noted to be high and was common in children with underlying co-morbidity.

Funding
None

Conflicts of interest
None
P11. [59] The short course of indacaterol/glycopyrronium (IND/GLY) in patients with pulmonary tuberculosis (TB) and COPD

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Introduction
COPD being comorbid disease can change the typical course of TB and leads to postoperative complications. TB patients receive several specific medicines that cause hepatic and cardiovascular system disorders. The aim to study the efficacy and safety of using a short IND/GLY course as an additional therapy in TB patients with moderate-to-very severe COPD.

Methods
This is a prospective, single center, observational study including pulmonary TB patients with a clinical and functional stable moderate-to-very severe COPD (GOLD) received of once-daily IND/GLY 110/50 µg during 6-12 days. Spirometry, CAT, mMRC, 6 minute walking test (6-MWT), ECG, ALT, AST were performed baseline and post IND/GLY therapy. The descriptive statistics and Mann-Whitney test were used.

Results
Of 23 randomized patients, 75% had significant improvement airways disorders, 96,8% - reduction dyspnea and other symptoms on the CAT score, 100% - physical activity tolerance increased by 6MWT data (Table 1).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline ( M±SD)</th>
<th>In 6-10 days ( M±SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC, l</td>
<td>3,20±1,26</td>
<td>3,71±1,18</td>
<td>0,027</td>
</tr>
<tr>
<td>FEV₁, l</td>
<td>1,79±0,88</td>
<td>1,95±0,82</td>
<td>0,036</td>
</tr>
<tr>
<td>MMEF, % pred.</td>
<td>19,44±18,04</td>
<td>22±16,57</td>
<td>0,024</td>
</tr>
<tr>
<td>6MWT, m</td>
<td>475,68±86,29</td>
<td>528,21±81,47</td>
<td>0,038</td>
</tr>
<tr>
<td>CAT-test, score</td>
<td>18,39±8,91</td>
<td>4,92±6,79</td>
<td>0,04</td>
</tr>
<tr>
<td>mMRC-test, score</td>
<td>1,65±1,17</td>
<td>1,17±0,79</td>
<td>0,173</td>
</tr>
</tbody>
</table>

There were no significant adverse events during IND/GLY therapy. There was no QT interval elongation in any patient by ECG, but a sinus bradycardia with a heart rate of 57 beats/min in 1 (4.3%) patient was observed. Also the significant deviations from the norm ALT and AST were not detected in any patient.

Conclusions
Our preliminary study showed the improving of ventilation parameters, the clinical COPD symptoms and exercise tolerance in TB patients with comorbid COPD. No adverse events were reported during IND/GLY short course.
The effect of lung function changes on respiratory muscle strength in patients with pulmonary tuberculosis (PT)

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Maximal respiratory pressures measurement is worldwide spread to assess respiratory muscle stress. Patients suffering from chronic lung diseases for a long time have respiratory muscle fatigue. In addition to the pathological process itself, which initially forms respiratory failure, its aggravation is caused by the weakness of the respiratory muscles. In a number of diseases that cause airway disorders with the development of pulmonary hyperinflation, as well as diseases affecting the interstitial lung, the external breathing apparatus performs a greater amount of work, which leads to a respiratory muscles failure. Measurement of the respiratory muscles function in patients with pulmonary tuberculosis has not been previously studied, although these patients have both obstructive ventilation disorders and pulmonary tissue damage.

Aim

to study the effect of lung function changes on the respiratory muscles in patients with PT.

Subjects and methods

Prospective observational study with verified PT patients during 2015-2018 years. The patients with lung resection and left ventricular ejection fraction less 60 mmHg were not included. Patients underwent evaluation of spirometry, bodyplethysmography, diffusion capacity, mouth occlusion pressure and respiratory muscle strength (maximal inspiratory and expiratory pressures (MIP and MEP respectively), neural ventilatory drive (P0,1)) by MasterScreen Body Diffusion (VIASYS Healthcare). We used descriptive statistics and Spearman correlation analysis.

Results

Two hundred eighty-seven patients were studied (187M/100F; mean age 39.5±12.1 years). The weakness of respiratory muscles was found in 137 patients (47%). The inspiratory muscles disorders were more frequent (59 patients, 43%), the expiratory muscles dysfunction was less frequent (19 patients, 14%), in 59 cases (43%) there were both the inspiratory and expiratory muscles dysfunction. Most patients with the respiratory muscles dysfunction (84%) had different types of lung mechanic changes: the obstructive airway disorders were in 83 cases (72%), significant violations predominated; 12 patients (10%) had mixed ventilation disorders and 4 (3%) patients had only restrictive disorders. MIP was positively associated with TLC, VC, FEV1, MMEF (r_s=0.31, 0.34, 0.55, 0.48 respectively, p<0.05) and negatively associated with RV/TLC (r_s=-0.61, p<0.05). MEP was also linked with TLC, VC, FEV1, MMEF (r_s=0.3, 0.44, 0.54, 0.41 respectively, p<0.05) and with RV/TLC (r_s=-0.5, p<0.05). MIP and MEP were also correlated with DLCO (r_s=0.38 and 0.55 respectively, p<0.05). Index P0,1 depended on FEV1, MMEF, VC, TLC, RV/TLC, DLCO (r_s=-0.53, -0.46, -0.6, -0.38, 0.4, -0.45 respectively, p<0.05). Also, there was a direct link between the disease duration, bacterial excretion and drug resistance (DR) and P0,1 (r_s=0.22, 0.24, 0.3 respectively, p<0.05), while the link between these clinical indicators and MIP and MEP was not found.

Conclusion

The respiratory muscles dysfunction was in 47% PT patients. The respiratory muscles strength depended on the airway disorders, lung volumes, lung diffusion. The respiratory center activity depended on the lung function disorders, the disease duration, DR and bacterial excretion.
P13. [181] DOES LOCALIZATION OF NON-CYSTIC FIBROSIS BRONCHIECTASIS PREDICT AIRWAYS MICROBIOTA?

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Non-cystic fibrosis bronchiectasis (NCFB) is a common disorder observed by pulmonologist in the outpatient setting. Chronic infection in NCFB patients is known to be associated with a worse outcome.

Aim of study
was to determine relation between bronchiectasis localisation and bacterial pathogen in patients with NCFB.

Study population
Subject with NCFB confirmed by high resolution computed tomography made the study sample.

Methods
Computed spirometry performed to detect pulmonary function. Isolation and identification of pathogens was carried out by classical bacteriological methods of inoculation on nutrient media, susceptibility for antibiotics was determined using disco-diffusion method according to CLSI guidelines.

Results
Between 2016 and 2018 years we included 25 subjects with NCFB (2 men and 23 women), mean age 50,6 ± 2,4 years. There were three patients after lobectomy: 1 – right middle lobe (RML), 1 – right lower lobe (RLL), 1 – left lower lobe (LLL). NCFB in only one lobe were detected in 9 cases (36.0 %), two lung lobes – 10 patients (40.0 %), three and more lobes – 6 cases (24.0 %).
In 7 (28.0%) patients NCFB were localized in the right upper lobe (RUL), in 8 (32.0%) cases in the RML, in 18 (72.0%) – in the RLL; in 7 (28.0%) – in the left upper lobe (LUL), in 16 (64.0%) cases – in the LLL.
22 samples of sputum were obtained: 6 (27.3 %) purulent, 11 (50.0%) mucopurulent, 5 (22.7%) mucus. In 19 (82.6%) samples the pathogen was detected. The combination of pathogens was in 4 (18.2%) patients (3 double pathogen combinations: P. aeruginosa with M. catarrhalis; P. aeruginosa with A. fumigatus, P. aeruginosa with K. pneumoniae; on triple combination: S. pneumoniae with H. influenza and M. catarrhalis).

The most common pathogens were P. aeruginosa – 16 (72.7%) strains. The others were S. pneumoniae – 2 (10.5%) samples, M. catarrhalis – 2 (10.5%), S. aureus (MSSA) – 1 (5.3%), A. fumigatus – 1 (5.3%), H. influenza – 1 (5.3%).
Detected S. aureus in LUL and RUL, RLL; S. pneumoniae–2 RML, 2 LUL and RLL; M. catarrhalis – 2 RML, RLL and LLL; H. influenza – RML, RLL and LUL; K. pneumoniae – 1 LLL; A. fumigatus – all lobes; P. aeruginosa – 3 RUL, 6 RML, 10 RLL and 13 LLL.
15 patients with P. aeruginosa have locations NCFB in lower lobe or lobes (p = 0.0036), 8 from 15 patients have NCFB in both LL (p = 0.71), no significant difference in involved RLL and LLL (p = 0.19).

Conclusions
There is no different between involved of the right and left lung in patients with NCFB. NCFB most often localized in lower lungs lobes. In patients with NCFB in lower lobes the most common pathogen is P. aeruginosa.
Optimizing the utilization of chemically modified Cas9 mRNA / sgRNA against the underlying genetic defect in Surfactant Protein B deficiency in lungs based on expression kinetics

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Background

Transcript therapy using chemically modified messenger RNA (cmRNA) possesses several advantages over plasmid DNA, e.g. negligible chance of integrating into human genome while nuclear entry is redundant. Modifying mRNA for enhanced expression and reduced immune response became the main focus of mRNA-based therapy. Comparison studies of various modifications have been published but no study has been conducted with the focus on comprehensive understanding of in vitro and in vivo kinetics. On the basis of these kinetics, we will strive to optimize the utilization of Cas9 mRNA and sgRNA in various monogenetic diseases, with focus on Surfactant Protein B (SP-B) deficiency, an orphan disease that results in progressive, hypoxemic respiratory failure in infants. Cas9/or gene, found to be a bacterial immune system, has become a powerful tool for engineering genomes in diverse organisms and showed promise for correcting disease-causing mutations. But random integration of promoter and/or Cas9 gene cassette at the DSBs (Double strand breaks) is a threat already featured in all various studies using double-stranded DNA and viral vectors.

Method

In this study, the kinetics of six commonly used and published modified cmRNAs have been evaluated. DsRed and mKate2 have been used as marker proteins and mRNA of these Red Fluorescent Protein (RFP) variants have been chemically modified and transfected into A549 and HEK293 cells. Expression at different time points (Eight time points from three hours to seven days) was measured using flow cytometry. Quantitative RT-qPCR was used to determine the amount of mRNA in the cells at those time points. Based on expression kinetics of marker proteins chemically modified Cas9 mRNA and sgRNA mediated gene correction approaches have been conducted. T7 endonuclease I assay, TIDE and TIDER analysis have been used to evaluate insertion and deletion (Indel) rate and Homology directed repair (HDR) respectively.

Results

Certain modifications reached their maximum protein expression as early as 12 hours (by flow cytometry) and almost undetectable after 3 days, whereas others had a delayed onset of expression, but could be detected even after seven days. mRNA level in cells (by RT-qPCR) also showed a direct correlation to expression pattern based on used modification. This expression pattern is also reflected in a functional study of Cas9 / sgRNA based indel induction where a certain chemical modification can achieve higher indel induction efficiency much faster than the rest of the chemically modified Cas9 mRNA.

Conclusion

Using Cas9 cmRNA for a controlled expression profile of the Cas9 protein will help to correct the underlying 121ins2 frame shift mutation, thus leading to an efficient and specific gene correction, while exhibiting very limited to no detectable off-target effects at the same time.


Isoniazide resistance tuberculosis (INHr TB) treatment outcome.

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Title
Isoniazid Resistance Tuberculosis (INHr TB) treatment outcome.

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Abstract

Background
Isoniazid (INH) is one of the most important first-line medicines for the treatment of drug susceptible tuberculosis, with high bactericidal activity and a good safety profile. The emergence of TB strains resistant to isoniazid is reduced the effectiveness of INH and worldwide estimated to have isoniazid resistance tuberculosis ranging from 5 to 11%.

Objectives
This study will assess the effectiveness of the treatment regimen of INHr TB, at the National TB Hospital Swaziland. The study result may assist on the recommendations of the standardized facility based regimen according to the result.

Method
A retrospective cohort study will be done on all bacteriologically confirmed INHr TB patients who have fulfilled the inclusion criteria, initiated on treatment from January 2015 to December 2017.

Results
A total of 55 patients are involved in the study. Female/ male ratio is 50.9 to 49.1%. Out of 55 patients 70.9% are cured, 7.3% completed treatment, with the total success rate of (cured and completed treatment) 78.2%, unsuccessful treatment outcome is 18.2% (failure rate of 10.9%, died 5.5% and defaulted 1.8%) and 3.6% of the patients not evaluated due to culture unknown results.

Conclusions
Even though the sample size is small and further study needed on the side effect profile, the extent of the disease and other contributing factors to the treatment outcome. In general the effectiveness of INHr treatment is satisfactory.

Key words
Isoniazid resistant tuberculosis (INHr TB), Tuberculosis (TB), Kanamycine (KM), Levofloxacine (LFX), Ethionamid (ETO), Terizidoone (TRD), Isoniazid (INH), Rifampicine (RFM), Pyrazinamid (PZA).
Radiological diagnosis of Allergic bronchopulmonary aspergillosis ABPA – Other Radiological features (ORF) and High Attenuating Mucus (HAM); are they important?

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Objective
Both HAM and ORF are recognized clinical features of ABPA. The prognostic significance and the exact prevalence of these radiological tools is not fully understood.

Method
50 patients with ABPA diagnosed using the ISHAM (International society for Human and Animal Mycology) criteria, presenting to our clinic underwent High Resolution CT Scans of the thorax. The patients were categorised as those without any radiological signs of ABPA (ABPA –S), ABPA with HAM, ABPA with ORF, ABPA with central bronchiectasis (CB) with or without HAM

Results
The prevalence of HAM in patients with ABPA at our centre was found to be 42%. This is much higher than the international data regarding the same, this discrepancy may be due to referral bias at a tertiary care centre. The prevalence of ORF was 78%. 100% of patients with HAM, had taken anti Tubercular therapy at some point of time in their life. The prevalence of HAM in patients of ABPA, was associated with a statistically significant higher risk of acute exacerbations, higher IgE levels, Worse lung functions on PFT. There was no association of HAM with the duration of disease or with the baseline IgE levels or the therapy taken for ABPA. The presence of ORF (other than HAM) was associated with a non significantly higher IgE in these patients.

Conclusions
Our study indicates that the presence of HAM in patients with ABPA, is associated with worse outcomes. If HAM is recognized on CT scans the treating team must take this into account and modify the management of these patients.
Differences in Tobacco smoke associated and Biomass fuel associated Chronic Obstructive Pulmonary disease (COPD) – A unique disease of the Indian Subcontinent

Objective

The objective of this study was to differentiate between the various epidemiological, clinical, radiological, laboratory and prognostic characteristics of Tobacco smoke (TS) associated and Biomass fuel (BMF) associated COPD. BMF associated COPD is a major cause of morbidity and mortality in the developing world. A large population especially in rural India still uses coal and indigenous gas stoves which lead to a large amount of air pollution. Current western literature does not distinguish between the characteristics of TS and BMF associated COPD.

Method

80 patients with COPD, defined using the GOLD spirometry criteria, were studied. 40 patients had significant exposure to smoked tobacco. 40 patients were never smokers, but had been exposed to BMF for at least 5-10 years, mostly for domestic cooking exposure. Both the groups were compared for various parameters.

Results

92.5%(37/40) in the smoking group were males. 85%(34/40) in the BMF group were females. The average age of the TS group at the time of diagnosis was 58 years, in the BMF group the average age of diagnosis was 69 years. All females from the BMF group were uneducated and 88.2(30/34) were brought to medical attention for the first time with an acute exacerbation. In the TS group the average FEV1 value(%age predicted ) was 52%. In the BMF group the average FEV1 was better at 64% predicted.65%(26/40) patients were on inhaled therapy for their disease as compared to 30%(12/40) in the BMF were on any kind of inhaled therapy. 97.5(39/40) in the TS group knew that Tobacco smoking could lead to COPD. In the BMF group only 17.5%(7/40) knew that BMF exposure could lead to respiratory disease. 72.5(29/40) in the TS group had associated Cardiovascular and metabolic disorders, this was 22.5(9/40) in the BMF group. The patients in both the groups were equally dyspnic at presentation, with an average MMRC of 3, depicting that most patients with COPD present to health care facilities late in our country. Both the groups had an average exacerbation of 2 / year, over the 2 years of study period. However, the TS group had a higher number of ICU admissions and worse exacerbations ( 10 in TS group vs 3 in BMF group). On HRCT Thorax BMF COPD had lesser percentage emphysema (low attenuation areas). The BMF group had a higher prevalence of associated Bronchiectasis on CT scans(53% vs 18%). Post discharge the TS group had higher adherence to the prescribed drugs and hospital follow up as compared to the BMF group (70% vs 45%).

Conclusions

BMF associated COPD is a unique group of COPD patients encountered in rural India. Majority of these patients are females, who are exposed to large a corpus of inhaled smoke via indigenous stoves and wood fire used for cooking. The health seeking behaviour of this group is worse than the classical TS COPD, as indicated by late age of first presentation , first presentation in exacerbation and poor post discharge follow up. Despite having better lung functions and less cardiovascular morbidities most of these patients are equally dyspnic and exacerbate at the same rates as their smoker counterparts. This special subgroup of COPD patients needs to be identified and treated early, for more favourable outcomes.
The role of blood biomarkers in predicting the risk of patients with unprovoked acute pulmonary embolism

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Background
The role of blood biomarkers in the risk assessment of acute pulmonary embolism (PE) have emerged as promising tools. However, biomarkers were studied in heterogeneous patient populations and were not verified in patients with unprovoked PE. There are also growing evidence of better outcomes of unprovoked than provoked PE. We sought to evaluate the value of biomarkers in unprovoked PE and validate the current risk stratification in this cohort.

Material and methods
This was a retrospective cohort study of patients with unprovoked acute PE from 2010 to 2017 at a single tertiary center in South Korea. Adverse composite outcomes were defined as thrombolysis, thrombectomy, extracorporeal membrane oxygenation, or death. Venous blood samples were collected at the first visit before anticoagulant treatment. Biomarkers associated with composite outcomes were analyzed and compared with preexisting risk models.

Results
A total of 265 patients (48.7% male) of median age 66.0 [interquartile range 52.0, 75.0] years were included. Total WBC and neutrophil counts, and concentrations of BUN, uric acid, glucose, lactate dehydrogenase (LD), CK-MB, troponin I, and BNP were significantly higher and concentrations of pO₂, HCO₃⁻, and SaO₂ were significantly lower in the intermediate-high to high risk group than in the low to intermediate-low risk group. Composite outcomes occurred in 20 (7.5%) patients; death (n=0), thrombolysis (n=16), embolectomy (n=2), and ECMO followed by thrombolysis or embolectomy (n=2). Hemoglobin, uric acid, and glucose were significantly and independently associated with adverse composite outcomes. This biomarker model showed the highest prognostic accuracy for adverse composite outcomes, with an AUC of 0.806 (95% CI: 0.702-0.911, p<0.001), which was significantly better than that of PESI or simplified PESI, and comparable to that of ESC risk classification.

Conclusion
The biomarker model including hemoglobin, uric acid and glucose has good prognostic performance comparable to ESC risk classification while PESI or simplified PESI score was not useful in unprovoked PE.
The IL-17s/IL-17Rs axis in airway defense and immunopathology during chronic respiratory disease associated to Pseudomonas aeruginosa infections.

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The pathophysiological mechanisms driving exaggerated inflammation and tissue damage associated to un-resolved airway infections during chronic lung diseases remain to be elucidated. Recent reports prompt the hypothesis that IL-17 immunity, through IL-17RA mediates host defense and immunopathology during chronic lung disease associated to persistent infections, such as P. aeruginosa. Thus, we are dissecting the pleiotropic activities of IL-17RA by the interaction with other IL-17 receptors (IL-17RC, IL-17RB, IL-17RE) during long term chronic infection by P. aeruginosa in murine models and human respiratory samples.

When C57Bl/6 mice were challenged with P. aeruginosa embedded in agar beads, we found that IL-17 cytokine family (IL-17A, IL-17F, IL-17E, IL-17B or IL-17C) increased during the early (2 days) and late (28 days) phases of chronic respiratory infection. We are evaluating the dynamic expression of IL-17 receptors by flow cytometry in C57BL/6 mice chronically infected by P. aeruginosa; preliminary data suggest that IL-17 receptors are differently expressed among stromal and immune cells in the lung. To directly address the contribution of each IL-17 receptor during chronic respiratory infections, three new knockout (KO) murine models for IL-17Rs were generated by CRISPR/Cas9 indel-mediated gene KO for each IL-17 receptors (IL-17RC, IL-17RB, IL-17RE). To date, functional validation of the three IL-17 receptors KO murine lines both in vitro and in vivo is in progress.

In respiratory samples from Cystic Fibrosis patients, we are evaluating the levels IL-17 cytokine family associated to both early and advanced stages of P. aeruginosa infection, strengthening the importance of IL-17 cytokine family mediated response in the overall progression of chronic airways disease.

In conclusion, targeting selectively IL-17s/IL-17Rs axis may provide a novel potential host-based intervention to limit immunopathology during chronic respiratory illnesses, mediated by opportunistic infections.

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Background
Indian COPD patients have variable pattern of risk exposure and response to treatment as compared to western patients.

Methods
Prospective interventional and observational study conducted after IRB approval in Pulmonary Medicine, MIMSR medical college & Venkatesh chest hospital Latur during Jan 2014 to June 2017, included 600 symptomatic COPD cases diagnosed by GOLD guidelines (FEV1/FVC <0.7) and FEV1<80% in all cases, eosinophilic predominance in sputum (4% or more), and having at least one exacerbation in last three years. All study cases received influenza vaccination before enrollment in study and received same treatment to all cases as ICS (inhaled corticosteroids) and LAMA (long acting antimuscarinic drug) combination (glycopyrronium bromide and salmeterol plus fluticasone in different dry powder inhalers). Statistical analysis was done by using Chi test and student's t test.

Observations and analysis
In study cases, we documented 67% study cases were having eosinophilic predominance in sputum. we observed FEV1 improvement by 124 ml±10 ml in 24% cases and 56% cases having 24 ml± 6 ml decline (p<0.0001). Total 69% of study cases were showing symptomatic improvement and change in mMRC grade & CAT score (p<0.001) Exacerbation was documented in 6% cases (36/600), of those 8 cases required ICU admission (p<0.0001). There is no increase in asymptomatic hyperglycemia & Pneumonia is observed in 2.5% study cases during 42 months study period.

Conclusion
Initiation of LAMA & ICS early in symptomatic COPD cases with FEV1 <80% with eosinophilic predominance in sputum will have successful treatment outcome in form of good symptom control & decrease in exacerbation. Rationale for response is predominant non-smoker class (heterogeneous class) in Indian COPD cases as compared to classically described Neutrophilic phenotype and having varieties dusts exposure especially agricultural dust. We recommend preferable use of LAMA and ICS combination in Indian COPD cases debatable to existing COPD guidelines.
A case of new onset asthma during pregnancy

Background
We report a case of new onset asthma during pregnancy following Mycoplasma Pneumoniae infection. Asthma is the most common chronic respiratory disease during pregnancy. Reports of new onset asthma during pregnancy are limited. It is thought that pregnant women are more susceptible to infections or that they are more severely affected. In addition, it is generally known that M. Pneumoniae infection is linked to asthma, yet there still remain certain question marks regarding the causal relationship in the development of asthma.

Case
A 33 year old healthy women, without a prior medical history of asthma was presented to our emergency department with progressive dyspnoea in her third trimester of pregnancy - at 32 weeks gestation. Patient had no family history of asthma and no personal history of atopy. Phadiatop test was negative. Lung auscultation revealed a strongly elongated expiratory wheeze with scattered rhonchi. Serum IgM was 16 (>10 positive) for M. pneumoniae, which indicates current infection. Chest radiograph showed no abnormalities. Treatment with prednisone(10 days 30mg followed by tapering), clarithromycin 500 mg twice daily, salbutamol/ipratropium inhalation, high dose ICS/LABA (beclometason/formoterol aerosol 200/6ug, two inhalations twice daily) and oxygen was started. After more than a week her symptoms improved and she was discharged after a hospital stay of 15 days. 2 weeks after discharge, and discontinuation of systemic steroids, spirometry and FeNO were performed at the outpatient clinic. This showed significant reversibility(13% and 262 cc) compatible with asthma and a strongly elevated FeNO(60ppb). In addition blood eosinophils levels were elevated (0.50x10^9/L ). FeNO normalised after 8 weeks(18ppb). Pregnancy outcomes of patient and new born were remarkably well. She gave birth to a healthy baby boy at AD of 39+3, birthweight of 3445 gram.

Conclusion
Pregnancy is a pro-inflammatory and immune modulating condition. M. Pneumoniae infection can lead to or worsen airway inflammation and thereby contribute to the development of asthma. Moreover M. Pneumoniae infection may result in T helper cell type 2 airway disease, which stimulate IgE production and eosinophil function(1). Based on pulmonary function testing, inflammatory biomarkers and clinical response to treatment, this patient seems to have new onset asthma triggered by mycoplasma infection during pregnancy. After treatment of the patient with systemic steroids, oxygen supplementation, antibiotics, and high dose ICS/LABA, she gave birth to a healthy child, without any pregnancy related complications. New onset asthma should be part of the differential diagnosis of a pregnant patient with respiratory symptoms, especially when mycoplasma infection is found. Moreover this case illustrates that asthma exacerbations during pregnancy should be recognized promptly and can be treated according to the existing guidelines to prevent adverse outcomes in mother and child.

References
P20. [265] Percutaneous coronary intervention in patients with chronic obstructive pulmonary disease

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Introduction
A recent systematic review and meta-analysis has confirmed the high risk of myocardial infarction in people with chronic obstructive pulmonary disease (COPD). Although the incidence of COPD in patients treated with percutaneous coronary intervention (PCI) is underestimated, it is not fully understood. It has already been documented that non-ST-segment elevation myocardial infarction (NSTEMI) was a more common clinical presentation of coronary artery disease in the COPD group, while ST-segment elevation myocardial infarction (STEMI) occurred more frequently in the group without COPD. However, the impact of COPD on periprocedural outcomes of PCI, as well as its relationship with clinical presentation and the type of coronary artery lesions, is not fully understood.

Objective
To analyze PCI procedures in patients with COPD

Methods

Results
There were no significant differences in the procedure-related mortality rates between the groups with and without COPD (0.11% vs 0.1%, P = 0.76 and 0.45% vs 0.34%, P = 0.34, respectively). The lesion that received the intervention was more often restenosis in the COPD group, whereas the primary percutaneous coronary intervention – in the non-COPD group (83.3% vs 69.8%, p < 0.0001). The prevalence of left main coronary artery involvement was significantly higher in the COPD group. Since in-hospital and long-term mortality and cardiac events were higher following PCI in patients with COPD, COPD should be considered a risk factor for the development of adverse clinical outcomes following PCI.

Conclusion
However, the long-term mortality was not clear and needs further investigation.
Daily physical activity in patients with severe asthma.

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Introduction
Daily physical activity in patients with asthma remains overlooked. Only limited evidence suggests reduced levels of daily physical activity in patients with asthma compared to healthy control subjects.1 Improving daily physical activity may be an important missing link in the successful management of asthma as higher adherence to physical activity has been associated with favourable outcomes including better overall asthma control, reduced exacerbations, and reduced health care use.2 Correspondingly, this may be even more relevant to patients with the severe phenotype of asthma.

Aims
We therefore aim to investigate the overall levels of daily physical activity in adult patients with severe asthma.

Methods
A prospective, observational study of continuous patients who fulfil the definition of severe asthma3 is ongoing. Patients have their daily physical activity recorded for 7 consecutive days using triaxial accelerometry (DynaPort MoveMonitor; McRoberts).

Results
Eleven patients have been studied to date (10 women; age 57.7±8.1; BMI 32.3±7.4; ACT score 15.6±5.2; pre-bronchodilator FEV1 1.78±0.9 L (69±28 %predicted); FEV1/FVC ratio 65.3±15.2; IgE 252±342 IU/ml; eosinophils 342±147 cells/ml (4.6±1.9%); daily beclomethasone-equivalent inhaled corticosteroid dose 1238±514 μg). Daily moving time (walking, stair climbing and cycling) was limited to 81.9±33.6 mins. Daily step count was 6610.8±2855.9, reflecting a low-active behaviour.4 Movement intensity was 1.80±0.21 m/s² (units of acceleration), which compares with that of generally older patients with moderate-to-severe chronic obstructive pulmonary disease.5 Weekly time in moderate-to-vigorous intensity physical activity (≥3.0 metabolic equivalents) was 474.9±184.6 mins; only one patient fulfilled current recommendations for weekly physical activity.6

Conclusions
The current findings demonstrate significantly reduced indices of daily physical activity in patients with severe asthma. They also call for targeted interventions as well as research into the potential effect of therapies on daily life activity of patients with severe asthma.

References
"Trends of COPD diagnosis and treatment in rural setting in India: Misdiagnosed and less efficiently treated; needs more awareness among doctor-patient-drug trio"

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**Background**

COPD is the leading cause of morbidity and mortality due to chronic respiratory illness in India. More than half of COPD patients are not getting adequate treatment including tertiary care or corporate and peripheral setting in India.

**Methods**

Prospective observational interview (questionnaire) based multicentric study conducted during June 2014 to June 2017 in Venkatesh chest hospital, & MIMSR Medical College Latur screened 9000 cases with chronic respiratory symptoms like cough, sputum production and shortness of breath and all cases were undergone spirometry. Finally study enrolled 6000 cases of COPD diagnosed by Spirometry. In this study we assessed disease diagnosis, methods of treatment offered to all patients by applying questionnaire. Statistical analysis by goodness of fit test (chi test).

**Observation and analysis**

In our study, 16% case are aware as if they are having ‘COPD disease’, 54% are not knowing the disease at all or similar terminology till enrollment (not counseled for COPD disease) and 30% cases are not convinced as they are having COPD (categorized as ‘difficult patient’) (p<0.0001). Inhaler treatment was offered in only 58% COPD cases, in form of Levosalbutamol only in 31% cases, Levosalbutamol plus beclometasone in 18% cases, and formoterol plus budesonide or salmeterol plus fluticasone only in 9% COPD cases (p<0.0001). Later being categorized as ‘difficult treatment’ as more costly than former ones and not patients pocket friendly. We also observed irrational and exuberant use of oral medicines in 42% COPD cases, in form of theophylline only in 16% cases, salbutamol in 7% cases, oral steroids in 19% cases and these medicines preferred by treating doctors over inhalation in spite of knowledge of inhalation treatment and categorized as ‘difficult doctor’ (p<0.0001).

**Conclusion:** We observed and faced ‘difficult doctor, difficult patient, and difficult treatment’ in COPD diagnosis and management routinely in peripheral setting in India. We recommend to use spirometry test as a routine in all chronic respiratory symptoms patients for exact diagnosis of COPD. We also recommend more awareness and sensitization of benefits and outcomes of Inhalation treatment in COPD to community physicians and needs more training in these group.
Non-infective exacerbations in COPD: relatively more common, misinterpreted in clinical practice and needs cautious evaluation to avoid irrational use of antibiotics

Background
Infective and non-infective causes of exacerbations in COPD have similar presentation with variable treatment response and outcome in intensive care setting.

Methods
Prospective interventional and observational study conducted in Pulmonary Medicine, MIMSR Medical College, Latur & Venkatesh Chest Hospital Latur during Jan 2014 to June 2017, included 400 cases of exacerbations of COPD (AECOPD) admitted in intensive care unit. All study cases were evaluated to differentiate infective from non-infective cause by performing CRP, Procalcitonin, total leucocyte count & sputum gram stain. Statistical analysis was done by using Proportion test (chi test) & student’s t-test.

Observations and analysis
In study of 400 AECOPD cases, we documented 44% of study cases were having non infective exacerbation and 56% cases were infective cause (p<0.018). Cardiac dysfunction were documented in 26 % cases and 12% cases in non-infective & infective group respectively (p<0.00001). GERD were documented 34% and 14% cases in non-infective & infective group respectively (p<0.00001). Duration of hospitalization in non-infective group was 4±2 days and 6±2 days in infective group (p<0.00001).

Conclusion
Non-infective exacerbations are relatively more common and routinely missed because of less utilization of CRP, Procalcitonin and sputum gram stain evaluation especially former tests not performed routinely. Cardiac dysfunction and GERD are commoner in non-infective AECOPD group as compared to infective type. De-escalation of antibiotics with more rational use of drugs can be possible with timely evaluation with these parameters. Additionally it will decrease overall ICU stay and cost effective treatment in all AECOPD cases.
Background

Pleural tissue (PT) has been reported to improve the yield of Xpert for diagnosis of tuberculosis pleural effusion (TPE). Studies on Xpert MTB/RIF in PT have used different reference standards and also reported varying yields with closed (CPB) and thoracoscopic pleural biopsies (TPB).

Objectives

To determine the utility of Xpert MTB/RIF and its additive yield to histopathology in PT for diagnosis of TPE. To determine if the difference in yield in CPB and TPB

Methods

Prospective multi-centric cohort of consecutive pleural biopsies over two years in CPB and TPB tissue against composite reference standard (CRS).

Results

Of the 304 pleural biopsies done in three centers over two years, 122 (40.13%) had Tubercular pleural effusion. Xpert MTB/RIF on PT samples and mycobacterial tissue cultures were also requested in another 84 suspected TPE and a final diagnosis of metastatic carcinoma (28/206, 9.2%), synpneumonic effusion (7.2%) or other conditions (8.2%) allowing calculation of specificity and positive predictive values. In TPE, histopathology was diagnostic in 81.1% overall and was not significantly greater with TPB (O.R 1.02, p=0.31). Xpert MTB/RIF was positive in 41.8% of TPE and was significantly higher with TPB (O.R 10.2, p=0.001). There was a trend towards higher Xpert MTB/RIF yield with rigid TPB (O.R 2.65, p=0.14). Xpert MTB/RIF had an additional yield to histopathology of 4.4% against CRS. PT mycobacterial cultures were positive in 5.7% only. 11.1% were diagnosed with TPE on follow-up despite negative histopathology, Xpert MTB/RIF and mycobacterial cultures on TPB.

Conclusion

Xpert MTB/RIF has a higher yield with TPB than CPB. Xpert MTB/RIF has an additive yield to histopathology and must be requested in PT samples in all suspected TPE. Histopathology alone is not an appropriate gold standard for TPE in a high prevalence area

WORD COUNT: 274
Chemical modified mRNA therapy for Cystic Fibrosis by targeting Lung cells.

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Background
Gene deficiency diseases where there is lack of functional protein, have found a potential cure in the form of mRNA therapy¹ but major challenges for achieving higher bioavailability concerning mRNA based therapy are higher rate of degradation, reduced ability to cross cellular barriers and immunogenicity². The advances in the field of nano-carriers and chemical modifications of mRNA bases and codon optimization have brought the mRNA based technology into therapeutics race, however, much more has to be achieved³,⁴. Cystic Fibrosis, a common genetic disorder among Caucasians is caused due to genetic mutation which results in high rate of mortality and reduced life quality⁵,⁶. Although, there has been huge progress since the cloning of CFTR and its delivery in plasmid form using viral vector, none has been proven efficient in restoring normal expression and function in human⁷,⁸. Lung cells consists of myriad of cell types among which Alveolar Type (I and II) cells, Endothelial cells, Club cells and Epithelial cells are the major CFTR expressing cells⁹-¹². CFTR channel protein restoration in these cells using mRNA can improve disease condition of Cystic Fibrosis patient significantly. Additionally, in the light of recent identification of Lung stem cells (Myoepithelial cells and Bronchio Alveolar Stem Cells)¹³-¹⁵, gene correction via sgRNA/Cas9 system could be also fruitful to target and repair stem cells.

Method
In this study, we have made an attempt to deliver chemically modified mRNA with the help of nano-carriers (Chitosan coated PLGA, Cationic Nano Liposomes) to specific lung cells via intratracheal and intravenous instillations. The reporter mRNA delivery and protein expression (mKate2) in different cellular population is identified with the help of cellular markers using Flow Cytometry. The lung function (Forced Expired Volume<sub>0.1</sub> and compliance) improvement is compared using Flexivent<sup>®</sup> to understand the effectiveness of different nanoparticles and route of administration.

Results and Conclusion
The study helps in easy characterization and localization of delivered mRNA for gene supplementation therapy. Lung function improvement of Cftr<sup>-/-</sup> mice was observed upon mRNA delivery using nanoparticles¹⁶. Chitosan coated PLGA nano-carriers have shown deep lung cell delivery (Endothelial cells) of reporter protein. In addition, this model has the potential to aid the development of delivery system for treating Lung diseases via Gene correction or Gene supplementation.

Conflict of Interest

References


Electrophoretic Alpha 1-globulin fraction for screening of alpha 1-antitrypsin deficiency

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Background

Alpha 1 antitrypsin deficiency (AATD) is an under recognized disease. The reasons for this underdiagnose are manifold: first, this is a rare condition and, moreover, the diagnostic pathway is not always readily available and both genotyping and phenotyping carry cost-related issues. Although the quantitative determination of AAT levels in blood is currently stated as the pivotal first test to identify AATD, it is often not prescribed; furthermore, to determine AAT circulating concentrations alone could be misleading since abnormally decreased or increased levels of this protein can be observed in other unrelated conditions. In this context, serum protein electrophoresis (SPE) represents a commonly used tool for assessing serum protein disorders and many subspecialists include it in the initial evaluation for numerous clinical conditions. This widespread use of SPE provides therefore an opportunity for incidental identification of people at risk for AATD, being the AAT protein the most abundant protein in the SPE alpha-1 globulin fraction.

Given these premises, we aimed at evaluate the ability of the α1-globulin percentage at plasma protein electrophoresis to detect A1AT genetic variants observed by phenotyping, genotyping or direct sequencing, and to compare the detection rate observed with the above described method with that resulting from a standard clinical-based approach and that resulting from a familiar screening of subjects with documented AATD.

Materials and Methods

This is a prospective, observational and monocentric study evaluating the effectiveness of a population screening, mainly based on the alpha 1-globulin fraction of serum protein electrophoresis, in comparison with a standard clinical screening and a familiar screening. We retrospectively analysed all those subjects who performed, besides a serum protein electrophoresis, the dosage of liver transaminases, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Subjects were then cross-matched for main serum biomarkers according to the following four classifications:

- Alpha 1 globulin ≤2.6% (Group A)
- Serum AAT level < 1 g/L (Group B)
- Alpha 1 globulin ≤2.9% and AST/GOT: > 37 U/L and ALT/GPT: > 78 U/L (Group C)
- Alpha 1 globulin %: 2.90-4.90 % and AST/GOT: > 37 U/L and ALT/GPT: > 78 U/L and ESR > 34 mm/h and CRP > 3 mg/L (Group D)

Results obtained from this administrative dataset were then compared with those coming from a standard clinical screening and a familiar screening.

The prevalence of Pi*M genetic variants was determined and the detection rate of each type of screening was calculated. The characteristics of participants with and without Pi*M genetic variants were compared.

The study protocol was approved by the Campus Bio-Medico University Ethical Committee (protocol number: ***) and all participants provided written informed consent.

Results

21094 subjects were eligible to be screened. 145 participants met the inclusion criteria: 31 (21%) deceased before the 2016, 32 (22%) refused to participate and 82 (57%) participated in the study. 52 out of 82 met the Group A, 11 the Group B, 5 the Group C and 14 the Group D criterion. Furthermore, 113 subjects were screened at the Respiratory outpatient clinic whilst 30 siblings of patients with Pi*M genetic variants were eligible for the study.
The overall detection rates were 51.3% in the alpha 1 globulin-based screened group, 15% in the standard clinical screening group and 53.3% in the familiar screening group. Focusing on the alpha1 globulin-based screening, Pi*M variant prevalence rate (N° of Pi*M variants/screened population) was 42/21094=0.00199. 34 of the 42 Pi*M variants were identified applying the Group A criterion, 4 the Group B criterion, 2 the Group C criterion and 2 the Group D criterion, with a detection rate respectively of 64%, 36%, 40% and 14%.

The lung function of subjects belonging to the population group was better than in the clinical screening group.

**Conclusions**

the application of the alpha-1 globulin-based algorithm might allow an earlier identification of carriers, and implement strategies to reduce other risk factors for accelerated lung function decline, to improve the detection of family members with the mutation, and also to follow up patients with steeper decline of lung function over time, and eventually candidate them to the augmentation therapy. Moreover, the earlier identification of a higher number of mutants will facilitate the design of longitudinal observational studies, which might provide new insights on the impact of such mutations over lung function.
Introduction
The post-bronchodilator test is a technique that allows the assessment of the reversibility of airway obstruction. It consists of recording the parameters of spirometry and plethysmography before and after the inhalation of a short-acting bronchodilator within a 15 minute interval. Currently, an improvement of 200 mL and 12% in forced expiratory volume in one second (FEV1) defines a positive post-bronchodilator test, which means the existence of a reversible ventilatory obstruction. The variation in the remaining parameters of pulmonary function, such as volumes, resistance or other flow is not covered by this definition.

With this work, we intend to study the impact of the bronchodilation test on the remaining pulmonary function parameters.

Methods
From a universe of 112 respiratory function studies with post-bronchodilator test, only studies of patients with obstructive ventilation (FEV1 / FVC <70%) were selected. There were excluded studies in which there was no increase in FEV1 after bronchodilation, resulting in a total sample of 68 elements (45 male and 23 female). The mean age was 61.9 years (SD 16.4 years). The effect-size (ES) of each pulmonary function parameter, which is the difference between the two means (pre and post bronchodilation) divided by the standard deviation of each pre-bronchodilation parameter, was then calculated.

Results
After the administration of the bronchodilator, a statistically significant increase of 4.2% of FEV1 was observed, with an ES = 0.27, as well as a 3% increase in FVC, with ES = 0.10. The ES of peak expiratory flow was 0.25. Regarding residual volume, it decreased by 15%, with an ES of 0.31. Finally, the ES for effective airway resistance was 0.56.
It should be noted that in this group of patients, statistically significant differences (p <0.05) were observed in almost all the parameters evaluated, except inspiratory capacity and total lung capacity.

Conclusion
With this study, it was verified that the alteration of airway resistance values in the bronchodilation test was more evident than the alteration of the remaining parameters of spirometry and plethysmography in patients with ventilatory obstruction. This study therefore suggests a greater impact of bronchodilation on airway resistance compared to FEV1, which is the parameter currently covered in the definition of a positive bronchodilation test.
Bronchiectasis - does etiology matter?

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Introduction
Bronchiectasis refers to structural alterations of the airways and whose superinfection commonly leads to hospitalization.

Objective
To describe the clinical features, comorbidities and outcome of hospitalized patients with non-cystic fibrosis bronchiectasis (NCFB) in our hospital, with particular emphasis on the impact of identification of the etiologic agent.

Methods
Review of the clinical processes of hospitalized adult patients with NCFB between 2012 and 2016. Statistical analysis was performed using chi-square test (significant level p<0,05).

Results
The sample consisted of 92 patients, of whom 50% were male. The mean age was 72 years-old (SD=18.2). Bronchiectasis were bilateral in 74 cases (80.4%). The most frequent comorbidities were smoking (42.4%; n=39), chronic obstructive pulmonary disease (31.5%; n=29) and arterial hypertension (27.8%; n=25). It was possible to identify the bronchiectasis’ etiology in 60.9% of the cases (n=56), of which 30 were due to tuberculosis, 15 due to other respiratory infections, 9 due to chronic obstructive ventilator disease and 2 due to graft rejection. There was no significant difference between the several comorbidity groups and etiologic categories of bronchiectasis. The median length of hospital stay was 14 days (P25=7 and P75=31), but no significant difference was seen in duration between the idiopathic bronchiectasis’ group and the other, neither in terms of mortality rate nor in number of Intensive Care Unit admission. Colonization and bacteriological isolation rates between the two groups also showed no statistical significance.

Conclusion
In this group of patients there was no significant difference in the clinical results obtained between patients with idiopathic bronchiectasis and of known etiology, which may lead to speculation that their management may be the same.
Case report
A 36 years-old female patient with NYHA class III-B heart failure due to hypertrophic cardiomyopathy in the “burnout” phase, ready for cardiac transplantation. Admitted in ward by decompensated heart failure.

Investigations
During hospitalization, she started dry cough and fever associated with leukocytosis, increased C-reactive protein and bibasal pulmonary infiltrates on chest radiography, admitting the diagnosis of nosocomial pneumonia. A slight clinical improvement was observed after the institution of empirical antibiotic therapy. The thoracic CT-scan documented, at the level of the lower lobes, "ground glass" densities and interlobular interstitial septal thickening at peripheral location, changes compatible with pulmonary stasis and with known heart failure, but without being able to exclude infection. After three bronchofibroscopies with sterile bronchoalveolar lavages, without evidence of another infectious site, she underwent transthoracic pulmonary biopsy that revealed enlargement of the alveolar septa due to juvenile fibrosis, hyperplasia of type II pneumocytes, and intra-alveolar fibrin balls, findings compatible with Acute Fibrinous and Organizing Pneumonia (AFOP). The autoimmunity study revealed ANA positivity of 1:160, being the infectious serologies negative.

Results and treatment
After admitting the diagnosis of AFOP, the patient underwent immunosuppression with methylprednisolone 1 mg/kg/day, with clinical improvement and gradual analytical and imaging stabilization, enabling cardiac transplantation.

Discussion
AFOP is an extremely rare entity, of unknown cause and whose differential diagnosis most often involves pneumonia of infectious origin. It may have a subacute or acute presentation with progression to ARDS. It has been reported that AFOP may occur in association with drug interactions, collagen vascular diseases, environmental exposures, and various respiratory infections, but several cases have no origin cause or association. To date, associations with other diseases, notably hypertrophic cardiomyopathy, have not been reported. This case aims to alert to the importance of considering AFOP in the presence of unusual imaging findings, as well as in the differential diagnosis of difficult-to-treat pneumonias, because of the possible evolution to ARDS and consequent very unfavorable prognosis.
Case history
A 74 years old man, non-smoker, locksmith, with no personal background. The patient referred dyspnea (mMRC=3) with eight months of evolution, with no other sign or symptom.

Investigations
The functional respiratory study revealed parameters within normality, and the gasometric analysis presented hypocapnia and slight hypoxemia in ambient air (PCO2 = 31.2mmHg, PO2 = 65mmHg and SatO2 = 95%). The patient walked 375 meters on 6 minute walking test (6MWT) with a minimum saturation of 89%. The chest radiography showed an exuberant bilateral hilar engorgement, especially on the right side. In this context, the patient later performed a thoracic angio-CT scan, which documented pulmonary parenchyma with a mosaic pattern, an enlarged pulmonary artery trunk, and filling defects attributable to pulmonary thromboembolism in the right pulmonary artery and in all lobes, bilaterally, involving interlobar, segmental and subsegmental branches. Transthoracic echocardiography revealed right cavity dilatation and severe pulmonary hypertension, with an estimated PASP of 86 mmHg. The study of thrombophilia was negative, such as the echo-doppler of the lower limbs. Pulmonary angiography revealed predominantly right embolic obstruction.

Results and treatment
The diagnosis of Chronic Thromboembolism Pulmonary Hypertension (CTEPH) was admitted. The patient started anticoagulant therapy and was submitted to a permanent filter placement in the inferior vena cava and pulmonary thromboendarterectomy, with significant clinical improvement, resting gasometric normalization and 60-meter increase in 6MWT of revaluation.

Discussion
CTEPH is an uncommon disease, with an incidence of 0.5 to 3.8% following an initial episode of acute pulmonary thromboembolism. Early diagnosis of CTEPH is hard, due either to the low specificity of the symptoms or the high rate of patients without a previous history of deep vein thrombosis or pulmonary embolism, that is estimated at around 30%. Beyond the hypocoagulation, the treatment of CTEPH is surgical, and for most patients, a successful pulmonary thromboendarterectomy is curative, which has occurred in this patient.
Characteristics of COPD patients residing in the urban area of South Korea categorized according to the GOLD assessment framework

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Background and aim
Chronic obstructive pulmonary disease (COPD) is characterized by chronic airflow limitation of the airways, and forced expiratory volume in one second (FEV1) has been the standard method for confirming a clinical diagnosis of COPD and for grading COPD severity. However, the importance of the impact of COPD on an individual patient and exacerbation prevention has been recently highlighted in the management of COPD.

Within this regards, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) proposed multidimensional approach to assess the severity of airflow limitation, its impact on the patient’s health status and the risk of future events. In particular, the 2017 GOLD framework focused on exacerbation risk based on a history of exacerbation history, along with symptoms measured by the COPD Assessment Test (CAT) or the modified medical research council (mMRC), proposing the separation of spirometric grades from the assessment of symptoms/risk of exacerbation. In South Korea, no study has assessed COPD population residing in the community, applying combined assessment of patients’ symptom and risk of exacerbation. This study was aimed to investigate the distribution and clinical characteristics of COPD population residing in the community in South Korea, applying the 2017 GOLD assessment framework.

Methods
A cross-sectional descriptive study was conducted with 110 stable COPD patients aged 69.9 (SD 8.7) years old and selected by a convenient sampling from an outpatient department of pulmonology in a tertiary hospital. Participants completed a constructed questionnaire including general characteristics, smoking history, dyspnea by mMRC scale, and health status by CAT. Medical records were reviewed to obtain disease-related characteristics including duration of the disease, FEV1, and a history of exacerbation in the last 12 months. Data were analyzed using PASW statistics 20.0.

Results
Ninety percent of participants were male and 82% of them were currently non-smokers. Time diagnosed was 9.6 ± 7.7 years and mean FEV1% was 62.0 ±21.7; 70% were in GOLD 2 or milder. Only 22.7% of participants had more than one exacerbation leading to hospital admission. Mean CAT scores was 17.4 ± 7.2 and 71.0% of participants reported mMRC ≤ 2. The distribution of participants into the ABCD group, as categorized by CAT or mMRC were as the following; 48.5% of participants were placed in the low symptom group (GOLD group A ad C) by the mMRC, compared to 28.2% categorized so by the CAT. Nearly half (51.6%) of participants were included in high symptom (group B and D) using the mMRC compared to 71.8% with CAT. There were significant differences in CAT scores by the mMRC (F=16.67, p< .0001), while differences in clinical characteristics of participants categorized into GOLD groups using the CAT or mMRC were not significant.

Conclusions
Majority of COPD patients in the community of South Korea were categorized into the low risk group and a higher proportion was judged less symptomatic by the CAT than by the mMRC. These results have clinical implications and warrant further studies for applying the GOLD framework to assess COPD population in the community and other settings.

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The Influence of Respiratory Function on Quality of Life in Patients with Stable Bronchiectasis

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Bronchiectasis (B) is a chronic irreversible disease of the respiratory tract, which is characterized by local dilatation of the bronchi, destruction of the elastic and muscular components of the bronchial walls. Morphology changes in the bronchi may be accompanied by functional bronchial obstruction and changes in the quality of life (QoL).

The aim of the study was to determine the effect of bronchial obstruction on the QoL in non-cystic fibrosis bronchiectasis (NCFB) patients.

Materials and methods
The study included 10 patients (2 men and 8 women) with NCFB (disease duration 1-8 years). In all patients, the presence of NCFB was confirmed by high resolution computed tomography. The respiratory function was investigated by computed spirometry, the QoL was assessed by Quality of life bronchiectasis questionnaire (QoL-B).

Results
The average age of patients was 48.4±3.7 years. In accordance with spirometry data signs of obstruction was detected in 100% of cases (FEV₁ from 36 to 82%, mean 57.42±5.34%). 3 (30%) patients had moderate, 3 (30%) – severe and 4 (40%) – very severe obstruction. Results of QoL-B questionnaire: “physical functioning” – 70.0[40.0-73.3] scores, “role functioning” – 53.3[40.0-66.7] scores, “vitality functioning” – 44.4[33.3-55.6] scores, “emotion functioning” – 62.5[41.7-75.0] scores, “social functioning” – 29.15[0.0-41.7] scores, “treatment burden” – 44.4[22.2-55.6] scores, “health” – 20.85[16.7-33.3] scores, “respiration” – 44.4[40.7-55.6] scores. A moderate positive correlation between FEV₁ and “role functioning” (R=0.66, p=0.03) was revealed. No significant correlation between FEV₁ and other aspects of the QoL-B questionnaire was found.

Conclusions
1. Most of patients with B had severe and very severe airways obstruction.
2. The most significant changes of QoL were determined in “social functioning” and “health” domains in patients with B.
3. The FEV₁ moderately positively correlate with the “role functioning” in accordance with QoL-B.
ASSESSMENT OF THE FACTORS AFFECTING QUALITY OF LIFE (QoL) IN PATIENTS WITH NON-CYSTIC FIBROSIS BRONCHIECTASIS (NCFB)

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Background
Bronchiectasis (B) is a chronic condition, which is accompanied by the dilatation of the bronchi, cough with sputum or, rarely, dry cough. The presence of B is associated with a deterioration in QoL and frequent hospitalizations in patients with NCFB.

The aim
of the study was to assess the QoL in patients with B and to determine the factors affecting it.

Materials and methods
The 11 women with stable NCFB confirmed by high resolution computed tomography were included in the study. The respiratory function was investigated by computer spirometry. Modified Medical Research council scale (mMRC) was used for dyspnea assessment and St. George Respiratory Questionnaire (SGRQ) was used for the QoL measurement.

Results
The mean age of patients was 44.5 ± 3.9 years. The signs of airways obstruction were found in 72.7% of patients (FEV1 28.8-98.1% (mean 63.4 ± 7.5)). The average mMRC score was 3 [2-3]. Results of SGRQ: symptoms – 81.9 [66.1–93.3] scores, activity – 61.0 [59.5–74.8] scores, influence – 68.4 [54.0–74.8] scores, total score – 69.7 [61.4–87.9]. There was a strong positive correlation between mMRC score and activity (R=0.715, p=0.013), moderate positive correlation between total score and mMRC score (R=0.606, p=0.047), moderate negative correlation between FEV1 and activity (R=-0.655, p=0.028)

Conclusions
1. The airways obstruction was found in most patients with NCFB.
2. During the survey, the majority of patients with NCFB noted a decrease in the QoL and moderate to severe dyspnea.
3. The most significant changes in QoL in patients with NCFB registered in symptoms.
4. Dyspnea and airways obstruction significantly influence on an “activity” domain evaluated by SGRQ.
P34. [92] Perception for risk and disease severity of NTM lung disease- physician survey in Germany, UK, Italy, France and the Netherlands

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Background
Bronchiectasis is one of the strongest risk factors for nontuberculous mycobacteria (NTM) lung disease The objective of this study was to measure current perception of NTM risk and disease severity by physicians treating adult non-CF bronchiectasis patients (NCFB).

Methods
An online survey with 280 physicians who spend at least 80% of their time in hospital setting and treated at least 10 adult NCFB patients in the previous 12 months was conducted in Germany, UK, Italy, France and the Netherlands.

Results
87% of respondents (range 77–93%) consider adult NCFB patients to be at particular risk of contracting NTM. 53% of respondents (range 36% [Italy] - 68% [UK] estimated that less than 20% of NCFB patients will contract NTM, 28% of respondents were not able to estimate that risk. The risk of contracting NTM was ranked as average compared to other micro-organisms. Most respondents (88%) were aware that NTM lung disease when left untreated can lead to severe consequences, including progressive worsening of respiratory function, increased morbidity and more frequent hospitalizations. Approximately 13% (range 7% [Germany] - 22% [France]) of physicians did not see NTM lung disease having a significant impact on mortality risk.

Conclusions
The results indicate that physicians treating adult NCFB patients are aware of the association between bronchiectasis and the risk of NTM lung disease. Majority of physicians perceive that NTM lung disease can lead to severe health consequences, although a minor part of physicians do not see that it lead to significant increase in mortality.
Screening for NTM lung disease in adult non-CF adult bronchiectasis patients - physician survey in Germany, UK, Italy, France and the Netherlands

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Background
Nontuberculous mycobacteria (NTM) lung disease has been increasing globally with bronchiectasis being a strong risk factor. The objective of this study was to evaluate the current screening practices of physicians for NTM disease in adult patients with non-CF bronchiectasis (NCFB).

Methods
We conducted an online survey with 280 physicians treating adult non-CF bronchiectasis patients in Germany, UK, Italy, France and the Netherlands. Respondents had to spend at least 80% of their time in the hospital setting and manage N³10 adult NCFB patients in previous 12 months.

Results
85% (range: 80-88%) of surveyed physicians tested at least some of their NCFB patients for NTM infection. In total 51% (range: 40% [France] - 70% [Netherlands]) of NCFB patients managed by these respondents were tested for NTM infection and 17% of those (range: 8% [Netherlands] - 21% [Germany]) were stated to have tested positive. The NTM infection was mostly suspected by physicians due to radiology exams or physical features of the lung (82%). Close to half of NCFB patients are tested for NTM on diagnosis or initial presentation. 64% of respondents (range: 52-76%) test for NTM in at-risk patients with NCFB at least once per year. Only 38% (range: 24-66%) of physicians test for NTM infection before initiating a macrolide monotherapy.

Conclusions
Physicians need to be educated to screen patients with NCFB for NTM infection before initiating macrolide monotherapy. Recommendations for NTM-screening in these patients need to be validated, and further research on risk factors associated with NTM infection is warranted.
Introduction
Since 2015, migratory flows to Italy from countries with high incidence of tuberculosis (TB), especially those in Sub-Saharan Africa and the Indian subcontinent, have increased. Social issues and political conflicts represent major reasons of migration. TB in the European Union affects mainly poor and marginalized people, including asylum seekers (AS) living in metropolitan areas. This study aimed at assessing incidence of TB and prevalence of latent TB infection (LTBI) among AS in the city of Milan, as well as the performance of the city surveillance and management system during the biennium 2016-17.

Methods
To face this public health issue in the Milan area, a two-level surveillance system was developed to screen AS for both TB and LTBI. AS hosted in receiving facilities could at any time self-report symptoms requiring further radiological and microbiological evaluations. However, all AS underwent an initial screening with tuberculin skin test (TST) and a questionnaire. Those presenting with a positive result were considered eligible for a chest X-ray (CXR) to assess signs compatible with TB. People under 35 years of age with negative CXR underwent further testing by Interferon Gamma Release Assay (IGRA) and received prophylactic treatment for LTBI if found to be positive to both TST and IGRA. Observed TB incidence and LTBI prevalence categorized by country and region were compared with literature data using incidence rate ratio (IRR) for incidence and Chi-square test for prevalence. A molecular surveillance, based on a 24-locus mycobacterial interspersed repetitive units/variable-number tandem repeats (MIRU/VNTR) typing system, was also implemented to evaluate if recent transmission had occurred.

Results
A total of 5,324 asylum seekers were enrolled. 89% belonged to the age groups 15-49; most were males (84%) and from Sub-Saharan African countries (69%). In 2016-17, a total of 69 active TB cases (rate 1,236/100,000 population) and a total of 865 persons with LTBI (prevalence 20%) were diagnosed. The incidence was 1,003 (IRR=4.357; p<.001) among AS from World Health Organization African Region (WHO AFR) countries and 3,043 (IRR=26.932; p<.001) among those from the WHO Eastern Mediterranean Region (WHO EMR) countries, that includes Somalia (20 TB cases). TB treatment success rate and defaulting rates were 80% and 12%, respectively. LTBI prevalence among AS from WHO AFR countries was 23%, similar to that observed in their countries of origin (p=.081), while a lower rate (11%) was observed in those coming from WHO EMR countries compared to that in their countries of origin (p=.012). A high rate of acceptance (93%) and adherence (90%) to LTBI prophylactic treatment were observed. The molecular surveillance by 24-MIRU/VNTR typing system allowed to determine that only 3 TB cases were due to recent transmission within Milan receiving centers.
Conclusions
Our study shows that TB incidence is high among AS and that well-coordinated screening measures are critical to early diagnosis and treatment. The high defaulting rate needs to be addressed through urgent community interventions. Prophylactic treatment of LTBI is feasible and successful in Milan, probably due to its short duration (3 months rifampicin and isoniazid). The attrition observed between the two levels of the surveillance system could be reduced through better data sharing i.e. including CXR data in databases.

Conflict of Interest/Disclosure
None.
Influenza hospitalizations in the 2017/2018 season – a retrospective study

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Introduction
Influenza causes an epidemics that is usually benign and mild but that can worsen other diseases. The impact is particularly significant in specific groups (elderly, pregnant, those with chronic disease) that present with higher risk of complications associated with Influenza leading to hospitalization and eventually death.

Aims
Characterization of clinical aspects and outcomes associated with patients hospitalized with Influenza in the 2017/2018 season in a local health unity in northern Portugal.

Methods: Retrospective analysis of adult patients (≥18 years) admitted with laboratory confirmed Influenza between October 1st 2017 and March 31st 2018. Data (demographic and clinical) was collected by chart review.

Results
One hundred and thirty two hospital admissions occurred (62,9% female and mean age of 74,1±12,3 years), with the majority of cases (70,5%) occurring in December 2017 and January 2018. Mean length of hospital stay was 13,9±15,1 days (median 10 days). The main comorbidities found were cardiovascular disease (43,9%; chronic heart failure and ischaemic heart disease), chronic respiratory diseases (28,8%) mainly COPD, diabetes (28,8%) and chronic kidney disease (17,4%). In 33,3% there were previous or current smoking habits. Seasonal Influenza vaccination was confirmed in 9,1% of patients. Dyspnoea and fever were the most frequent manifestations with 72,0 and 43,2% of patients respectively – the mean length of symptom development before hospitalization was 4,2 days. On admission, mean PaO₂/FiO₂ ratio was 261,7 mmHg and mean C-reactive protein level was 86,4 mg/L. Type B Influenza was identified in 76,5% of cases. Considering organ complications 22,7% developed acute heart failure and 13,6% bacterial pneumonia; two myocarditis occurred. Intermediate/intensive care admission was needed in 30 patients (22,7%) – 66,7% of which required ventilatory support (invasive and/or non-invasive). Antiviral treatment was given to 58 patients (43,9%). Sixteen patients died (12,1%) during hospitalization – patients were older (mean age 78,8±9,4 years) with female predominance maintained (68,8%); the majority (75) had not been vaccinated and Influenza type B was more frequent (75%). A statistically significant relation was found between PaO₂/FiO₂ ratio and admission on intermediate/intensive care units (p=0,045).

Conclusions
Our study revealed the higher impact of Influenza on the elderly age group with cardiovascular disease as a major comorbid/complication associated, as has been published. We observed a low immunization rate among hospitalized patients which may justify the admissions, especially considering the age group for which the vaccine is recommended (≥65 years). Influenza B was the most frequent type identified, including among deceased patients. Our results reveal the awareness of the risks associated with influenza infection and the importance of vaccination are never over-emphasized and virological surveillance is of most importance in understanding the relationship of virus strains and disease severity.

Conflict of Interest/Disclosure
None to declare.
P38L [243] Influenza hospitalizations – a comparative analysis between two seasons

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Introduction
Influenza viruses are among the most common causes of human respiratory infections and are associated with significant morbidity and mortality. Elderly, infants and people with chronic diseases are the ones at higher risk of developing severe complications. Estimates of the burden of seasonal influenza can help to evaluate the impact of vaccine programs and contribute to development of prevention policies.

Aims
Identification of clinical characteristics and outcomes associated with Influenza hospitalizations in the 2016/17 and 2017/18 seasons.

Methods: Retrospective analysis of adult patients (≥18 years) admitted with laboratory confirmed Influenza between two seasons - October 1st 2016 to March 31st 2017 and October 1st 2017 to March 31st 2018. Data was collected by chart review.

Results
A rise of 50 hospital admissions was observed between the 2016/17 and the 2017/18 seasons (with 82 and 132 hospitalizations, respectively). A prevalence of female sex was observed in 2017/18 season (46.9% vs 62.9%) but no significant difference in age was observed. In both seasons, most admissions occurred in December and January, especially in 2016/17 (93.9% vs 70.5%). Influenza vaccination rate was superior in the 2016/17 season (40.2% vs 9.1%). Regarding previous medical history, smoking habits, chronic respiratory diseases, cancer and renal disease were more frequent in 2016/17, while cardiovascular disease and obesity were more prevalent in 2017/18 season. All cases identified in season 2016/17 were influenza type A, while on 2017/18 season 76.5% were type B. Hospitalization length was higher in 2017/18 season (10.0±8.8 vs 13.9±15.1 days, respectively). Admission on intermediate/intensive care units was similar (26.8% and 22.7%), but length of stay was longer in 2017/18 (6.0±4.4 vs 17.0±13.2 days). More patients received antiviral treatment in the last season (20.7% vs 43.9%). Death rate was similar (14.6% and 12.1%), but men were the most affected in 2016/17 (75%) while women were in 2017/18 (68.8%). A statistical significance was found in the 2016/17 season between PaO₂ levels on admission and risk of death while in 2017/18 this was observed between PaO₂/FiO₂ ratio and admission on intermediate/intensive care units.

Conclusions
Factors that determine the severity and extent of the outbreak are not completely understood, but type A is usually associated with a more severe disease. In our study, an increase of hospitalizations in the last season was observed, with higher severity translated in more admissions on intensive/intermediate care units despite the similar number of deaths. These results are in line with the described by the ECDC for the 2017/18 season, were type B predominated - this season had also a lower rate of vaccination which can by itself explain these numbers. We highlight nor only the importance of epidemiologic patterns characterization but also that vaccination promotion, especially among risk groups is one of the keys to avoid/reduce severe complications.

Conflict of Interest/Disclosure
None to declare.
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