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Respiratory Diseases and *Immune Response*

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10TH INTERNATIONAL WORKSHOP ON LUNG HELATH

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The abstracts in this book are listed in alphabetical order
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RISING STARS

SEX DIMORPHISM CONTRIBUTES TO INITIATION AND PROGRESSION OF BLEOMYCIN-INDUCED PULMONARY FIBROSIS IN MICE

Danilo D'Avino[1]; Lucianna Maruccio[2]; Ida Cerqua[1]; Elisabetta Granato[1]; Domenico Galati[3]; Rita Di Matteo[1]; Armando Ialenti[1]; Marialuisa Bocchino[4]; Fiorentina Roviezzo[1]; Antonietta Rossi[1]

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Background/Aim: Pulmonary fibrosis (PF) is a chronic and progressive interstitial lung disease, where the normal lung architecture is lost and replaced by fibrotic tissue leading to an irreversible and progressive respiratory insufficiency[1]. PF has previously been considered the end result of chronic inflammation, but accumulating evidence indicates that fibrosis and inflammation are two separate pathways[2]. Epidemiology shows that men are more affected than women and, more interestingly, the female sex is associated with major survival[3]. The cellular and molecular mechanisms underlying this sex dimorphism are not known. Considering this evidence, the aim of this study is to evaluate sex-related differences in the initiation and progression of PF.
Methods: PF was induced in male and female adult C57/Bl6 mice by s.c. injections of bleomycin (2 mg/kg, BLM), 3 times/week for 1-4 weeks. Lungs were harvested for:
histological assessment using Hematoxylin & Eosin (H&E), Masson's Trichrome (MTC) and Picro Sirius Red (PSR) stains; immunohistochemistry (IHC) analysis for neutrophils; lipid mediator and cytokine measurement by ELISA assay.
Results: Histological analysis of lung sections with H&E staining revealed an onset of cell infiltration 1 week after BLM treatment along the subpleural area and alveolar spaces, with an increase up to 2 weeks, followed by a loss of lung architecture caused by the onset of fibrotic tissue more in males than females. Immunohistochemical analysis confirmed this evidence, revealing a higher neutrophilia in males compared to females up to 2 weeks. According to this, proinflammatory leukotriene B_4 and interleukin-1β levels increased significantly only in male mice. MTC and PSR staining showed a significant and progressive increase of collagen expression starting from 1 week in males, while in females a slight increase of collagen was observed up to 2 weeks, with a return to basal level at 4 weeks, showing a resolution of fibrotic process. Accordingly, anti-fibrotic prostaglandin E_2 levels were significantly increased only in lungs from female mice.
Conclusions: The data suggest that in early stage of PF both inflammatory reaction and fibrotic process occur in parallel in males and females, but an exacerbated fibrosis process takes place only in males.
References:
E. King, et al. Lancet. 2011; 378: 1949–1961.
Rydell-Törmänen K, et al. Lab Invest. 2012; 92(6):917-25.
Gribbin J, et al. Thorax 2006; 61:980–985
I declare that I have no conflict of interests and that the studies have been approved by institutional committees on ethics of experimental and human investigations.

X INTERNATIONAL WORKSHOP ON LUNG HEALTH
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NINTEDANIB AND ITS OUTCOME AMONG POST-COVID PULMONARY FIBROSIS PATIENTS RESIDING IN HIGH ALTITUDE. CASE REPORT

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Background The COVID-19 pandemic has caused major issues in our healthcare system. Even though shreds of evidence add up to the knowledge, a lot remains unknown. Much research is going on for treating the disease and its consequences as pulmonary fibrosis. This study aimed to see the effect of Nintedanib among post-COVID pulmonary fibrosis patients both clinically and radiologically.

Case Study Case report of four patients having critical COVID-19 who despite being given remdesivir, anticoagulants, and steroid therapy developed Pulmonary fibrosis. They were given a targeted anti-fibrotic drug Nintedanib for initial 3 months and assessed for improved clinical symptoms, oxygen requirement and lung function using pre- and post-treatment High-Resolution Chest Computed tomography (HRCT) Scan and Spirometry. If not, they were continued for 6 months of therapy and reassessed. Two patients were under regular follow-up for 9 months period, one lost follow-up, and the next patient's drug was stopped due to frequent seizure episodes as he was under Na Valproate.

Discussion The pathogenesis of lung fibrosis seems to be due to impaired healing of the alveolar epithelium; COVID-19 act as a trigger. IPF and COVID-19 lung seem to have similar mechanisms thus anti-fibrotic therapy (Nintedanib) had been used as an adjunct treatment though its use has been questionable. It has been a treatment option for prevention and during post-COVID-19 pulmonary fibrosis which has been seen as early as by 3 weeks. In our scenario, Nintedanib was given for a total of 6months resulting in clinical and radiological improvement as seen in HRCT chest and spirometry.

Conclusion In our study administration of Nintedanib to critical COVID-19 patients was found to be associated with improvement both clinically and radiologically with improvement in lung function.

ABSTRACTS FOR POSTERS

12. SPHINGOSINE-1-PHOSPHATE SIGNALING AS A SEXUALLY DIMORPHIC TARGET FOR ASTHMA TREATMENT

Ida Cerqua[1]; Elisabetta Granato[1]; Maria Antonietta Riemma[1]; Antonietta Rossi[1]; Rosalinda Sorrentino[2]; Maria Francesca Nani[1]; Giusy Ferraro[2]; Giuseppe Cirino[1]; Fiorentina Roviezzo[1]

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Background: Asthma has a higher incidence in adult females. The prevalence and severity of asthma are strongly influenced by hormonal fluctuation during the menstrual cycle. Moreover, women seem to experience more asthma symptoms than men and use more rescue medications with a negative impact on life quality. Conversely, asthma during puberty is more prevalent in boys compared to girls. Also, in pre-clinical models, females tend to have a more severe asthma phenotype than males. Among the several mediators involved in asthma, sphingolipids have emerged as potential key contributors. Polymorphisms of Orosomucoid-like 3 (ORMDL3) proteins playing an integral role in sphingolipid homeostasis and synthesis have been associated with an increased risk of childhood asthma. Sphingolipids constitute key structural elements in cellular membranes, but they are also sources of critical signaling molecules such as sphingosine-1-phosphate (S1P) involved in several cellular functions including signal transduction, immune response, and cell proliferation. S1P levels result significantly increased in bronchoalveolar lavage fluid from subjects with asthma following allergen challenge and well correlate with lung eosinophilic inflammation. S1P level is remarkably higher in women *versus* men in adulthood, whereas plasma S1P levels decrease dramatically in post-menopausal women. Also, estrogens improve the synthesis and release of S1P in vitro. Based on this evidence, the aim of this study is to investigate whether ORMDL3 and S1P are linked to female asthma susceptibility and their role in sex dimorphism in asthma features.
Methods: Male and female mice expressing high (BALB/c) or low (C57/Bl6) Th2 immunophenotypes were used. In vitro and in vivo experiments have been conducted to assess lung function and the contribution of S1P signaling in atopic and sensitized mice.
Results: Lungs and bronchi harvested from female BALB/c mice show an upregulation of ORMDL-3 and S1P signaling when compared to males or to C57/Bl6 mice of both sexes. This finding well correlates with differences in lung function as well as serum IgE and pulmonary IL-5 levels between sexes in BALB/c mice. Administration of 17β-estradiol to male BALB/c mice promotes a significant increase in bronchial reactivity and upregulation of S1P signaling abrogating the sex differences in lung function. The 17β-estradiol-induced bronchial hyperreactivity in males is reversed by $S1P_2$ or $S1P_3$ antagonists. In perfect tune, an upregulation of ORMDL-3 occurs in the lung of 17β-estradiol treated male mice. Conversely, tamoxifen treatment induces a significant reduction in bronchial reactivity and downregulation of S1P signalling. Systemic exposure of BALB/c mice to S1P induces asthma-like disease only in females. Following sensitization, asthma features result more marked in BALB/c female mice and ameliorated by pharmacological inhibition of S1P signaling.
Conclusion: In conclusion, S1P signaling plays a key role in driving asthma susceptibility and in exacerbation of asthma feature in females. Thus, S1P signaling could represent a sexually dimorphic target for a sex-tailored therapy of asthma.
I declare that I have no conflict of interests and that the studies have been approved by institutional committees on ethics of experimental and human investigations.

20. INFLUENCE OF DOSE AND EXPOSITION TIME IN THE EFFECTIVENESS OF NAC TREATMENT IN HUMAN BRONCHOALVEOLAR BASAL EPITHELIAL CELLS

Poster Winner

Paula Montero[1,2]; Ines Roger[3,1,2]; Cristina Estornut[2]; Javier Milara[4,1,3]; Julio Cortijo[1,3,5]

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Background: N-Acetyl-L-cysteine (NAC) acts as a precursor of the tripeptide glutathione (GSH), one of the principal cell mechanisms for reactive oxygen species (ROS) detoxification. Chronic obstructive pulmonary disease (COPD) is associated with enhanced inflammatory response and oxidative stress and NAC has been used to suppress various pathogenic processes in this disease. Studies show that the effects of NAC are dose-dependent, and it appears that the efficient doses *in vitro* are usually higher than the achieved *in vivo* plasma concentrations. However, to date, the inconsistencies between the *in vitro* and *in vivo* data have not been explained in depth.

Objective: This study aims to investigate and corroborate the beneficial effects of both low and high doses of NAC *in vitro,* as well as to confirm the *in vivo* hypothesis that the effects of NAC administration are dependent on the concentration and duration of treatment.

Methods: A549 were transfected with polyinosinic-polycytidylic acid (Poly (I:C)) and treated with NAC at different treatment periods (24h, 72h and 144h). Oxidative stress was analyzed by ROS and thiols detection. Inflammation was analyzed by IL-6, IL-8 ELISA and NFkB activation with Western blot analysis. NAC concentrations tested reproduce the plasma levels reached after oral NAC 600 and 1200 mg, as well as 2 commonly *in vitro* used concentrations (in the range of mM).

Results: In A549 cells challenged with Poly (I:C), NAC at low doses in chronic administration has sustained antioxidant and anti-inflammatory effects, while acute treatment with high dose NAC exerts a strong antioxidant and anti-inflammatory response. These results present novel evidence in A549 cells by confirming that the effects of NAC are concentration dependent not only *in vivo* but also in the *in vitro* setting.

Conclusions: Overall, these findings add new data to the existing body of experimental and clinical evidence of the beneficial activity profile of NAC in chronic inflammatory lung diseases such as COPD. Our results strongly support the idea that chronic administration of NAC, even at low doses, is a good strategy to maintain the redox state and thus prevent possible exacerbations in patients with chronic respiratory diseases.

26. D-DIMER LEVELS AND RESPONSE TO RESPIRATORY SUPPORT WITH HELMET CPAP IN PATIENTS WITH COVID-19 PNEUMONIA

Poster Winner

Stefano Pini; Marina Saad; Fiammetta Danzo; Eleonora Maratta; Anna Casartelli; Linda Pelosi; Walid Karimeh; Dejan Radovanovic; Pierachille Santus

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Background: Continuous positive airway pressure (CPAP) is widely employed as a respiratory support in COVID-19 pneumonia. Increased D-dimer indicates endothelial dysfunction, which could hinder the effectiveness of CPAP by worsening ventilation/perfusion ratio.

Aim: The aims of this study was to assess if D-dimer levels are associated with changes in indexes of lung recruitment after starting CPAP in patients with COVID-19 pneumonia.

Methods: This was a retrospective, observational study conducted on adult patients with COVID-19 pneumonia that underwent respiratory support with helmet CPAP from March 2020 to March 2021 in the High Dependency Respiratory Unit of L. Sacco University Hospital, Milan (Italy). Biochemistry and gas exchange parameters, including arterial partial pressure of oxygen (PaO2) and carbon dioxide (PaCO2), were assessed at admission and regularly tested during the hospital stay. Severity of respiratory failure was assessed by means of the PaO2/ fraction of inspired oxygen (FiO2) ratio and alveolar-arterial gradient (A-a O2). CPAP failure was defined as death in the High Dependency Unit in patients with a Do-Not Intubate (DNI) order or need for endotracheal intubation (ETI).

Results: During the observation period a total of 172 patients (mean age 69 years, 73% males) were enrolled. At baseline, median PaO2 was 66 (inter quartile range – IQR: 59-80) mmHg and PaO2/FiO2 was 148 (89-252) mmHg. One hour after starting CPAP, PaO2/FiO2 had improved by 67.0 (standard deviation 88.6) mmHg ($p<0.001$) and the alveolar-arterial (A-a O2) gradient by 133 (97) mmHg ($p<0.001$). The highest D-dimer reached before or during CPAP treatment (DDmax) was 1877 (943-6706) µg/L FEU. In total, 44 patients (25.5%) died and 27 (15.7%) underwent ETI. DDmax was an independent predictor of CPAP failure (AUROC=0.80, $p<0.001$; Figure 1), but did not correlate with the degree of lung recruitment with CPAP assessed by PaO2/FiO2 ($R=-0.046$, $p=0.640$) and by A-a O2 gradient ($R= -0.002$, $p=0.985$).

Conclusions: D-dimer levels do not correlate with improvements in gas exchange after CPAP but can predict CPAP failure in patients with COVID-19 pneumonia.

Disclosure: The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

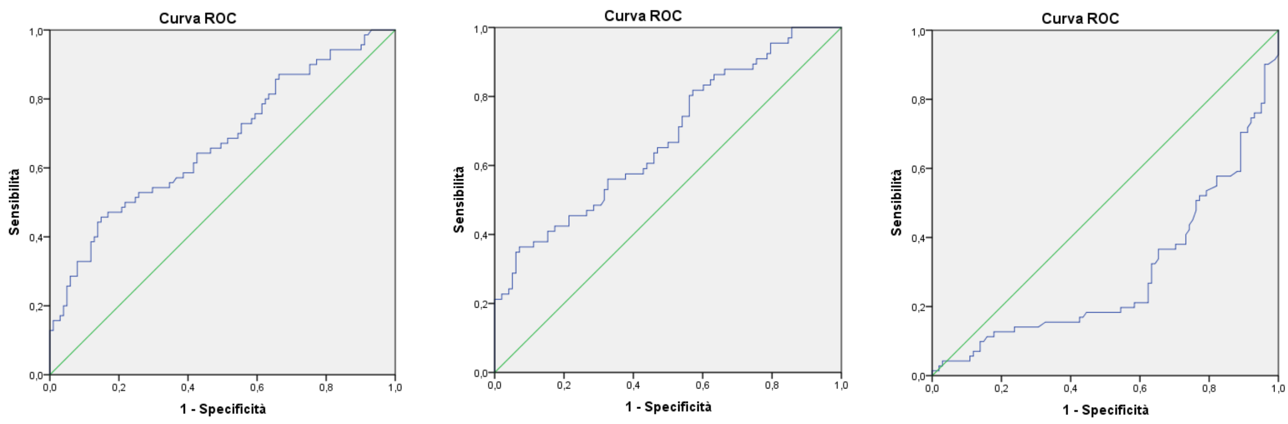

Figure 1. ROC curves of the D-dimer at the admission to the ward (left), the PCR value (in the middle) and the lymphocyte count at the admission (right) for the prediction of CPAP failure in the study population.

16. BLOOD EOSINOPHIL COUNTS AS A PREDICTOR OF COPD EXACERBATIONS

Élin Almeida[1]; Filipa Jesus[1]; Fernando Pereira Silva[1]; Sara Braga[1]; Joana Ribeiro[1]; Mariana Tavares[1]; José Manuel Silva[1]; Luís Ferreira[1]

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Background: There has been controversy over the implications of eosinophilic inflammation in COPD exacerbations, and whether this phenotype could be used as a biomarker for predicting exacerbation and hospital admissions in COPD.

Aim: To establish whether there is an association between blood eosinophil counts and the frequency of hospital admissions and the length of stay for COPD exacerbation.

Methods: We retrospectively analyzed data of patients admitted due to COPD exacerbation between October 2019 and March 2021. The 1-year frequency of COPD-related admissions and length of stay were compared between eosinophilic and non-eosinophilic patients, using as a cut-off point an eosinophil level ≥300 cells/μL and/or ≥2% of the total count of white blood cells on the first complete blood count.

Results: A total of 85 patients were included, of whom 22.4% had an eosinophilic phenotype. The median of eosinophil count and their percentage was 0.07×10^9cells/μL (0.01-0.17) and 0.6% (0.1-1.75). Although not significative, patients with blood eosinophilia had less exacerbations than patients without eosinophilia (mean 0.41 versus 0.11). The median length of stay of the patients without eosinophilia was 10 days (7-14) versus 8 days (5-13) in the eosinophilic group, with no significant difference. No correlation was observed between eosinophil count and the frequency of hospital readmissions or length of stay.

Conclusion: Although being recommended as a predictor of response to inhaled corticosteroids, eosinophils may not be useful predictors of future exacerbation, as we found no evidence of an association between blood eosinophils at admission for a COPD exacerbation and hospital readmission, nor with the length of hospital stay.

21. TELEMONITORING: IMPROVING MULTIDISCIPLINARY CARE IN LUNG TRANSPLANTED PATIENTS

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Background Telemedicine has been successfully employed in a wide range of fields. We hereby present the results of a pivotal study our group ran in our Centre just before the COVID19 pandemic.

Methods This was a prospective study including all adult cystic fibrosis patients who underwent lung transplant (LuTx) from September 2017 to August 2019. Patients were randomized into two groups; patients assigned to the first arm (intervention) received a home medical assistant (HMA) system device, to which a pulse oximeter and a spirometer with reusable turbine were integrated; they were asked to perform a spirometry and register their SpO_2 at rest and on effort on a twice-weekly basis. All the data were digitally transmitted to our Centre, where physiotherapists and physicians were able to analyze them real-time. Both the groups received traditional hospital-based follow-up.

Results 32 patients were enrolled, 16 for each group.

At the beginning of the study, several technical problems were reported with the equipment (55 registrations not obtained due to technical problems and one change of equipment). A total of 2470 events was registered.

Baseline patient characteristics and relevant respiratory complications during the study period are presented in Table 1; no significant difference was found between the two groups. With reference to the intervention group, adherence to telemonitoring significantly decreased during the 12 months period of follow up (see figure 1). Hospital reported data were consistent with the last being registered with the HMA device (median difference between the devices 54 (33; 102) mL).

Groups were compared in terms of Acute Lung Allograft Dysfunction (ALAD) (see Figure 2): no statistically significant difference was found in terms of incidence ($p = 0.137$), time from onset of symptoms to diagnosis (although a trend can be recognized towards a faster diagnosis) and time of occurrence from LuTx.

7 patients were requested to anticipate their hospital routine, in order to rule out possible ALAD. 4 contacted attending physicians by phone call because they were experiencing respiratory symptoms (cough, sputum, dyspnea): these individuals were all later hospitalized for a respiratory infection. 3 were instead contacted by our Centre, because the physiotherapists detected a significant FEV1 decrease at HMA measurement. All these patients received an anticipated visit (as opposed to their routine evaluation) with the aim to investigate the source of these problems.

13 out of 16 patients reported a high degree (score > 7/10) of satisfaction with the telemonitoring experience. Complaints mainly concerned the required frequency of measurements (which the patients considered excessive) and the malfunction of the equipment.

Table 1 Baseline characteristics of study population

	Total	Cases	Controls	p	Missing
	32	16	16		
Baseline characteristics					
Age at time of lung transplant (years)	32 (24; 36)	28 (23; 36)	33 (25; 38)	0.289	32 (24; 36)
Sex, males (no, %)	18 (56)	10 (63)	8 (50)	0.479	18 (56)
Occurence of acute rejection (no, %)	5 (16)	3 (19)	2 (13)	0.437	5 (16)
Hospitalizations for respiratory infection (no, %)	9 (28)	6 (38)	3 (19)	0.197	9 (28)
Walking test (in terms of distance, expressed in meters)					
At discharge	479 (426; 534)	492 (455; 532)	460 (412; 569)	0,289	0
At 3 months from LuTx	610 (550; 640)	615 (540; 652)	583 (555; 636)	0,715	3
At 6 months from LuTx	600 (542; 622)	590 (529; 636)	600 (555; 625)	0,756	5
At 9 months from LuTx	598 (549; 650)	585 (520; 636)	600 (581; 655)	0,434	7
At 12 months from LuTx	620 (576; 661)	611 (570; 665)	620 (576; 662)	0,999	4
SGRQ (expressed as no./100)					
At discharge	24 (9; 45)	24 (5; 42)	24 (13; 57)	0,724	0
At 3 months from LuTx	5 (2; 15)	3 (1; 16)	7 (4; 11)	0,428	6
At 6 months from LuTx	5 (3; 9)	4 (3; 11)	6 (4; 9)	0,65	6
At 9 months from LuTx	5 (1; 7)	4 (1; 7)	6 (3; 7)	0,695	6
At 12 months from LuTx	3 (3; 7)	3 (2; 6)	4 (3; 8)	0,435	7
PFTs, expressed as % of predicted					
FVC, at 3 months from LuTx	78 (68; 93)	80 (68; 95)	73 (70; 91)	0,586	1
FEV1, at 3 months from LuTx	81 (69; 90)	83 (70; 93)	76 (62; 83)	0,586	1
FVC, at 6 months from LuTx	87 (74; 96)	90 (75; 100)	82 (74; 92)	0,565	1
FEV1, at 6 months from LuTx	83 (72; 94)	87 (73; 98)	82 (68; 91)	0,357	1
FVC, at 9 months from LuTx	87 (77; 102)	92 (82; 104)	84 (75; 101)	0,466	2
FEV1, at 9 months from LuTx	84 (73; 96)	91 (74; 96)	78 (67; 97)	0,486	2
FVC, at 12 months from LuTx	91 (78; 103)	97 (83; 103)	85 (76; 107)	0,653	2
FEV1, at 12 months from LuTx	87 (74; 97)	92 (77; 98)	78 (72; 97)	0,285	2

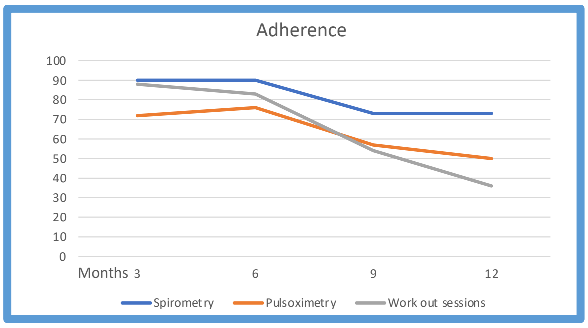

Figure 1 Adherence to telemonitoring during the observation period

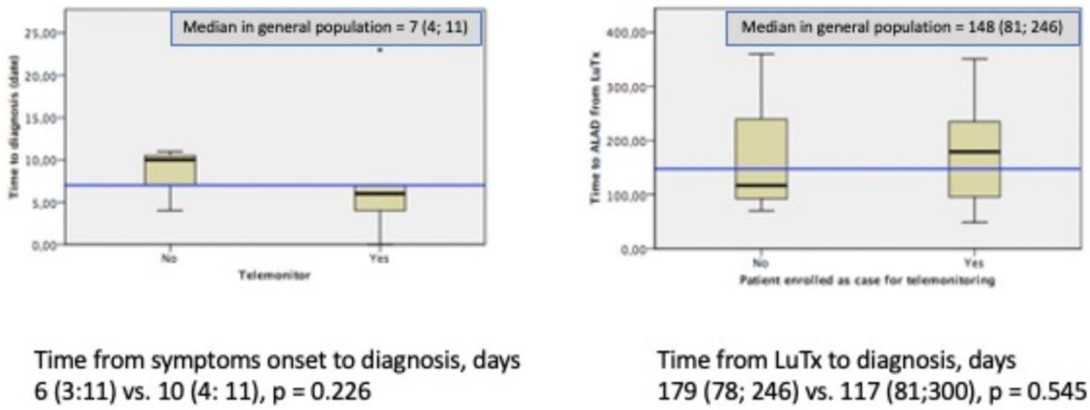

Figure 2 Acute Lung Allograft Dysfunction (ALAD) in study population

Conclusion Telemonitoring can be a valuable and reliable tool to improve quality health care to LuTx recipients. Our patients seemed willing to adopt HMA device, showing a good adherence to registrations; home spirometry has proven again to be a reliable device for measuring pulmonary function, with results that were equivalent to those obtained with hospital – based instruments. This RCT lends empirical support for the potential benefit of home spirometry, enabling the identification of cases warranting urgent evaluation for functional decline.

22. PROCALCITONIN AND C-REACTIVE PROTEIN TO RULE OUT EARLY BACTERIAL COINFECTION IN COVID-19 CRITICALLY ILL PATIENTS

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Background: Although the frequency of community acquired respiratory bacterial coinfection upon hospital admission in COVID-19 patients has been reported to be <4%, almost three-quarters of patients received antibiotics. We aim to investigate whether procalcitonin (PCT) or C-reactive protein (CRP) upon admission could be helpful biomarkers to identify bacterial coinfection among patients with COVID-19 pneumonia. **Methods**: Multicenter, observational cohort study including consecutive COVID-19 patients admitted to 55 Spanish ICUs. Primary outcome was to explore whether PCT or CRP serum levels upon admission could predict bacterial coinfection among patients with COVID-19 pneumonia. Secondary outcome was to evaluate the association of PCT and CRP levels and 30-day mortality. The kinetics of PCT and CRP serum values were also considered. **Results**: Between 5 February 2020 and 21 December 2021, 4,076 patients were included, 140 (3%) of whom presented a bacterial coinfection. Both PCT and CRP at hospital admission were independently associated with bacterial coinfection, particularly PCT ≥0.38 ng/ml (OR 1.57, 95% CI 1.10-2.24, p=0.012) and CRP ≥134 mg/L (OR 1.99, 95% CI 1.37-2.90, p<0.001). PCT values ≥0.38 ng/ml were independently associated with higher 30-day mortality (HR 1.25, 95% CI 1.09-1.44, p=0.002). PCT and CRP had higher values in the bacterial coinfection patients in the first 48 hours since symptoms onset (PCT p=0.001, CRP p=0.018), while after that an increase was shown only for CRP values (p=0.003). A relation between biomarkers levels and bacterial coinfection was shown in the first 48 hours from symptoms onset for PCT≥0.44 ng/ml (p= 0.031) and after 48 hours for CRP≥134 mg/L (p= 0.002). **Conclusion**: Based on our findings, PCT and CRP upon admission were independently associated with bacterial coinfection among patients with COVID-19 pneumonia. PCT <0.44 can be a valuable indicator of the absence of bacterial coinfection within the first 48 hours after symptoms onset. Considering symptoms timing is crucial for the interpretation of PCT and CRP levels.

17. LUNG CANCER AS A COMORBIDITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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COPD is a risk factor for lung cancer development independent of smoking status, with three to six times more likely to develop lung cancer at a rate of 0.8–1.7%/year. This may be associated with genetic susceptibility to cigarettes, chronic inflammation caused by toxic gases. Inflammatory mediators may promote the growth of bronchioalveolar stem cells, and activation of nuclear factor-κB and signal transducer and activator of transcription 3 play crucial roles in the development of lung cancer from COPD. The aim of the study is to evaluate the prevalence of lung cancer in patients with COPD.

We performed a retrospective study, from 2012 to 2022, among patients with pathologically confirmed diagnosis of lung cancer, aged 40-75 years. Patients with lung cancer that had COPD diagnosed >= 10 years before lung cancer diagnosis, were investigated group. Histological subtypes of lung cancer were determined based on histopathology reports and were categorized as squamous carcinoma, adenocarcinoma, small cell lung cancer (SCLC), large cell lung cancer (LCLC; including large cell neuroendocrine carcinoma), and other histological types according to 2015 WHO classification of lung tumors. At the time of registration, sex, age, BMI, smoking status, treatment history, and symptoms, including the CAT score, were recorded. In addition, at the time of registration, spirometry was performed both before and after inhalation of a bronchodilator, and a blood test and chest CT were also performed. The GOLD criteria was used to diagnose and assign severity of COPD: patients with a postbronchodilator FEV_1/FVC <0.70 were classified as having COPD; FEV_1 ≥0.8 was defined as mild, 0.5≤ FEV_1 <0.8 as moderate, 0.3≤ FEV_1 <0.5 as severe, and FEV_1 ≤0.3 as extremely severe. Patients were excluded if they presented with simultaneous or sequential second primary cancers or had a history of asthma, bronchiectasis, tuberculosis, pulmonary fibrosis, or other confounding diseases.

The middle age of lung cancer diagnosis was 61.1±8.5 years. Of the total number of patients with COPD and lung cancer (260), 195 (75.0%) were male and 65 (25.0%) female. 190 (73.07%) were current smokers or ex-smokers. The histological subtypes identified were as follows: squamous carcinoma (96 [36.9%]), adenocarcinoma (115 [44.2%]), SCLC (26 [10.0%]), LCLC (13 [5.0%]), and other histologic types (including adenosquamous, carcinoma carcinoid tumors, sarcomatoid carcinoma; 16 [6.15%]). The proportion of squamous carcinoma was higher in smokers/ex-smokers with COPD, while adenocarcinoma was more frequently observed in COPD non-smokers. Emphysema-predominant phenotype was an independent prognostic risk factor for squamous carcinoma. The prevalence of COPD in lung cancer patients was 35.5%. Compared with lung cancer patients with non-COPD, those with COPD were older (*P*<0.001), had a lower BMI (*P*<0.001), and majority were male (*P*<0.001) and smokers (*P*<0.001).

Annual low-dose computed tomography (LDCT) is an effective procedure for the early detection of lung cancer in high-risk patients like patients with COPD.

18. PREVALENCE OF BRONCHIECTASIS IN COPD PATIENTS

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Introduction - There is increasing recognition that radiological bronchiectasis is present in many patients with COPD. Computed tomography scan images have been used to identify different radiological COPD phenotypes based on the presence and severity of emphysema, bronchial wall thickening, and bronchiectasis. Bronchiectasis is defined as an abnormal dilation of the bronchi, usually as a result of chronic airway inflammation and/or infection. The prevalence of bronchiectasis in patients with COPD is high, especially in advanced stages, estimated prevalence varies from 4% to 50%.

Methods - COPD patients underwent chest CT as part of their clinical assessment. Patients were included if COPD was diagnosed based on spirometry and clinical assessment and excluded if there was clinical bronchiectasis. Scoring was by a simplified system based on Smith (Thorax, 1996) and returned a score of 0 (no bronchiectasis), 1 (0–50% of bronchi involved), or 2 (50–100% of bronchi involved) for each lobe, with a total score of 12 including the lingula; emphysema, interstitial lung disease (ILD), or other pathology was noted. A total of 220 COPD patients (77.2% ex- or current smokers, 79.5% male) were consecutively enrolled.

Results - Bronchiectasis was present in 54.5% of patients (score ≥2/12) and there was significant inter-observer correlation in the scoring ($r=0.63$, $p<0.0001$). Scores were highest in the lower lobes and lowest in the middle lobes (1.66 vs 0.86, $p<0.000$). Patients with widespread bronchiectasis (score ≥6/12) had a trend towards reduced bronchodilator reversibility (4% vs 9%, $p=0.08$) than those with limited bronchiectasis. Emphysema was present in 77.2% and ILD in 11.36%. The overall prevalence of emphysema was not different between patients with and without previous pulmonary tuberculosis (PTB) n=30 (13.63%), but in those with previous PTB, a higher number of subjects with middle ($p=0.002$) and lower ($p=0.017$) lobe emphysema, higher severity score ($p=0.029$), higher prevalence of panlobular emphysema ($p=0.015$), and more extensive centrilobular emphysema ($p=0.036$) were observed.

Conclusions - In this study, we found a higher prevalence of bronchiectasis than previously reported which may reflect the heterogeneity of COPD patients in a general respiratory clinic. Radiological features of bronchial wall thickening and mild bronchiectasis were commonly seen and when widespread this may result in reduced bronchodilator reversibility; however, the presence of radiological bronchiectasis was not related to disease severity. COPD patients with previous PTB had unique features of bronchiectasis and emphysema on HRCT, which were associated with significant dyspnea and higher frequency of severe exacerbations.

11. NEUTROPHILIC INFLAMMATION

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Background Neutrophilic airway inflammation is defined as a pathologically unique form of asthma. This problem has been found to appear in adults who are symptomatic. However, the specific clinical impacts as well as the mechanisms of the neutrophilic inflammation have still not been properly evaluated till today. Asthma is defined as a specific inflammatory airway disorder in human beings (1). This disorder is associated with eosinophils and mast cell infiltration. However, neutrophil infiltration also occurs and is strictly associated with the severity of asthma. In some of the previous research works, it has been observed that neutrophilic infiltration correlates with asthma which is specifically refractory to the corticosteroids, which are the mainstay of asthma treatment (2). Moreover, it has been recognized that these neutrophils are specifically heterogeneous in nature and thus more phenotyping is needed in order to delineate various asthma subtypes. The present review will discuss the current knowledge of neutrophilic inflammation and its role in asthma, highlighting the various future research areas in this field.

Methods Secondary research will be conducted in this study. A systematic review of literature or SLR will be the chosen format of research, for the present study. This study design will be chosen since there is no scope of conducting primary research without ethical approvals from the respective authority. Thus, the conduct of secondary research can be stated to be justified. A keyword-based search strategy will be followed in order to collect data for this research. This type of search strategy has been used in many secondary research studies or review papers (3). Therefore, the selection of this type of search strategy can be stated to be justified. The collected research papers will be screened based on a specific group of inclusion as well as exclusion criteria. The collected data will be recorded in a table and from there data will be extracted and synthesized.

Results The results will show the association between neutrophilic inflammation and severe asthma under the criteria of non-type 2 inflammation (4). Various mediators will be implicated in neutrophils and the recruitment to airways will be observed as an effect of the asthmatic condition. Respiratory tract infections by pathogens will be observed to induce a neutrophilic response. This response will be associated with neutrophilic inflammation or neutrophilia (4). The process will be observed to be associated with protease secretion and will also have severe consequences in the lung airways. Failing to suppress the neutrophilic inflammation can even promote the survival of neutrophils. Some information regarding alternate therapeutic agents for the condition will also be obtained from the research. For example, macrolides are successful in reducing the neutrophil numbers in blood (5). The specific molecules associated with the higher neutrophilic burden including CXCR2 chemokine receptor have also been observed to be targeted in various clinical trials. However, controlling for these specific cofounders, it will be observed that some factors also modify the neutrophilic inflammation process. These factors include IL-17, IFN-γ, and TNF-α. Controlling these confounders in the research will increase the precision of neutrophilic inflammation as a response to asthma.

Conclusions On a concluding note, it can be said that the abstract has discussed the mechanism of neutrophilic inflammation and various factors associated with it. The abstract has also discussed one of the most used therapeutic strategies to neutralize the effect of neutrophilic inflammation. Future works should focus on the conduction of primary research studies, in order to accumulate and analyze live data, which will open further research avenues.

References

Ray A, Kolls JK. Neutrophilic inflammation in asthma and association with disease severity. Trends in immunology. 2017 Dec 1;38(12):942-54.

MacDowell AL, Peters SP. Neutrophils in asthma. Current allergy and asthma reports. 2007 Nov;7(6):464-8.

Habibi MS, Thwaites RS, Chang M, Jozwik A, Paras A, Kirsebom F, Varese A, Owen A, Cuthbertson L, James P, Tunstall T. Neutrophilic inflammation in the respiratory mucosa predisposes to RSV infection. Science. 2020 Oct 9;370(6513):eaba9301.

Tomar B, Anders HJ, Desai J, Mulay SR. Neutrophils and neutrophil extracellular traps drive necroinflammation in COVID-19. Cells. 2020 Jun 2;9(6):1383.

Rosales C. Neutrophil: a cell with many roles in inflammation or several cell types?. Frontiers in physiology. 2018 Feb 20;9:113.

1. LTBI (LATENT TUBERCOLOSIS INFECTION) MOBILE SCREENING FOR REFUGEES IN MILAN METROPOLITAN AREA. EFFICACY OF THE INTERVENTION

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For more than two centuries, tuberculosis has been one of the leading causes of mortality and morbidity from an infectious disease with more than 10 million cases and 1.5 million deaths per year. It is estimated that over one billion people are infected and of these 5-10% will develop an active form.

The cases and the infected patients are mainly concentrated outside Europe, but migratory and climatic phenomena, social unrest and adverse economic evolution contribute to changing the epidemiology even in low endemic countries. In Milan, there are about 12,000 homeless and, depending on socio-political evolutions, migrants/refugees who are hosted in community structures are added to this number.

Following a previous screening project (2016-2018), in 2019 Lombardy region approved a collaborative project by TB Ref. Centre (CRR-TB), public health (ATS Milano) and STOP TB Italia ONG for the detection of latent and active TB.

In 2020, the Sars-Cov2 pandemic temporarily stopped this project that resumed in mid-2021.

At the request of the host communities or ATS Milano, the CRR-TB sent a mobile vehicle with a team of one pulmonologist, nurses and health assistants. The team submitted to the subjects a clinical questionnaire and performed tuberculin test (TST) with confirmatory IGRA test. Until mid-2021, the vehicle was equipped with X-ray machine, so X-rays were taken on-site and immediately evaluated by the pulmonologist. Subsequently, positive subjects were sent to the CRR-TB to complete the diagnosis and start the appropriate treatments (therapy or preventive therapy/TP).

From June 2019 to June 2022, more than 1,500 subjects were reported but only 1138 made a complete screening (due to refusal or transfer to another facility). Three subjects were found to have active TB (264/100,000) and three had already been treated in the past. Of the remaining 1132 (Table), 89 (7.8%) were from Eastern Europe, 54 (4.7%) were from South America, 467 (41%) were from Asia and 495 (43%) were from Africa. 271 (23%) were diagnosed with latent TB infection by IGRA test and of these 258 (95%) started anti-TB preventive therapy with a short regimen (R+H) for three months. 202 (78.3%) completed the treatment correctly and 56 refused or discontinued it.

In conclusion, the screening project allowed to identify, in addition of the three cases of active TB, a large number of infected subjects who received PT with a favorable outcome, preventing the further spread of the disease (END TB Strategy).

	TOTAL	EST EUROPE	SOUTH AMERICA	ASIA	AFRICA
TOTAL	1132	89	54	464	492
IGRA-	861	79	34	351	367
IGRA+	271	10	20	113	125
TP	258	10	20	106	121
TP completed	202	6	12	97	87

2. HUMORAL IMMUNITY AND BRONCHIECTASIS (BE) EXACERBATION RATE (ER)

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Background. The measurement of total serum IgA, IgM, IgG levels in patients (pts) with Bx is proposed by guidelines for humoral immunodeficiency detection. However, the influence of increased immunoglobulins (Igs) levels on the course of the disease is not established well. **The study aimed** to assess the connection between serum Igs levels and ER in pts with BE.

Materials and methods. 99 pts with stable BE confirmed by chest HRCT were included. ER during the previous year was defined by medical source documentation. Serum IgA, IgM, IgG were measured by immunoturbidimetry.

Results. The median age was 55 (39-63) years, 33.3% j – men. The median number of ER per year was 2 (1-4), 48 pts (48.5%) had frequent exacerbations (FE) (3 and more per year). The level of serum IgA was higher among pts with FE (3.69 (2.48-4.57) vs 2.63 (1.89-3.5) g/l, p=0.009), also there was a higher proportion of pts with elevated levels of IgA among pts with FE (48.9% vs 20%, p=0.003). The levels of total serum IgM were equal between studied groups (1.7 (1.01-2.52) *vs* 1.34 (1.07-2), p=0.43). Total serum IgG was higher in pts with FE (13.69 (10.97-15.76) *vs* 10.82 (8.86-13.24) g/l, p=0.001). By ROC-analyses conducted, the cut-off of IgA level for FE predicting was >3.84 g/l, AUC 0.65 (0.54-0.74), p=0.02; the cut-off of IgG level for FE predicting was >13.76 g/l, AUC 0.67 (0.56-0.76), p<0.001. Univariate logistic regression analysis showed a significant predictive value of IgA and IgG levels for FE risk prognosis: OR 5.4 (2.02-14.4), p=0.0003 and OR 5.03 (1.95-12.9), p=0.0004 respectively. After confounders were excluded, the level of IgA >3.84 g/l remained significant for FE predicting (p=0.03).

Conclusions. In the group of pts with FE 48.9% had elevated IgA while stable. IgA>3.84 g/l seems to be an independent significant predictor of FE, which reflects the mucosal immune response against airway pathogens.

3. RATE OF SPUTUM CULTURE CONVERSION ON EXTENSIVE DRUG RESISTANCE TREATMENT TB PATIENTS WITH THE BACKBONE REGIMEN OF BEDAQUILINE

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Background: Drug resistance tuberculosis (DR TB) is a major public health problem and sub Saharan Africa is the highest burden area. XDR TB is raising according to the reports and its difficult to treat due to lack of effective anti TB drugs. This study will provide analysis of culture conversion rate of XDR TB cases on the new FDA approved anti TB drug bedaquiline (BDQ).

Method: This is a retrospective study done on bacteriological confirmed XDR TB cases who are initiated on BDQ based individualized regimen from July 2015 to January 2016 and the sputum culture followed for 6 months.

Result: Data analysis done by using SPSS data analyzer. A total of 27 cases involved, who are on individualized BDQ based anti TB regimen according to their resistance pattern and/or drug exposure history. All of the cases were culture positive during initiation of treatment and sputum culture followed at 2nd, 4th and 6th months of treatment. From 27 (100%) cases; 19 (70.37%) converted at 2nd month, 5 (18.5%) converted at 4th month, 1(3.7%) converted at 6th month, 1(3.7%) not converted at the end of 6 month and 1(3.7%) died before 6 month. A culture conversion rate at 4th month is 88.87% and at 6th month is 92.59%.

Conclusion: BDQ based XDR TB individualized regimen is a promise for better treatment outcome in the management of debilitating XDR TB cases. The result from this interim sputum culture conversion rate is high when it is compare to WHO convertional XDR TB treatment regimen, which has a cure rate of 20%.

Key words: Tuberculosis (TB), Drug resistance Tuberculosis (DR TB), Extensive drug resistance tuberculosis(XDR TB), Bedaquiline (BDQ)

23. CORRELATION OF VARIOUS BIOMARKERS WITH DISEASE SEVERITY IN COVID-19- A PROSPECTIVE COHORT STUDY

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BACKGROUND In late December 2019, an unexplained pneumonia outbreak ,with symptoms including fever, dry cough, fatigue, and occasional gastrointestinal problems occurred in Wuhan, Hubei, China, which later became the COVID-19 pandemic. After many researches, it was found that the use of biomarkers allows for a more confident interpretation of these clinical symptoms. So, our aim in this study was to evaluate the correlation of various biomarkers in the pathophysiology of COVID-19 and how their levels change with disease severity, thereby which, it provides clinicians a tool to categorize patients and predict prognosis and mortality as well.

METHODS We conducted a prospective cohort study in 100 COVID-19 RT-PCR (real time- polymerase chain reaction)positive adult patients (>18 years), who were having symptoms of dry cough, shortness of breath, sore throat and myalgia, from a period of September 2020 to September 2021. Biomarkers like Serum Ferritin, interleukin-6, lactate dehydrogenase and D-Dimer were evaluated in the 1st and 6th month after hospital discharge. High resolution computed tomography was taken in the 1st and 6th month and the CT Severity Score (CTSS) was noted to assess disease severity. Correlation was measured using Spearman rank coefficient and statistical significance was accepted at p value <0.05.

RESULTS Out of the 100 patients, majority came under the 41–60-year group with mean and standard deviation of 50.3 $\pm$ 15.41 and majority were male patients (56%). Significant positive correlation was found with various biomarkers and disease severity - Serum ferritin (r=0.725,0.325, p<0.001), interleukin-6 (r=0.638,0.473, p value<0.001), Lactate dehydrogenase (r= 0.813,0.487, p value<0.001) and D-dimer (r=0.744,0.567, p value<0.001) at 1st and 6th month after discharge from the hospital. It was also noted that around 27% of the patients had residual fibrosis 6 months after the covid infection which was statistically significant.

CONCLUSION The majority of COVID-19 patients ultimately recover, however according to the most recent researches, 10% to 20% of patients may continue to have mid- or long-term consequences after their initial illness. The term "post COVID-19 state" or "long COVID" refers to these effects combined short- and long-term consequences. From this prospective cohort study, we came to a conclusion that the follow-up of the post covid patients with specific biomarkers as mentioned in our study and the imaging parameters can predict the outcome including the challenging post covid fibrosis also. More studies in large cohort of patients are needed to further analyze these effects and measures to prevent the post covid sequalae.

4. IMMUNODEFICIENCY IN CYSTIC FIBROSIS AND CYSTIC FIBROSIS-RELATED DISEASE: RESULTS FROM A SYSTEMATIC SCREENING IN AN ADULT COHORT

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BACKGROUND Cystic fibrosis (CF) is the most common life-limiting genetic disease in Caucasians. Despite multiorgan involvement, mortality is mainly secondary to end-stage lung disease. Chronic bacterial infection is accountable for irreversible structural airway damage leading to bronchiectasis, which are, in turn, the optimal substrate for further pathogen proliferation. This process generates a self-sustaining vicious vortex of infection and local inflammation. The term CFTR-RD (cystic fibrosis-related diseases) defines clinical entities associated with CFTR (cystic fibrosis transmembrane conductance regulator) dysfunctions that, however, do not fulfil the diagnostic criteria for CF.

Immunodeficiencies (ID) are defined as any dysfunction of the immune system responsible for an impaired response to infections and encompass a wide spectrum of heterogeneous disorders. IDs are among the most prevalent aetiologies of diffuse bronchiectasis in both adults and children.

Although CF, CFTR-RD and ID might share similarities in the pathophysiological mechanism of bronchiectasis development, they each offer different treatment options. The diagnosis of IDs, especially in the case of CF and/or CFTR-RD overlapping, might lead to the presence of a double component which sustains the previously mentioned vicious vortex inflammatory mechanism favouring the manifestation of the clinical phenotype. However, data on ID prevalence and clinical characteristics in adults with CF and CFTR-RD bronchiectasis are currently lacking.

METHODS We conducted an observational, prospective, consecutive study on a cohort of 169 adult patients affected by CF and 21 adult subjects affected by CFTR-RD. A blood sample was collected during a phase of clinical stability and it underwent a standardized immunological screening, including complete white blood count, IgG, IgA, IgM, IgG subclasses, total IgE, lymphocyte subsets and HIV test. We studied the prevalence of ID among CF and CFTR-RD patients. Subsequently, CF patients were divided into immunodeficient and non-immunodeficient patients according to the screening results and the two groups were compared for statistically significant differences.

RESULTS A total of 34 (20.1%) patients affected by CF had at least one immunological alteration. Primary immunodeficiencies accounted for the majority and were diagnosed in 33 (19.5%) patients while 15 (8.9%) had potentially treatable immunodeficiencies. Among CFTR-RD patients, primary immunodeficiencies were detected in 10 (47.6%) patients. Patients with treatable IDs were more frequently identified in the CF group (15 patients, 8.9%) compared to the CFTR-RD group (1 patient, 4.8%), p=0049. No statistically significant difference was found between immunodeficient and immunocompetent CF patients in terms of respiratory and extra-respiratory involvement, microbiology, comorbidities and chronic treatment were found.

CONCLUSIONS This study shows that ID are common in CF and even more in CFTR-RD patients. ID can represent a treatable trait and, for this reason, it should be actively looked for in CF and CFTR-RD patients and even more so in this last group, since it might lead to significant changes in the management and prognosis of these patients. Therefore, we should include Ig screening in the essential bundle of tests in these patients.

8. TESTING AT-RISK PATIENTS FOR NTM-PD IN CURRENT CLINICAL PRACTICE: RESULTS OF AN INTERNATIONAL SURVEY

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Background: Non-tuberculous mycobacterial pulmonary disease (NTM-PD) is a rare pulmonary disease that may manifest in patients at risk due to underlying lung disease and/or other risk factors. Understanding the characteristics of patients at risk of NTM-PD is important, but current clinical practice for testing is largely unknown.
Methods: In total, 455 clinicians from Europe, North America, Australasia and Japan completed an online survey of current clinical practice with respect to identification and testing of patients at risk for NTM-PD.
Results: Across the survey, respondents' caseloads varied with 42% having >10, 28% having 6–10 and 29% having 1–5 new patients with NTM every year. Persistent cough was the most reported symptom initiating NTM testing, followed by weight loss and haemoptysis, while gastroesophageal reflux disease was least likely. Inter-country differences existed with broad alignment in Europe and North America, which differed from Japan. Respondents were most likely to test patients with non-cystic fibrosis bronchiectasis (NCFBE) (mean 90%) or those with chronic obstructive pulmonary disease (COPD) (mean 64%), and those using immunosuppressants (mean 64%); however, there were large inter-country differences.
In NCFBE, radiological features or clinical symptoms suggestive of infection prompted testing for NTM, while only a minority tested for NTM when initiating macrolide therapy (15%) or at initial NCFBE presentation (24%), despite guideline recommendations.
In COPD, radiological exams or clinical symptoms triggered testing, but inter-country variability exists when considering exacerbations as a prompt to test (Japan 23% vs Canada 78%) and there was limited testing in patients receiving inhaled corticosteroids (9%).
In patients with cystic fibrosis (CF), where NTM testing is recommended annually, 60% of respondents tested for NTM. Of those who test in CF, 50% tested tested all adults with CF; respondents in Canada and Australia/New Zealand were much more likely to test all adults (71% and 73%, respectively).
Use of steroids (oral and inhaled) was the most common prompt for testing (66% of respondents) among clinicians who test for NTM in patients in receipt of specific medications. Few respondents tested those in receipt of anticancer agents and anti-TNF alpha inhibitors (19% and 10% , respectively)A mean of 4.8 risk factors (range 3.4–5.5) prompted NTM testing; most combinations included symptom(s) and underlying disease, except in Japan where symptoms only were paired together most often. The most common combinations prompting testing were persistent cough with weight loss or fatigue or bronchiectasis. Other symptoms (e.g., purulent sputum, exacerbations) prompted testing among clinicians with larger NTM patient caseloads.
Conclusion: These data show that testing for NTM is influenced by underlying disease and presence of clinical/radiological symptoms. However, context is key, and the decision to test for NTM may depend on the overall patient profile, not individual symptoms. Clinical practice varies considerably across geographies and is not always aligned with the existing recommendations for NTM testing in certain patient subgroups. International expert recommendations on which patients should be screened for NTM are warranted.

7. A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS OF PATIENT RISK FACTORS FOR NON-TUBERCULOUS MYCOBACTERIAL PULMONARY DISEASE (NTM-PD)

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Background: Non-tuberculous mycobacteria (NTM) are ubiquitous in the environment and can cause pulmonary disease (NTM-PD). Patients with NTM-PD typically experience reduced lung function, increased morbidity, and substantial reduction in health-related quality of life. NTM-PD is often diagnosed when the disease has become established and is difficult to treat. Understanding risk factors for NTM-PD can prompt testing and initiation of early, effective treatment. Results from a systematic literature review (SLR) and meta-analysis (MA) of the identified risk factors are reported.

Methods: Electronic searches on Medline and EMBASE were performed in July 2021 to identify publications (2011–2021) reporting attributable risk factors for NTM-PD. Systematic screening of 7,246 citations against agreed inclusion and exclusion criteria identified 99 publications for inclusion in the SLR and were subjected to full data extraction. Of these, 24 publications contained data on attributed risk factors that could be included in the meta-analysis (MA). Patient demographics, NTM species, symptoms identified, risk factors and co-morbidities were recorded, and results were analysed. Due to high heterogeneity in the data, random effect modelling was used for MA which was performed using R based meta package.

Results: Underlying lung disease was associated with NTM-PD, notably non-cystic fibrosis bronchiectasis (NCFBE), chronic obstructive pulmonary disease (COPD), asthma, and a history of tuberculosis (Table). Use of inhaled corticosteroids and immunosuppressive drugs, specifically anti-tumour necrosis factor alpha (TNFα), were also positively associated as was infection with *P. aeruginosa*. Low body mass index was positively associated with risk of NTM-PD and cardiovascular disease (CVD) was marginally associated. In this analysis lung function (FEV1) as well as macrolide use were not statistically significantly associated with NTM-PD.

Table: MA of identified attributable risk factors

Identified risk factor	No. of studies (n)	Baseline population	Combined OR	95% CI	I^2 (%)
Non-cystic fibrosis bronchiectasis	4	General population Symptoms of TB	21.43	5.90, 77.82	95
History of TB	7	General population Symptoms of TB Rheumatoid arthritis COPD	12.69	2.39, 67.26	99
COPD	8	General population Symptoms of TB Rheumatoid arthritis	6.10	3.96, 9.40	90
Infection with *Pseudomonas aeruginosa*	5	General population COPD CF	5.54	2.72, 11.26	95
Inhaled corticosteroids	4	General population Pulmonary disease	4.46	2.13, 9.35	97
Asthma	4	General population Symptoms of TB	3.73	2.21, 6.27	89
Low BMI (<18 kg/m^2)	2	General population COPD	3.04	1.95, 4.73	88
Use of anti-TNFα treatment	2	Rheumatoid arthritis	2.13	1.24, 3.65	0
CVD	2	Rheumatoid arthritis General population	1.73	1.01, 2.97	50
FEV1% of predicted	3	CF	1.01	0.97, 1.05	97
Macrolide use	3	CF	0.80	0.47, 1.39	96

Conclusion: This is the first SLR and MA to explore a comprehensive range of risk factors predisposing patients to NTM-PD and provides insight into other factors that influence the risk of developing NTM-PD such as comorbid diseases e.g. NCFBE and COPD, and presence of *Pseudomonas* infection, CVD and inhaled steroid use. For BMI it is unclear if low BMI is associated with an increased risk for NTM-PD or if NTM-PD results in reduced weight. However, this MA is limited by a paucity of data regarding the attributable risk for NTM-PD and a high degree of heterogeneity across studies compared. Similarly, some studies are performed in defined patient groups e.g. cystic fibrosis which may not be reflective of data in a more general population. Understanding risk factors, as explored in this MA, may identify patients for NTM testing and further treatment if appropriate.

19. EFFECTS OF BRONCHODILATION ON FLOW LIMITATION AND ON MORPHOLOGY OF THE LOOP OF SPECIFIC LUNG RESISTANCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Background: Chronic obstructive pulmonary disease (COPD) patients often experience tidal expiratory flow-limitation (tEFL), a condition causing respiratory and cardiovascular detrimental effects: to date, the evidence regarding the impact of flow-limitation on the bronchodilator response is scanty.
Moreover, tEFL in patients with stable COPD is one of the major determinants of the expiratory part of the alveolar flow-pressure relationship and distortion of the expiratory loops of specific airway resistance (sRaw).
Aims and objectives: The aim of this study was to analyze the acute effects of bronchodilator therapy on tEFL and on the shape of the sRAW expiratory loops
Methods: This was a prospective, observational study conducted in the outpatient clinic of Respiratory Disease Unit of Luigi Sacco University Hospital in Milano (Italy).
Consecutive patients with COPD with a forced expiratory volume in 1 second (FEV1)<75%predicted and stable clinical conditions underwent body plethysmography, single breath nitrogen washout test (SBN2) and negative expiratory pressure during resting breathing to assess tEFL before and after salbutamol pMDI 400 µg delivered with a spacer. Expiratory area of the sRAW expiratory loop was calculated by a dedicated software as previously described (*Pecchiari M et al. J Appl Physiol (1985). 2020;129(1):75-83*).
Results: Nineteen patients (mean age 74 years, 68.4% males) with a median (IQR) FEV1 of 55 (45-66) %predicted value were enrolled. Eleven patients (58%) had tEFL at rest. Lung function characteristics in flow-limited and non-flow-limited patients had overlapping baseline characteristics.
After bronchodilation, patients showed an average increase in FEV1 of 12% from baseline ($p < 0.005$) with an improvement of vital capacity (VC) of 160 ml (+5% vs baseline; $p = 0.044$). sRaw were significantly reduced (-15.5%, $p < 0.001$) with a concomitant significant reduction of the area of the expiratory loop normalized for maximum expiratory flow (ΔEA' : -18.7%; $p = 0.003$). All patients with tEFL at baseline remained flow limited after bronchodilator administration.
In patients with tEFL, the administration of salbutamol resulted in a significant improvement of FEV1 (+12.3%; $p = 0.014$), associated with a reduction of sRaw (-14.9%; $p = 0.011$), and of the EA' (25.9%; $p = 0.007$, Figure 1). Static volumes and parameters of ventilation inhomogeneity tended to decrease after bronchodilation but did not reach statistical significance (Phase III SBN2 test, residual volume and functional residual capacity all $p > 0.05$)
Conclusions: Our results confirm that tEFL can be rarely reversed by the administration of bronchodilators, but the presence of tEFL does not negatively affect the response to bronchodilators in terms of airflow obstruction and airway resistances. The reduction of expiratory loop area of sRAW in tEFL patients is not apparently linked to the modification of static volumes, hyperinflation, and ventilation inhomogeneity
Disclosure: The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

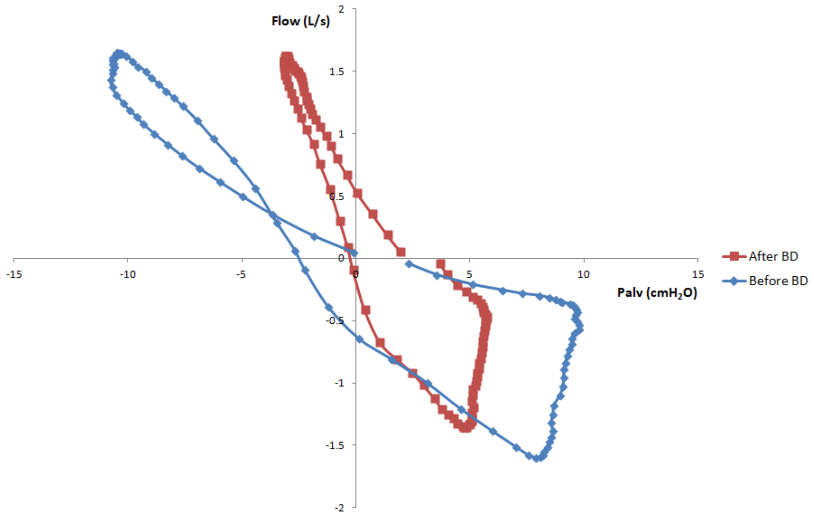

Figure 1 Alveolar flow-pressure loop in a flow-limited subject during plethysmography, before (red) and after (blue) bronchodilation.

9. THE HOSPITALIZATION BURDEN AMONG POTENTIALLY TREATMENT-REFRACTORY NONTUBERCULOUS MYCOBACTERIAL LUNG DISEASE PATIENTS IN JAPAN

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Background/Aims: Nontuberculous mycobacterial lung disease (NTMLD) is increasing in incidence and prevalence in Japan. This life-threatening pulmonary infection is associated with progressive lung damage and increased healthcare use, particularly among patients who are refractory to treatment and therefore left with limited treatment options. As there are a lack of data describing treatment patterns and quantifying healthcare resource utilization in patients with refractory NTMLD, this study aimed to assess treatment patterns and hospitalizations among patients with potentially refractory NTMLD in Japan.

Methods: This retrospective cohort study utilized claims data from the Japan Medical Data Center (Feb 2015-Feb 2020). Baseline treatment was defined as the regimen during the first 6 months after NTMLD antibiotic treatment initiation with the index date defined as the date 6 months after treatment initiation. Regimen changes from baseline treatment during the post-index period were used to categorize patients who received NTMLD treatment for ≥18 months as potentially refractory (those who added drug classes or added/switched drugs) or potentially non-refractory (those who remained on baseline treatment or reduced drugs). Patients who discontinued within 6 months of treatment were also considered potentially non-refractory, and those who discontinued after 6–18-month treatment were classified as having uncertain refractory status. Hospitalizations were assessed at 6-month intervals for a total of 30 months after treatment initiation.

Results: Of 1030 treated patients identified, 230 (22.3%) showed potentially refractory treatment patterns over 24 months of post-index treatment: 163 patients were treated persistently (defined as <30 consecutive days without drug supply) and 67 had drug gaps (defined as ≥30 consecutive days without drug supply). At baseline, potentially refractory patients had the highest prevalence of bronchiectasis (28%), chronic obstructive pulmonary disease (COPD, 50%), hemoptysis (17%), idiopathic interstitial lung disease (13%) and gastroesophageal reflux disease (GERD, 34%). Patients with potentially refractory NTMLD treatment patterns had higher rates of hospitalization, especially all-cause and respiratory-related hospitalizations, over 30-months after treatment initiation. Despite receiving persistent treatment for ≥18 months, hospitalization rates among potentially refractory patients (n=163) remained high (15.3%-20.2% all-cause, 8.6%-11.7% respiratory-related, 6.1%-9.8% NTMLD-related) over the 30-month study period. In contrast, hospitalizations for potentially nonrefractory patients generally decreased over time. In a sensitivity analysis of potentially refractory patients who added/switched drugs during the 12-month post-index period (vs 24-month period used in the primary analysis), 138 patients were identified (~60% of the potentially refractory patients in the primary analysis). There were even higher proportions of potentially refractory patients with hospitalizations in this group than the primary analysis, especially during the first 18 months following treatment initiation (13.5%- 25.7% vs 10.4%-20.2% all-cause; 8.1%-15.8% vs 6.0%-13.4% respiratory-related; and 8.1%-16.2% vs 4.5%-11.9% NTMLD-related).

Conclusions: Most patients identified in this study as having potentially refractory treatment patterns had a high hospitalization burden that remained high over the 30-month study period despite receiving persistent treatment for at least 18 months. These findings suggest that refractory NTMLD imposes a substantial burden on patients and highlights the need for timely identification and appropriate management of patients with refractory NTMLD in Japan.

13. RELATIONSHIP BETWEEN ASTHMA CONTROL AND OBSTRUCTIVE SLEEP APNEA IN VIETNAMESE CHILDREN WITH ASTHMA

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Background: Asthma and obstructive sleep apnea (OSA) are common chronic respiratory disorders in children. The relationship between asthma and OSA is bidirectional, both of these conditions share multiple epidemiological risk factors. Untreated OSA may cause attention deficit/hyperactivity disorder (ADHD)symptom. The aim of study is to assess prevalence of ADHD in asthmatic children with OSA and link between asthma control, lung function and children with OSA and asthma.

Methods: A total of 96 children aged 6- 15 years who was diagnosed asthma according to GINA 2020 were enrolled in this study. All main data including age, gender, BMI, Vanderbilt ADHD Diagnostic Parent Rating scale, asthma control status, lung function and exhaled nitric oxide were collected. Home respiratory polygraphy were used to identify OSA in study subjects.

Results: There were 96 patients (mean: 8.38 yrs) included in the present study. OSA was identified in 60.42% asthmatic children with mean AHI 3.45 event/hour. Inattention ADHD subtype was significant higher in OSA asthmatic group than non- OSA group (34.48% vs 7.89%, $p<0.05$). OSA was associated with a higher probability for the presence of ADHD (OR: 6.15, 95%CI: 1.678- 22.474, $p< 0.05$). A significantly higher risk of OSA was found among children with poorly controlled asthma (82.98% vs 17.02%, $p<0.001$) than among children with controlled asthma. Logistic regression analysis showed that allergic rhinitis (OR: 8.217, 95%CI: 3.216-20.996, $p< 0.05$) increased the odds of having OSA.

Conclusion: The prevalence of OSA is increased among poorly controlled asthma. Without treatment, OSA may cause ADHD in children. Early diagnosis of OSA in asthmatic patients will lead to the appropriate asthma control strategy.

5. TUBERCULOSIS AND ITS PREVALENCE AMONG RESIDENTS RESIDING IN HIGH ALTITUDES OF NEPAL

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Introduction: This study was performed to assess the prevalence of tuberculosis (TB) and its form in Nepal's high-altitude western rural district. TB infection, disease, and mortality seem to be less common at high than low altitudes as studies suggest that low oxygen pressures inhibit the ability of Mycobacterium tuberculosis organisms to survive and multiply.

Methods: Jumla is a high-altitude mountainous region ranging from 915m- 4679m with a population of 119,337 (2021) having 8 municipalities. Data were collected from all the municipalities starting from July15th2021-July14th2022 and th2021-July14th2022 and were compared with prior years in number and diagnosis with annual data of Nepal.

Results: A total of 84 cases were recorded of which 52.4% (n=44) were females. The group affected most was between the age16-30 years (34.5%) and 61-75yr (22.5%). The cases were mostly detected by the sputum Xpert MTB/RIF testing (54.7%) with positive sputum Acid-fast bacilli being 27.4%. Most of the patients were diagnosed to have Pulmonary bacteriologically confirmed (PBC) tuberculosis 52.4%, PCD (Pulmonary clinically diagnosed) 16.7%, Extra-pulmonary 28.6% with one case of each multi-drug resistant tuberculosis (MDR-TB), and Pre-XDR (Extensive drug resistant) TB. Among them, 12% of people have a history of TB undergone ATT (anti-tuberculosis drugs) in past with 6% having a close contact history.

Conclusion: Tuberculosis infection, disease, and mortality seem to be less common at high than low altitudes. As in Karnali Province, Humla with the second being Jumla has the lowest number of TB patients in other parts of Nepal, affecting younger people.

6. AMIKACINE LIPOSOME INHALATION SUSPENSION (ALIS) FOR REFRACTORY MYCOBACTERIUM AVIUM COMPLEX (MAC) PULMONARY DISEASE: OUR EXPERIENCE

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Nontuberculous mycobacteria (NTM) are environmental organisms that can cause pulmonary disease (PD). Among them, the most common species responsible for PD in Europe is Mycobacterium Avium Complex (MAC), which includes M. avium, M.intracellulare and M.chimaera.

The management of MAC lung disease can be complex and treatment outcomes are often poor.

Failure to achieve culture conversion is common despite treatment with a guideline-based multidrug regimen.

Treatment failure is defined as the re-emergence of multiple positive cultures or persistence of positive cultures after ⩾ 12 months of antimycobacterial treatment. Refractory MAC Lung Infection is defined as having positive MAC cultures during treatment with a multi-drug antimicobacterial regimen for a minimum of six consecutive months and no documented successful treatment.

A treatment strategy for refractory MAC-PD involves adding Amikacin liposome inhalation suspension (ALIS) to the standard therapy.

The CONVERT study showed that this therapy is responsible for a higher culture conversion rate compared to the standard treatment. Patients treated with ALIS also continue to have negative cultures during the 12 months of post-conversion therapy.

We discuss a case of a patient who was treated with ALIS in our reference center.

She was a 66-year-old woman, with a history of breast cancer treated with left radical mastectomy and chemotherapy. She had a previous diagnosis of MAC-PD with positive bronchoalveolar lavage (BAL) for M. intracellulare treated with a combination of clarithromycin, rifampicin and ethambutol for six months, then discontinued for ethambutol-induced optic neuropathy.

The clinical presentation at referral to us was with recurrent episodes of haemoptoe, non-productive cough, anorexia and fatigue. The spirometry showed a moderate airway obstruction with ppFEV1 62%. Chest CT demonstrated disease progression with bronchiectasis and pseudonodular thickening in every lobe. She repeated a BAL, which revealed M. intracellulare. Initial treatment included clarithromycin, rifampicin, clofazimine and levofloxacin for 24 months, after which she did not achieve culture conversion. The symptoms persisted and there were no radiological changes. Moreover, M. intracellulare showed newly developed clarithromycin resistance.

Because of treatment failure, we considered adding ALIS to oral therapy on a daily regimen. Shortly after initiation of treatment, she experienced dysphonia and haemoptoe that led to discontinuation of treatment. She restarted ALIS on a triweekly regimen, which was better tolerated. At 12 months of ALIS plus oral therapy, there was the first evidence of negative sputum culture. This was associated to clinical and functional improvements, with a raise in ppFEV1 up to 80%. CT scan at 12 months showed the reduction of the diffuse thickenings.

At the end of the 24-months treatment sputum culture confirmed negative.

Our results are consistent with what is reported in literature. ALIS appeared to be the determinant factor responsible for culture conversion, but results regarding sputum culture after the discontinuation of the treatment are still ongoing. In our experience ALIS was relatively safe, showing only minor adverse events which decreased importantly after optimization of the dosage. As of today, guidelines recommend the use of ALIS only for refractory PD, but, even in these cases, it is not of easy access for patients and physicians. Further evidence are needed to determine whether its use could be extended to patients without refractory PD.

24. SHUNT FRACTION IN COVID-19 RELATED ACUTE RESPIRATORY FAILURE

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Background: Failing autoregulation of pulmonary vessels and higher shunt have been described in Covid-19 related Acute respiratory failure (ARF). The aim was to investigate shunt fraction in patients with Covid-19-ARF compared to patients with other causes of ARF.

Methods: Observational study of hospitalized patients with Covid-19-ARF and other causes of ARF at Papa Giovanni XXIII Hospital, Bergamo, Italy between June 2020 and November 2021. Shunt fraction was measured by a non-invasive system during spontaneous breathing (Beacon®Caresystem).

Results: We enrolled 51 adult patients (8 female), mean age (±SD) 65±13 years and mean BMI 28,3±5,3 Kg/m2. Covid-19-ARF patients represented 71% (36/51). Community acquired pneumonia was the most common cause of other ARF (11/15). No differences in terms of age and BMI were described between Covid-19 related and other causes of ARF patients. Pulmonary gas exchange impairment was similar, median PaO2/FIO2 ratio was 254 [IQR 162,297] in Covid-19-ARF and 269 [IQR 201,296] in other causes of ARF patients (p=0.41). Nevertheless, mean shunt fraction resulted significantly increased in Covid-19-ARF (18±6%) than other causes of ARF patients (12±9%; p=0,03). Lung radiological involvement analysis is ongoing with AVIEW software, Coreline Soft, Seoul, Korea.

Conclusion: Shunt fraction appears to be increased in Covid-19-ARF if compared to patients with other causes of ARF. However, this is the first study proposing this non-invasive method to measure shunt fraction in ARF and further investigations are needed to validate this technique.

27. DEVELOPMENT AND VALIDATION OF A NOVEL DEEP LEARNING MODEL FOR DIAGNOSIS OF VENTILATOR-ASSOCIATED PNEUMONIA (AI-VAP)

ANIMESH RAY[1]; Shrawan Kumar Raut[1]; Kolin Paul[1]; Surabhi Vyas[1]; Naveet Wig[1]

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INTRODUCTION: Ventilator-associated pneumonia (VAP) is defined by infection of the pulmonary parenchyma in patients initiated on invasive mechanical ventilation for at least 48 hours. VAP remains one of the most common infections in mechanically ventilated patients. Early diagnosis of VAP is critical so as to initiate early antibiotics targeting the pathogens causing pneumonia. Despite recent advances in microbiological tools, the diagnosis of VAP is difficult as the current tools like Clinical Pulmonary Infections Score (CPIS) is difficult to calculate at the bedside. On the other side, performing biopsies for diagnosis of VAP is technically difficult and potentially dangerous in critically ill patients. Moreover, a number of parameters used for diagnosis viz. respiratory secretions culture (available only after several days), poorly defined clinical parameters (worsening oxygen requirement, increasing tracheal secretions) and chest radiograph changes (with considerable interobserver variation) makes early diagnosis of VAP difficult. As a result, the physician often uses part of the available data combined with 'clinical intuition' for diagnosing (atleast initially) VAP (physician-diagnosed VAP). So, there has been an unmet need for developing a novel and reliable tool for diagnosing VAP, which is the focus of this study.

METHODS: This was a prospective observational study done in collaboration with IIT Delhi. The primary objective of the study was to develop and determine the diagnostic accuracy of artificial intelligence (the AI based support system called AI-VAP) in detecting Ventilator-associated pneumonia (VAP) as compared to final diagnosis of VAP by combination of clinic-radio-microbiological data (both CPIS and physician-diagnosed VAP). An improvised version of CheXnet model was used to capture imaging data and to develop the final joint model. Consecutive patients with suspicion of VAP were recruited in the study. Initial 100 radiographs were used for training the AI algorithm. After that 200-300 radiographs along with clinico-radio-microbiological data (including CPIS score and ET aspirate culture) were used for validation of AI algorithm, with a ten times cross-over, followed by estimation of diagnostic accuracy. The details of the process of development is given in the figure 1 below.

RESULTS: A total of 232 patient on mechanical ventilation were screened, among which 157 patients included in the study. Out of these, 61 patients had VAP. Analysis of 300 chest radiographs (of 32 patients) for diagnosis of AI based VAP was done which showed overall accuracy of 83%(for image data using chest X-rays only) and 89%(for joint model using combined clinic-radio-microbiological data) respectively (in comparison with CPIS). In comparison to CPIS, diagnostic accuracy of physician diagnosed VAP was 70%. On an average, the AI-VAP was able to diagnose VAP earlier by a median of 2.3 days (0-2) as compared to physician diagnosis of VAP. Sample predictions is depicted in figure 2 below.

CONCLUSION: The overall accuracy of the novel AI algorithm for diagnosis of VAP was significantly higher in comparison to physician diagnosis of VAP. Also the AI algorithm lead to earlier diagnosis of VAP as compared to physician diagnosis. Thus, the newly developed AI algorithm for diagnosis of VAP is promising and needs to be validated further in larger studies.

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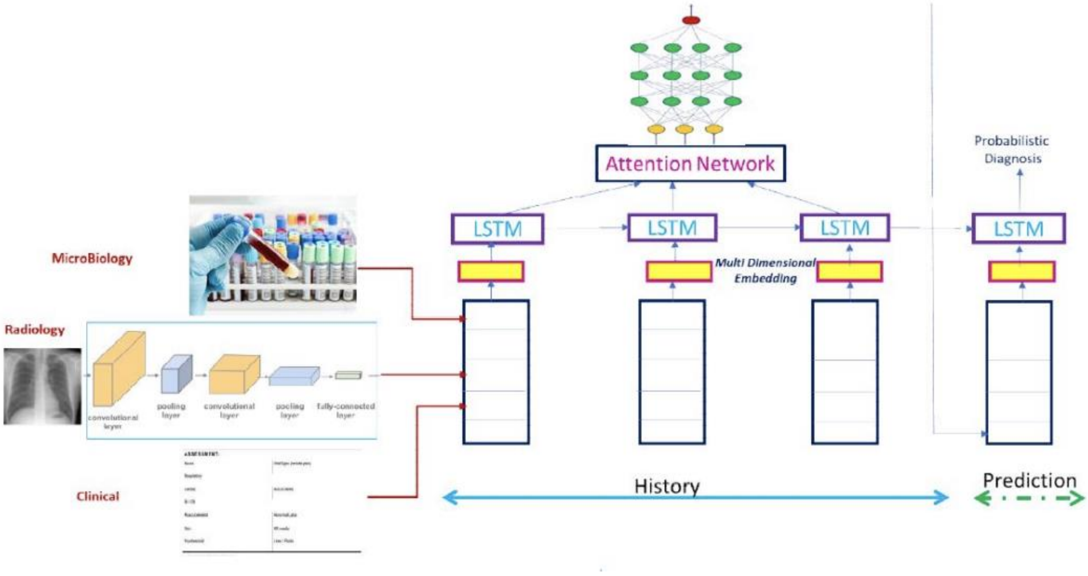

Attention Network
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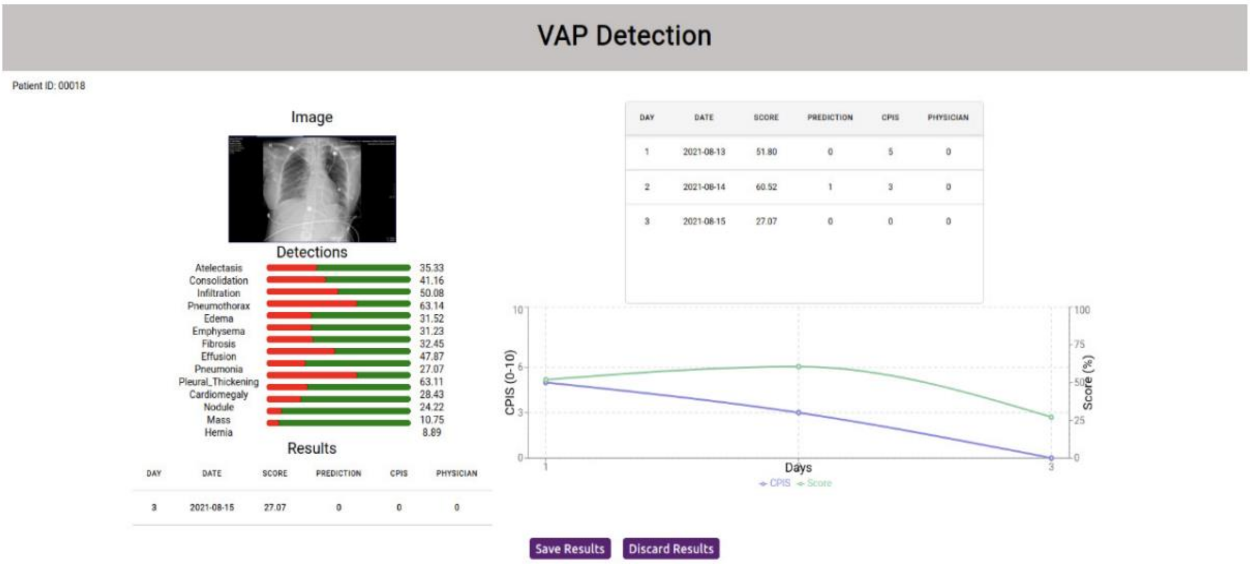
LSTM
LSTM
Probabilistic Diagnosis
LSTM
MicroBiology
Radiology
Multi Dimensional Embedding
Clinical
History
Prediction



VAP Detection
Patient ID: 00018
Image
Detections
Atelectasis 35.33
Consolidation 41.16
Infiltration 50.08
Pneumothorax 63.14
Edema 31.52
Emphysema 31.23
Fibrosis 32.45
Effusion 47.87
Pneumonia 27.07
Pleural_Thickening 63.11
Cardiomegaly 28.43
Nodule 24.22
Mass 10.75
Hernia 8.89
Results
DAY DATE SCORE PREDICTION CPIS PHYSICIAN
3 2021-08-15 27.07 0 0 0
DAY DATE SCORE PREDICTION CPIS PHYSICIAN
1 2021-08-13 51.80 0 5 0
2 2021-08-14 60.52 1 3 0
3 2021-08-15 27.07 0 0 0
CPIS (0-10)
Score (%)
Days
CPIS Score
Save Results
Discard Results

14. IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE QUESTIONNAIRES WITH BIOLOGIC THERAPIES IN SEVERE ASTHMA AND COMORBID CHRONIC RHINOSINUSITIS WITH OR WITHOUT NASAL POLYPOSIS: A REAL-LIFE EXPERIENCE

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Background Patients with severe asthma frequently have comorbid chronic rhinosinusitis (CRS) with or without nasal polyps, increasing disease burden and complicating treatment. The emergence of biologic therapies for the treatment of asthma has provided promising targeted treatment for these patients but real-life clinical data are still scarce.

Aims and objectives To evaluate in a real-life setting improvements of disease-specific health-related quality of life (HRQoL) as measured by SinoNasal Outcome Test-22 (SNOT-22, 0 – 110), Visual Analog Scale symptom scores (VAS, 0-10), and Asthma Control Test (ACT, 5-25) in patients with severe uncontrolled asthma associated with CRS with or without nasal polyposis and treated with different biologic therapies.

Methods In this retrospective real-life study, data from consecutive patients with severe uncontrolled asthma treated in our severe asthma outpatient clinic with comorbid chronic rhinosinusitis with/without nasal polyposis were collected at baseline, and 3, 6 and 12 months after starting different biologic treatments.

Results A total of 39 patients (mean ± SD age 54 ± 12) were enrolled: 8 patients on omalizumab, 8 on mepolizumab, 15 on benralizumab, and 8 on dupilumab. Of these, 30 (77%) patients presented CRS with nasal polyposis.

SNOT 22 and VAS score significantly improved in all patients at 3, 6, and 12 months of treatment compared with baseline (median (IQR) SNOT-22: 14 (0-52) vs 10 (0-30) vs 0 (0-15) vs 0 (0-12), $p<0.001$; VAS score: 1 (0-5) vs 0 (0-3) vs 0 (0-2) vs 0 (0-1), $p<0.001$).

Patients on omalizumab and dupilumab had significantly higher baseline SNOT-22 and VAS scores ($p<0.01$). When divided by biologic therapy, patients on omalizumab and dupilumab presented significant improvements at all timepoints in SNOT-22 and VAS compared with baseline (respectively SNOT-22 $p=0.010$ and $p<0.001$, VAS score $p=0.015$ and $p<0.001$), while no difference was found in patients on mepolizumab and benralizumab (respectively SNOT-22 $p=0.392$ and $p=0.290$, VAS score $p=0.999$ and $p=0.465$).

Asthma control improved in all patients at all timepoints compared with baseline (median IQR, 13 (12-16) vs 21 (20-24) vs 23 (22-25) vs 23 (22-25); $p<0.001$). Subgroup analysis for each biologic therapy showed significant improvement of ACT score for all treatments.

No differences in terms of ACT, SNOT-22, and VAS scores at all time-points were found between patients with and without nasal polyposis.

Conclusions This study confirms the general efficacy of omalizumab, mepolizumab, benralizumab, and dupilumab in patients with severe asthma in a real-life setting. For the first time we demonstrated that both dupilumab and omalizumab are equally able to rapidly improve CRS-specific HRQoL and general health status, while the lack of signal in patients with benralizumab and mepolizumab is probably secondary to the lower baseline CRS specific

symptom burden. These data highlight the importance of targeting type 2 inflammation in patients with coexisting upper and lower airways disease.

Disclosure The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

	All patients (N=39)				
Characteristics	Before biologic therapy	After 3 months of biologic therapy	After 6 months of biologic therapy	After 12 months	*P* value[a]
Asthma Control Test (ACT)	13 (12-16)	21 (20-24)	23 (22-25)	23 (22-25)	<0.001
SNOT-22	14 (0-52)	10 (0-30)	0 (0-15)	0 (0-12)	<0.001
VAS score	1 (0-5)	0 (0-3)	0 (0-2)	0 (0-1)	<0.001
	Omalizumab (N=8)				
Asthma Control Test (ACT)	12 (10.3-13.0)	20.5 (19.3-21.8)	23 (22-25)	23 (22-25)	<0.001
SNOT-22	34 (0-43.8)	11 (0-37.8)	12.5 (0-37.8)	10 (0-18)	0.010
VAS score	2 (0-3.5)	2 (0-2)	2 (0-2.8)	0.5 (0-1)	0.015
	Mepolizumab (N=8)				
Asthma Control Test (ACT)	15 (13.3-17.8)	22.5 (20.3-24.8)	22 (21-24.8)	22 (21-24.8)	0.026
SNOT-22	0 (0-24)	0 (0-26.3)	0 (0-26.3)	0 (0-26.5)	0.392
VAS score	0 (0-3)	0 (0-3)	0 (0-3)	0 (0-3)	0.999
	Benralizumab (N=15)				
Asthma Control Test (ACT)	15 (12-19)	23 (20-25)	23 (22-25)	23 (22-25)	<0.001
SNOT-22	7 (0-21)	0 (0-14)	0 (0-14)	0 (0-14)	0.290
VAS score	0 (0-2)	0 (0-1)	0 (0-1)	0 (0-1)	

15. DELINEATING THE MOLECULAR MECHANISM OF TSLP-DRIVEN NON TYPE INFLAMMATION IN SA

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Background: Patients with severe asthma (SA) represent a group of asthmatics that is poorly responsive to standard of care treatment thus leading in some cases, in life-threatening disease exacerbations. Currently-available biologic therapies display superior efficacy mainly in patients with mild-to-moderate allergic or eosinophilic asthma. Hence, targeting factors that hold broader effects on airway inflammation than existing biologics could constitute an attractive therapeutic approach for SA patients. Thymic stromal lymphopoietin (TSLP) is an upstream initiator of the inflammatory cascade thus representing one such appealing therapeutic target. Still, the precise role of TSLP in SA pathogenesis remains elusive. Our aim was to investigate whether inhibition of TSLP in vivo can restrain excessive non-type inflammatory responses that prevail in SA and ameliorate disease phenotype.

Methods: 8-12 week-old female C57BL/6 were sensitized with HDM and c-di-GMP intranasally (i.n.) on days 1, 3, and 5. Mice were then rested for 5 days and subjected to 3 challenge sets involving 3 consecutive challenges with HDM and c-di-GMP with a rest of 4 days between challenge sets. c-di-GMP was administered i.n. along with HDM, on the first day of each challenge set, followed by HDM administration in the next 2 challenges. For the preventive protocol, anti-TSLP or the respective isotype control were given i.n. for three consecutive days prior to allergen sensitization. Mice were sacrificed 24 hours after the last challenge. BALF, lungs and serum were isolated from all experimental groups. BAL inflammatory cell counts, peribronchial and perivascular inflammation, mucus production and cytokine release were measured in serum, BALF and lung homogenates by ELISA. Mice with SA were also compared with mice with mild-to-moderate asthma that received HDM i.n. on days 1, 3, and 5, then rested for 5 days and subjected to 3 challenge sets involving 3 consecutive challenges with HDM.

Results: We observed significantly increased TSLP levels in the BALF, lung homogenates and serum of mice with SA compared to mice with MMA and to a greater extent to control mice (naïve). In vivo blockade of TSLP before allergen sensitization significantly decreased the levels of peribronchial and perivascular inflammation, mucus production by goblet cells as well as total numbers of BAL infiltrating inflammatory cells and especially neutrophils. We also detected decreased levels of IL-17, IFN-γ and IL-13 in the serum, BALF and lung homogenates of SA mice that received anti-TSLP compared to SA and to a greater extend MMA mice. Finally, in vivo ablation of TSLP also diminished the expression levels of type1, 2 and 17 cytokines in mediastinal lymph node cell culture supernatants upon ex vivo allergen stimulation.

Conclusion: Our data reveal that inhibition of TSLP before allergen sensitization in a well-established murine model of SA restrains pulmonary inflammation and attenuates key asthma features. Our studies may pave the way for delineating the molecular mechanisms through which TSPL orchestrates non type inflammatory responses that prevail in SA.

28. RIBAVIRIN FOR TREATMENT OF SUBJECTS WITH RESPIRATORY SYNCYTIAL VIRUS-RELATED INFECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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[1] *CIBERES, Madrid, Spain;* [1] *Hospital de Donosti, Donosti, Spain*

Introduction: Respiratory syncytial virus (RSV)-associated diseases have caused an estimated 1.8 million hospital admissions and 40,000 deaths among children. RSV can cause lower respiratory tract infections (LRTIs) in all age groups, adults with comorbidities, and immunocompromised patients. The aim was to summarize the evidence concerning efficacy and safety of ribavirin in subjects diagnosed with RSV associated with LRTI.

Methods: A systematic review and meta-analysis were performed. Eligible studies were observational (10 subjects) and RCTs of subjects with aerosol/oral ribavirin for RSV-LRTI. Comparator was supportive care/placebo. Systematic search on PubMed, Cochrane Library, and Web of Science databases was conducted between January 2001 and January 2022. PROSPERO register number: CRD42022308147.

Results: After retrieving 907 studies, 10 observational studies and 1 RCT were included (4/11 high quality of evidence). Seven studies included subjects with haematological malignancy/stem cell transplant, two lung transplants, and two healthy individuals. A total of 788 subjects diagnosed with RSV infection were included; 14.3% of them presented with only LRTI. Among 445 subjects treated with ribavirin, 195 (43.8%) received an aerosolized formulation. Pooled meta-analysis showed no differences in mortality (RR: 0.63; 95%CI: 0.28–1.42) in all subjects treated with aerosol/oral ribavirin compared to supportive care. In subgroup analysis, mortality was significantly lower in haematological subjects (RR: 0.32; 95%CI: 0.14–0.71), but did not differ significantly in lung transplant recipients (RR: 0.89; 95%CI: 0.31–2.56). Oral ribavirin (vs. supportive care) was associated with increased viral clearance (RR: 2.60; 95%CI: 1.35–4.99). Seventeen adverse events were reported among 119 subjects, but none were severe.

Conclusion: Ribavirin should be considered for treatment of RSV-LRTI in haematological subjects. There is a lack of evidence to support its use in lung transplant recipients. Oral formulation appears to be an easier, safe, and cost-effective alternative to aerosolized ribavirin. Further advances needs to focus on newer antivirals.

10. TRENDS IN HOSPITALIZATIONS AND OUTPATIENT VISITS WITH EARLY OR DELAYED ANTIBIOTIC TREATMENT INITIATION IN NONTUBERCULOUS MYCOBACTERIAL LUNG DISEASE

Kevin Winthrop[1]; Catherine Waweru[2]; Mariam Hassan[2]; Sara Burns[3]; Anjan Chatterjee[2]; Roald Van der Laan

[1]*OHSU-PSU School of Public Health, Portland State University, Portland, United States of America;* [2]*Insmed Incorporated, Bridgewater, United States of America;* [3]*Panalgo, Boston, United States of America*

Background/Aims The most recent (2020) treatment guidelines recommend initiating antibiotic treatment rather than “watchful waiting” for patients diagnosed with nontuberculous mycobacterial lung disease (NTMLD). However, there is a lack of evidence regarding how delays in treatment (DT) impact healthcare resource utilization (HRU). This study aimed to assess potential differences in HRU among patients with NTMLD receiving early treatment (ET) with antibiotics compared with those experiencing DT.

Methods This retrospective observational cohort study identified patients from MarketScan® claims data (July 2014 to June 2020) with: ≥2 NTMLD medical claims; continuous enrollment spanning 12 months pre–index date to ≥24 months post–index; concomitant treatment (ie, from ≥2 drug classes within 30 days of each other) with antibiotics used in NTMLD; and no tuberculosis diagnosis. Index date was defined as the date of the first NTMLD claim; baseline was defined as 12-months pre-index. The mean time to antibiotic initiation (TT) from index date was used to categorize patients into ET (TT ≤3 months) and DT (TT >3 months) groups. For each group, hospitalization trends (any hospitalizations and respiratory-related hospitalizations) and emergency room (ER) visits at baseline, year 1 (Y1), and year 2 (Y2) post–index were described.

Results The study identified a total of 481 patients with NTMLD: 364 (76%) ET and 117 (24%) DT patients. ET patients were younger and more likely to be male compared with the DT group. The DT group had a higher proportion of patients with bronchiectasis, asthma, and emphysema. In the ET group, the overall proportion with any hospitalization decreased from baseline (33.2%) to Y1 (30.5%) and to Y2 (21.7%) as did the mean (standard deviation [SD]) number of any hospitalization per patient (0.50 [0.94] to 0.47 [0.93] to 0.35 [0.80]). The DT group increased from baseline to Y1 in both the proportion (31.6% to 35.0%) and mean (SD) number (0.40 [0.67] to 0.61 [1.11]) of hospitalizations per patient. This was followed by a decrease in Y2 for both the proportion (28.2%) and mean (SD) number (0.44 [0.86]), although the mean number of hospitalizations in Y2 remained higher than at baseline. Similar trends were observed in respiratory-related hospitalizations in both the proportion of patients and mean hospitalizations per patient. For ER visits, decreases were observed from baseline through Y2 in the ET group for both the proportion (31.0% to 24.7%) and mean (SD) hospitalizations per patient (0.50 [1.12] to 0.45 [1.41]); in contrast there was little change from baseline to Y2 among DT patients in either proportion (33.3% to 29.9%) or mean hospitalizations per patient (0.54 [0.93] to 0.53 [1.06]).

Conclusions While patients with NTMLD who received early antibiotic treatment experienced improvements in hospitalizations and ER visits over the first 2 years after diagnosis, those whose antibiotic treatment was delayed experienced little to no improvement from baseline.

29. EFFECTS OF ANTIVIRAL THERAPY ON MORTALITY AND HOSPITAL STAY DURATION IN COVID - 19 PATIENTS: A RETROSPECTIVE ANALYSIS

Pavel Yordanov[1,2]; Valentina Dimitrova[1,2]; Tanya Dobreva[1,2]; Figen Mustafa[1,2]; Yanitsa Dimitrova[1,2]; Merlin Efraim[1,2]; Aleksandar Yordanov[1,2]; Nataliya Usheva[2]; Georgi Gerganov[2,1]; Pavlina Peneva[1,2]; Diana Petkova[2,1]

[1] *University Hospital "St Marina" Varna, Varna, Bulgaria;* [2] *Medical University "Prof. Dr. Paraskev Stoyanov" Varna, Varna, Bulgaria*

Aims: To assess the effect of Remdesevir added to the standard of care compared to the standard of care alone in patients hospitalized with COVID – 19 pneumonia in relation to disease outcome and hospital stay duration.

Methods: We retrospectively analyzed 295 patients, mean age was 61.13 ±13.87 years. 167 (56.61%) were male and 128 (43.39%) were female. 126 (42.88%) of all patients received Remdesevir in standardized treatment regimen for 5 days in addition to the standard of care. Data for comorbidities, hematological and some biochemical markers was also gathered.

Results: Statistically significant decrease in mortality rate in Remdesevir group (15.9%; n=20) was found, compared to those on the standard of care alone (45.8%; n=77) (Pearson Chi-Square=29.23; $p<0.0001$), Pearson's $R=-0.32$; $p<0.0001$, where the risk for death was three times higher (OR=2.89; 95% CI 1.87÷4.46). Adjusted to age, gender and presence of cardiovascular comorbidities, the correlation with mortality weakens, but remains negative and statistically significant. (Pearson's $R=-0.21$; $p<0.0001$). The same is valid for the mean hospital stay duration 12.62 ±9.164 vs. 15.50 ±8.888. t-2.702; p= 0.007 and the mean value of the days spent in RICU 6.60 ± 6.8 vs. 3.46 ±5.67 ($p<0.005$).

Conclusions: The administration of the Remdesevir leads to reduction of the mortality rate, total hospital stay and number of days in intensive care.

25. COVID – 19 IN PATIENTS WITH ORGAN TRANSPLANTS

Pavel Yordanov[1,2]; Figen Mustafa[1,2]; Tanya Dobreva[1,2]; Yanitsa Dimitrova[1,2]; Aleksandar Yordanov[1,2]; Georgi Gerganov[1,2]; Merlin Efraim[1,2]; Diana Petkova[1,2]; Valentina Dimitrova[1,2]

[1] *University Hospital "St Marina" Varna, Varna, Bulgaria;* [2] *Medical University "Prof. Dr. Paraskev Stoyanov" Varna, Varna, Bulgaria*

Introduction: The treatment of COVID – 19 in transplant patients on immunosuppressive therapy can be an enormous challenge to all healthcare professionals.

Aim: To analyze the course of the SARS – CoV – 2 infection and its outcome in transplant patients.

Methods: A retrospective analysis of 6 patients with kidney and 1 patient with heart transplantation and confirmed SARS – CoV – 2 associated pneumonia was performed. All patients were admitted to the COVID ward in the Department of thoracic surgery and the RICU at St Marina University Hospital - Varna for the period from September 2020 to March 2022.

Results: The average age of the patients included in the study was 52.43±7.91, the average time after transplantation was 7 years with a rank from 1 to 14 years, 85.7% of them were men and 14.3% were women. One of the patients was vaccinated, one had previous COVID - 19 infection before the current admission. All patients are currently being treated with mycophenolate and corticosteroids, 57.1% with tacrolimus, 28.6% with sirolimus, 14.3% with cyclosporine. 71.4% of patients received antiviral treatment. The average Charlson Comorbidity Index (CCI) index was 3.43±1.27. In 71.4%, oxygen therapy was included as a method of respiratory support, and in 42.9%, ventilatory support - NIV or MV – was required. The average hospital stay duration in the studied group was 17.86±8.78 days. Death occurred in one patient.

Conclusion: Considering the ongoing immunosuppressive therapy transplant patients are at risk of more severe course of the COVID - 19 infection. They should be treated by a multidisciplinary team.

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