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# **XXII National Congress of Italian Pulmonology - XLVI ITS-AIPO Congress**

## **Respiratory health. The answers of 21st century Pulmonology to the new environmental, technological and organizational models**

25 October–27 November 2021

### **Abstracts**

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### **Disclosure Statement Abstract Review Committee**

The members of the Abstract Review Committee have no conflicts of interest to declare.

## Abstracts

### Respiration

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ID# 2

#### The Care Pathway of the Patient with Coronavirus-19 in the Intensive Respiratory Care

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**Introduction:** An organizational-managerial-economic model is presented for the patient suffering from hypoxic respiratory failure from coronavirus pneumonia (COVID-19) that arrives at the Intensive Respiratory Care Unit (IRCU) of Monaldi Hospital.

**Objects:** To create a diagnostic-therapeutic-care pathway for hospitals and territorial management that goes from taking charge of the patient, to management and discharge, with a diagnostic and care quality based on skills and with an appropriate use of resources.

**Methods:** The patient is recovered: 1) in the low of assistance intensity of the Ordinary Department of Pulmonology or Infectious disease, if  $\text{PAO}_2/\text{FIO}_2 > 200$  in ambient-air, and he is responsive to oxygen therapy with venturi mask (MV) or high flow (HFNO); 2) in the average intensity of IRCU if he needs non-invasive mechanical ventilation (NIMV), if  $\text{PAO}_2/\text{FIO}_2 < 200$  with  $\text{FIO}_2$  at 60% with MV or HFNO; 3) in the high intensity of Intensive Care (ICU) for orotracheal intubation if  $\text{PAO}_2/\text{FIO}_2 < 100$  with respiratory distress, after 12 hours of NIMV. The patient remains in IRCU, if intubation is not indicated, due to advanced age or serious comorbidities. The subsequent transfer of the patient between ICU, IRCU, Ordinary Department depends on the patient's response to therapy. These pathways also have economic goals for the difference in daily costs of hospitalization: ICU (£ 1300), IRCU (£ 600), Ordinary Department (£ 450). The patient who does not have respiratory insufficiency from pneumonia or serious comorbidities, but that is positive at nasopharyngeal swab for SARS-CoV-2 must be managed at home, in fiduciary isolation by the USCA (Special Continuity Care Units) at a daily cost of £ 100.

**Results:** 160 patients with COVID-19 pneumonia had need hospitalization: 40 patients with  $\text{PAO}_2/\text{FIO}_2 < 250$  performed HFNO, while 80 patients with  $\text{PAO}_2/\text{FIO}_2 < 200$  and 40 patients with  $\text{PAO}_2/\text{FIO}_2 < 100$  who were not candidates for orotracheal

intubation, were undergoing at the NIMV. All 40 patients in HFNO and 60 patients in NIMV improved and were discharged after 20 days of hospitalization, among these 10 patients in fiduciary isolation by the USCA. On the other hand, 20 patients in NIMV with  $\text{PAO}_2/\text{FIO}_2 < 200$  and comorbidities and the most serious 40 patients with  $\text{PAO}_2/\text{FIO}_2 < 100$  died.

**Conclusions:** The path of the COVID-19 patient in relation to the intensity of care optimizes the patient as he is admitted to the most appropriate setting, avoiding improper hospitalizations in Ordinary Department, ICU and IRCU, with an increase in survival, reduction of the average hospital stay and consumption of resources.

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ID# 3

#### Remdesivir in the Treatment of Coronavirus Disease 2019: Our Experience

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**Introduction:** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection includes two moments: viral replication that can worsen in interstitial pneumonia, and the cytokine storm with the inflammatory response that can lead to death. Remdesivir is a drug that inhibits viral replication. It should be administered in the first 10 days from the onset of symptoms, when the viral load is high, in hospitalized patients with respiratory failure due to coronavirus disease 2019 (COVID-19) pneumonia, who do not require high flow oxygen (HFNC) or mechanical ventilation (MV) or Extra Corporeal Membrane Oxygenation (ECMO).

**Objects:** Evaluate the efficacy and the safety of Remdesivir in COVID-19 pneumonia and its effect in long covid syndrome.

**Methods:** We evaluated 30 patients with COVID-19 pneumonia in Venturi mask with FIO<sub>2</sub> averaging 40% (range 24%-60%). Their median age was 62 years (range 41-80), 60% were male, 50% had comorbidities (obesity, diabetes mellitus, cancer, ischemic heart disease, systemic arterial hypertension). The median chest CT score was 11/20 (range 5-18). They were treated with remdesivir at a dosage of 200 mg on the first day and 100 mg in the following 4 days, in combination with methylprednisolone, enoxaparin, N-acetylcysteine. All patients underwent blood gas analysis, electrocardiogram, blood chemistry tests (complete blood count, coagulation, inflammation indices, renal and hepatic function) before treatment and every 3 days thereafter.

**Risultati:** All patients completed the therapeutic course with Remdesivir, without adverse effects. After 20 days, in 20 patients pneumonia, hypoxemia and the indexes of inflammation regressed, the molecular swab was negative and they were discharged home without any respiratory support. In the remaining 10 patients the disease progressed and gas exchanges worsened (PAO<sub>2</sub>/FIO<sub>2</sub> 100). Of these, 3 patients underwent HFNC and after 1 month they recovered and discharged home. The other 7 patients who were more advanced in age and severe comorbidities, required non-invasive mechanical ventilation (NIMV), subsequently orotracheal intubation and died. The 23 recovered patients complained of a mild long COVID syndrome (fatigue, myalgia, shortness of breath, anxiety, decline in memory) in the following months.

**Conclusions:** Remdesivir therapy, started early, was effective in patients with COVID-19 pneumonia who do not require HFNC or MV or ECMO, with short hospital stay and less need for HFNC or NIMV. The drug was well tolerated and the long Covid syndrome was mild.

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ID# 4

## COPD during COVID-19: A Cross-sectional Observational Study of Narrative Medicine

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**Introduction:** The COVID-19 pandemic has disrupted everyone's life, particularly that of people in fragile conditions such as Chronic Obstructive Pulmonary Disease (COPD) patients and their caregivers. Moreover, it has harmed our economy, society, and healthcare system. Narrative Medicine is a valuable approach to understand the current caring and social practice.

**Objects:** The main aim of this study was to explore how the pandemic impacted on the organization and quality of care, in people affected by COPD, their caregivers and health care professionals, also exploring the role of telemedicine to overcome the isolation and access to care.

**Methods:** A cross-sectional observational study of narrative medicine was conducted between July and November 2020 across Italy. An online semi-structured questionnaire enriched by a narrative plot were completed by 146 participants (79 COPD patients, 24 caregivers and 43 health care professionals). Narratives were analysed throughout descriptive statistics and were evaluated both in aggregate form, breaking down the text and identifying the recurrences and the main semantic clusters using the software NVivo 11.

**Results:** During the lockdown period, 19 (24%) were followed via telemedicine by the General Practitioners (GPs), while 38 (48%) were followed in similar ways by the Pulmonologist. Only 2 people (2%) received home visits from their GPs and 9 (11%) had access to outpatient visits, compared to 32 (41%) who were seen in the hospital by the Pulmonologist as needed. As expected, only 12.6% COPD people reported regular access to visits, while 59.1% of GPs and Pulmonologists experienced telemedicine. This approach was perceived as satisfactory by both patients and caregivers. 22 (15.06%) patients were not able to access the visits either in presence or in telemedicine, although all Pulmonologists shifted physical to virtual visits. Indeed, the habit of telehealth is still under construction and some preferred to postpone visits. This finding becomes even more relevant if we consider that the most

frequently reported emotions and behaviours were apprehension, terror, and fear (25% participants and 32% caregivers), followed by thoughtfulness and vigilance for caregivers (16.6%).

**Conclusions:** The results highlight the need to implement a system of continuous care, able to manage the possible lockdown, distance and isolation. Telemedicine is in the hands of physicians but does not cover enough needs of patients and caregivers because of unequal infrastructures, though the results are promising.

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#### ID# 5

### Non-invasive Respiratory Support in Patients with Coronavirus Disease 2019

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**Introduction:** The Coronavirus disease 2019 has swept the world, with over 3 million deaths since the start of the pandemic. The disease is mild in most people, but in the elderly and those with comorbidities it can progress to pneumonia, which in 20% of cases can result in respiratory failure requiring high flow oxygen (HFNO) and ventilation therapies.

**Objects:** Verify the HFNO and the non-invasive ventilation (NIMV) effectiveness in acute respiratory distress syndrome (ARDS) due to COVID-19 pneumoniae to avoid the endotracheal intubation.

**Methods:** 200 patients required hospitalization: 65% men, mean age 66, 40% obese, 60% with systemic hypertension and diabetes mellitus, 25% with cancer, 20% with chronic obstructive pulmonary disease (COPD). 80 patients had moderate ARDS ( $\text{PAO}_2/\text{FIO}_2$  ratio >140) and 120 patients had severe ARDS ( $\text{PAO}_2/\text{FIO}_2$  ratio >100 but <140). All patients showed bilateral ground glass opacity and consolidation on high-resolution tomography of the chest. 50 patients with moderate ARDS received HFNO with flow 60 l/min and  $\text{FiO}_2$  100%, 30 patients with moderate ARDS received continuous positive airway pressure (CPAP)/NIMV with oronasal interface; the positive end-expiratory pressure (PEEP) did not exceed 12 cmH<sub>2</sub>O. 120 patients with severe ARDS received bilevel positive airway pressure (Bilevel)/NIMV.

**Results:** After a few days, 40 patients in HFNO, 50 patients in CPAP/NIMV and 30 patients in BILEVEL/NIMV improved their gas exchange and twenty days later were discharged to home. For the other 80 patients (40%), with severe comorbidities, the NIMV therapy failed, so they needed intubation and died later.

**Conclusions:** Depending on the clinical condition, we used HFNO and CPAP/NIMV and BILEVEL/NIMV obtaining clinical improvements. In this way, fewer patients have undergone endotracheal intubation. As a result, the prognosis improved and the length of hospitalization, along with resource consumption, was reduced.

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#### ID# 6

### Rehabilitation to Post-COVID-19 Patients: Effects of a Remote Treatment Protocol. Pilot Study

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**Introduction:** COVID-19 affected subjects have a syndrome comparable to that of ARDS. They have a reduction in muscle strength with a likely reduction in physical function. A long term exercise program is necessary for these patients. Patients have to stay at home and physiotherapists can't go to their domicile due to restrictions about COVID-19. For this reason, physiotherapists are not able to follow patients with rehabilitative sessions in hospital as outpatient or at this could modify the effects of exercise programs. We consider that remotely monitoring these patients could be an effective solution.

**Objects:** The first aims are physical function and Hand Grip Strength in COVID-19 affected subjects, verifying if there are differences between the remote monitored subjects and the self-managed ones. Secondary aims are strength assessment, gait speed, the quality of life and Activities of Daily Living.

**Methods:** Controlled randomised prospective pilot study. All patients included in the study do an early exercise program, that include both an aerobic and a strength training, provided by the physioterapist at the moment of the discharge. The intervention group (IG) is followed remotely 3 times a week and the control group (CG) self-managed at home. Assessments were performed at time of discharge and after two months of training. A non-parametric statistical analysis was performed. Mann-Whitney U Test was used to see the effect differences between the 2 treatments. Wilcoxon Test was used for intra-group comparisons. P value < 0.05 was considered statistically significant.

**Results:** 16 adult COVID patients with a mean age of 62 years were included. There has been a significant improvement in both groups in Short Physical performance Battery and 1 minute sit-to-stand test (STST). In the MRC-strength score only patients of the IG achieved a statistically significant improvement ( $p<0.046$ ). Performance in the 5 repetition STST has significantly improved in both groups. In gait speed a statistically significant greater

enhancement was achieved by the intervention group (IG: p<0.028; CG: p<0.043; IG versus CG: p<0.003). Both groups achieved the maximum level of independence in the ADL on average. No significant differences in handgrip test. Significant differences between the two groups were found in scores of 3 SF-36 questionnaire domains: Social functioning, Pain, General Health. CG felt more positive perception than IG.

**Conclusions:** COVID-19 affected patients who were regularly monitored 3 times a week achieved greater improvements in strength and gait speed. All patients (monitored and self-managed) followed the assigned rehabilitation program and obtained significant improvements in endurance physical performance.

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### ID# 8

## Radon and Public Health in the Light of Legislation 101 of 31.07.2020

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**Introduction:** Radon causes annually 10% of lung cancers in Italy. The risk for smokers is 25 times higher than for non-smokers. With the Legislation n.101 of 31.07.2020, Italy received last year the European Directive 2013/59/Euratom of 05.12.2013 (Health protection of the population and workers from the risks deriving from ionising radiation). The limit defined by the new rules, for exposure in terms of equivalent dose in workers, goes from 150 millisievert per year to 20 millisievert/year. For public and private work and living environments the reference value goes from 500 Becquerel per year to 300 Becquerel/year. As of 31.12.2024, the limit for newly built houses will be lowered to 200 Bequerel/year.

**Objects:** Radon gets harmful by binding with the particulate; the complex is deposited in the respiratory tract releasing alpha particles which interact with cellular DNA causing cancer. The concentration in an indoor environment is related to: soli properties, method of construction, building materials used, poor ventilation of the premises. It is useful to evaluate the radiation levels in indoor environments.

**Methods:** In this study we analyzed the presence of Radon inside a three-storey private house, starting from the basement and going up to the 3rd floor; we used a Geiger device with dedicated software, by carried out one hundred measurements and examined only the most significant ones.

**Results:** On average the level of radioactivity in the basement, with the due proportions, considering 1 month of continuous measurement, exceeded the acceptable levels of 300 Becquerel/year. This percentage fell within the norm on the first and second floors and then abruptly rose above 300 Becquerel/year on the

third floor, in rooms renovated according to modern criteria and with cutting-edge materials.

**Conclusions:** Pending the implementation of Legislation Decree 101 of 31.07.2020, the actions to be enforced against Radon are: frequent air exchange, putting in place of anti-radiation membranes, mechanical ventilation controlled by a special fan that creates a depression (with expulsion to the outside of the air contained in closed environments) or over-pressure (creating a flow opposite to that of Radon), suction of air in floors with crawl space below, by positioning suitable collection channels.

## Reference

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### ID# 9

## A Strange Case of Cerebral Tuberculosis in COVID-19 Era

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**Introduction:** Central nervous system tuberculosis is one of the worst manifestations of Mycobacterium Tuberculosis infection. Risk factors include young age, immunosuppression, malnutrition, alcoholism and malignancies. Clinical presentations are seizure, headache, hemiplegia and signs of raised intracranial pressure. Brain CT and MRI aid in diagnosis, assessment for complications, and monitoring of the clinical course. Treatment is a four-drug regimen for 2 months followed by isoniazid and rifampin for the rest of the course of 18 months. Steroids should be used for the first 2 months as well. We report a case of a young woman with brain tuberculoma simulating a glioma with simultaneous SARS-CoV-2 infection.

**Case report:** We report the case of a 35-year-old woman hospitalized for tonic-clonic epileptic crisis, paresthesia in the left arm with reduction of the state of alertness with suspected lung neoplasia and brain metastasis. Cerebral end chest CT scans showed right paramedian parietal neoformation and ground glass opacities in the right middle lobe. We administered levetiracetam, dexamethasone, ceftriaxone and clarithromycin. Magnetic resonance imaging showed extra-axial expansion formation at the right lateral face of the posterior region of the large sickle, with irregular margins (2.2x1.2 cm), slightly hyperintense in the sequences T1w and hypointense in T2w sequences, with perilesional edema. Spectroscopic study confirmed presence of an expansive process of the low-grade glial series. Was performed fibrobronchoscopy with TBNA at 11R lymph node station and bronchial washes (no neoplastic cells, no BK and common germs). After improvement

of symptoms, patient was discharged. Unfortunately, about a week after, patient was hospitalized again with SARS-CoV-2 pneumonia. Chest CT scan shows multiple ground glass opacities in the upper right lobe, in the upper left lobe and in the lower lobes. After three weeks of steroid therapy and negativization of nasopharyngeal swabs was discharged. After two month patient was hospitalized again with the same symptoms of first hospitalization. She underwent brain MRI which showed an increase in cerebral lesion with surrounding edema (shown in Fig. 1). Neurosurgeon indicated a craniotomy with removal of the mass. Before surgery, was performed chest CT scans showed right middle pulmonary field parenchymal thickening (the same site at the first hospitalization). Histological examination described chronic granulomatous necrotizing multinucleated giant cell inflammation, alcohol-acid resistant bacilli, Ziehl-Neelsen positive.

**Conclusions:** Some brain tumeculomas can be mistaken for cerebral gliomas. It is necessary to investigate the mechanisms that could influence this association between COVID-19 and tuberculosis, as seen more and more in literature.

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ID# 10

## Influence of Fascial and Soft Tissue Treatment on Respiratory Efficiency and Chest Mobility

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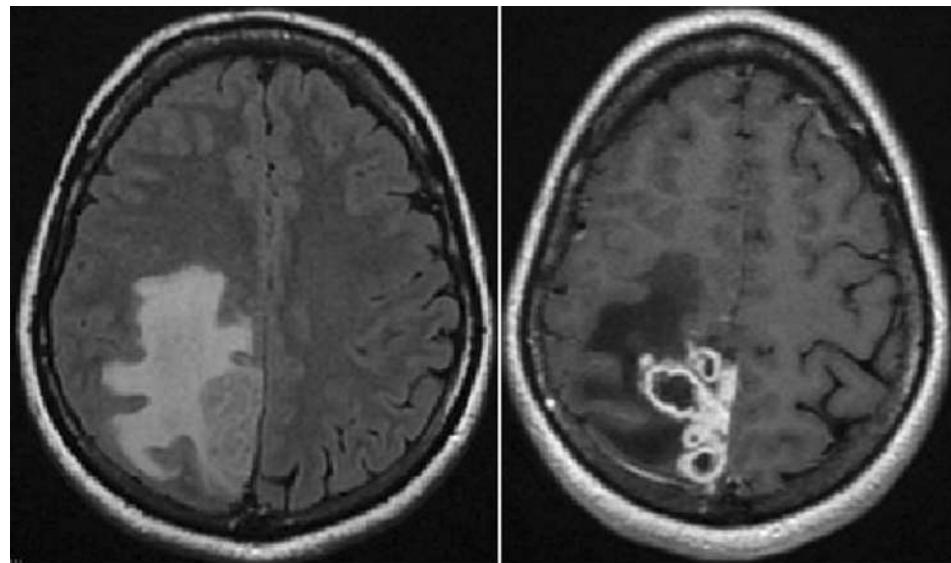
**Introduction:** In 2020 COVID-19 pandemic brought the respiratory system at the top of the pyramid of attention from every point of view. As physician we have decided to investigate different approaches in order to help people without using drugs, if possible. From this point of view sport activity and physical different therapies (e.g. osteopathic treatment) have shown to be very helpful in recovery and prevention of COVID-19's conditions.

**Objects:** The aim of the study was to determine the influence of fascial and soft tissue treatment on respiratory efficiency and chest mobility of men and women between 22 and 54 years old.

**Methods:** Subjects between 22 and 54 y.o., vaccinated or healed from COVID-19 and without any other pathologies were recruited. Fascial and soft tissues manual treatment was made on mesentery's roots, right pillar of diaphragm and ileo-cecal valve. Spirometry was executed before and after the treatment. Patients had been adequately instructed on how to make a spirometry.

**Results:** FEV<sub>1</sub> showed an average increase of 2% meanwhile FEF2575 showed an average increase of 14.38% (from a minimum increase of 0.26% to a maximum of 31.76%).

**Conclusions:** Although FEV<sub>1</sub>'s improvement is not indicative, there is an improvement in FEF2575 indicating better



**Fig. 1.**

spontaneous return of the diaphragm to its resting state after the treatment. The treatment doesn't act on filling because we have seen that the increase in FEV<sub>1</sub> is not significant but it affects emptying so it could be interesting to evaluate how patients are able, after the treatment, to better empty themselves and, since better emptying is a prerequisite for better filling, whether and how the residual functional capacity improves. It is as if with the treatment we had made patients learn to better empty themselves, getting therefore a more elastic return of the diaphragm in its relaxed position. There is a gain except for smokers who always remain hyper-inflated emphasizing then how the share of emphysema is already measurable for smokers.

## Reference

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ID# 13

## A Rare Case of Histiocytosis

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**Introduction:** Erdheim-Chester disease (ECD) is a rare, non-Langerhans histiocytosis characterized by tissue xanthomatous infiltration by spumous histiocytes CD68+ CD1a-. Recent identification of the clonal nature of the disorder have been found that ECD histiocytes express a pattern of proinflammatory cytokines and chemokines responsible for local activation and recruitment of histiocytes ; this consists of elevated levels of interferon (IFN)- $\alpha$ ,

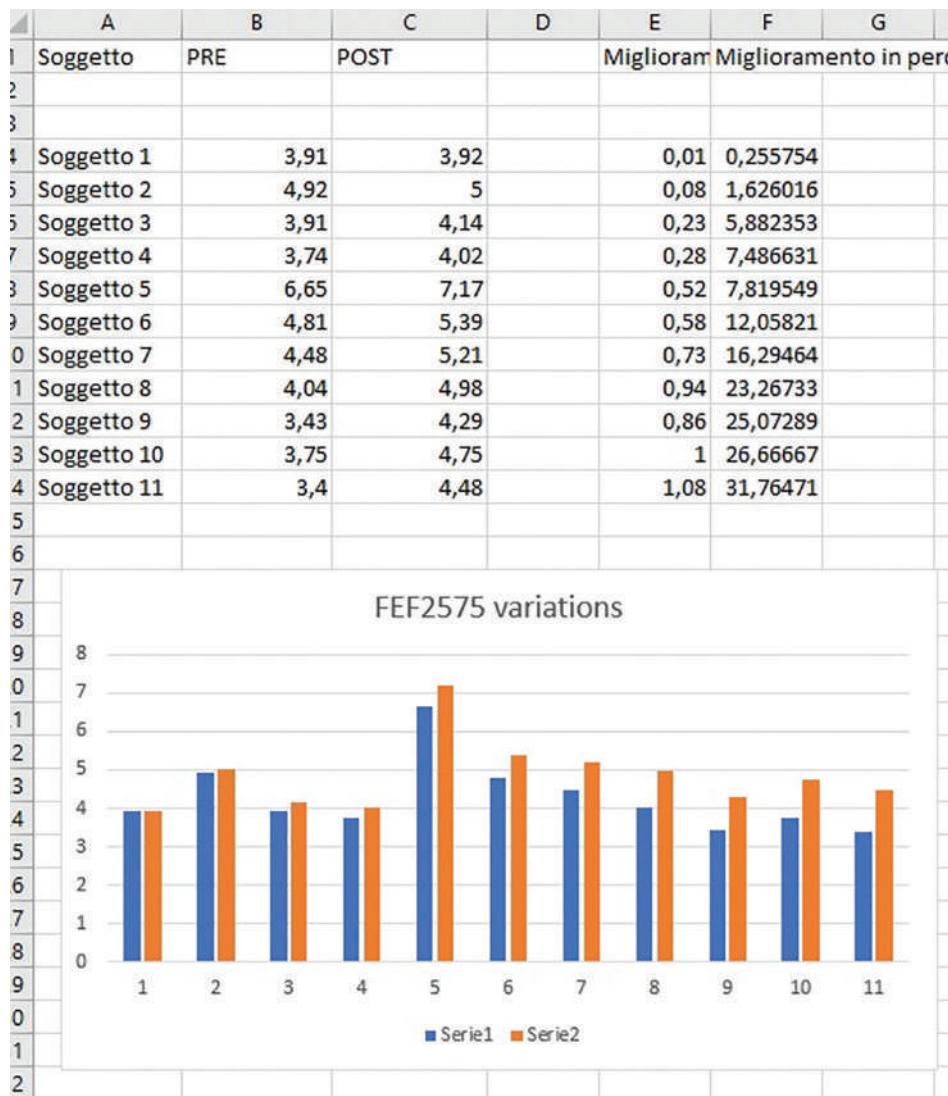


Fig. 1.

interleukin (IL)-12, monocyte chemotactic protein-1, and decreased IL-4 and IL-7. The majority of the patients with ECD have osseous involvement. Around half of ECD patients may also have extraskeletal manifestations, including central nervous system (CNS) and cardiovascular involvement, retroperitoneal and adrenal infiltration, diabetes insipidus, exophthalmos, xanthelasma, and pulmonary involvement. The manifestation of pulmonary involvement may be due to infiltration of the lungs or to cardiogenic pulmonary edema resulting from primary cardiac involvement. The clinical course of ECD is largely dependent on the extent and distribution of the disease. The natural history of the lung disease remains unclear. Pulmonary involvement in ECD has been overlooked, HRCT reveals typical lesions in most patients. There is no clear response of these lesions to corticosteroids and IFN\_. The overall prognosis of the disease is poor, but pulmonary involvement does not appear to be a major prognostic factor in ECD.

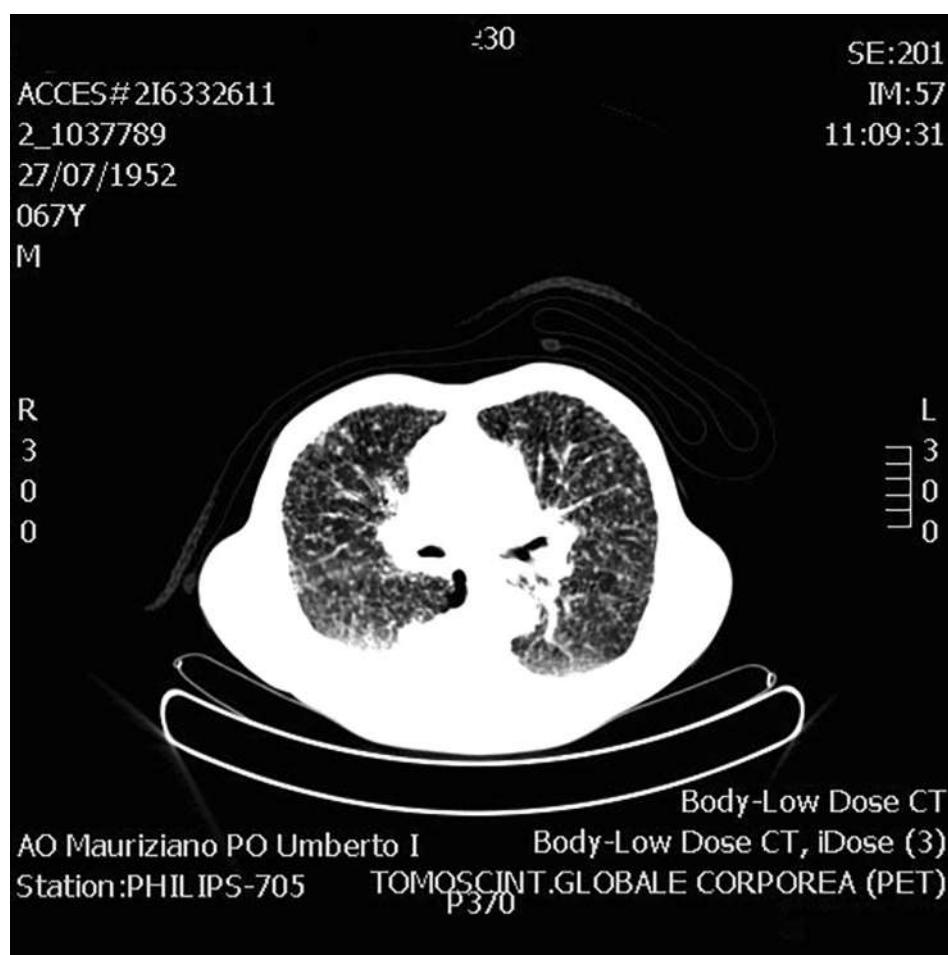
**Case report:** A 67yo male was seen in our office in november 2019 because of diffuse micronodular lesion on CT scan. He used to be a heavy smoker (60 py) and alcohol abuse. The patient suffer from hepatic chirrosis CHILD A6 MELD 8 (HCV/HBV neg). A CT scan also showed thickening of the abdomen/thorax arteries.

PET CT showed a diffuse lung radiotracer uptake, pleural effusion, radiotracer uptake in the left femoral shaft, focal uptake in the thyroid gland. Respiratory Function Test showed severe obstructing syndrome (FEV<sub>1</sub> 36%) and severe reduction of the CO diffusion capacity (33%). We performed a fibrobronchoscopy that turned out negative both for tumoral cells and bacteria. A surgical lung biopsy were done. The histologic result was presence of foamy histiocyte CD68 and 163 pos, CD1 and S100 negative. No necrosis and/or granuloma were found. Diagnosis: Erdheim-Chester Disease. BRAF V600 turned out negative. Brain RMN didn't show ocular involvement.

**Conclusions:** In consideration of the liver disease we couldn't use interferon therapy. At the moment the patient is under steroid therapy (prednisone 50 mg/die) and is showing clinical improvement. As the therapy was started recently, no restaging is yet performed.

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**Fig. 1.**

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ID# 15

## Healthcare Resource Use & Costs of Pertussis in Adults with Asthma: a Retrospective Study in England

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**Introduction:** Pertussis is an infectious disease whose burden in the older adult population is under-recognized, especially among those with chronic conditions like asthma.

**Objects:** This study evaluated the healthcare resource utilisation (HCRU) and associated costs among cohorts of individuals ≥50 years with asthma, diagnosed or not with pertussis.

**Methods:** A retrospective observational study was conducted using the Clinical Practice Research Datalink, linked to Hospital

Episode Statistics. Patients ≥50 years with asthma and a pertussis diagnosis code between 2009–2018 were selected and matched to patients without pertussis, using propensity scores. HCRU in primary and secondary care settings were measured for both cohorts during a baseline period from 18 to 6 months prior to diagnosis, and from 1 month prior to diagnosis to 11 months after. Analysis also included HCRU and costs from 1 month to 1 day prior to diagnosis. Annualised direct medical costs (DMC) were estimated from identified HCRU multiplied by relevant unit costs. A generalised linear model (GLM) compared both cohorts' DMC from 1 month prior to pertussis diagnosis to 11 months after.

**Results:** Matched pertussis (N=314) and non-pertussis patients (N=1,256) were comparable for most baseline HCRU measures. From 1 month prior to diagnosis to 11 months after, general practitioner (GP)/nurse visits, and accident & emergency visits were more frequent in the pertussis cohort ( $p<0.001$ ). Primary and secondary care costs were respectively 1.54 and 1.20 times the costs in the pertussis cohort ( $p=0.005$ ) (Table 1A). Similarly, from 1 month to 1 day prior to diagnosis, primary and secondary care costs were respectively 3.30 and 1.29 times the cost in the pertussis cohort ( $p<0.001$ ) (Table 1B). The GLM showed that the total annualised cost per patient was £370 higher on average in the pertussis cohort corresponding to a 26.38% increase ( $p=0.0018$ ) (not shown in tables below).

**Table 1.**

Table 1. Annualised costs (2019 UK £)

A. 1 month before to 11 months after diagnosis date

		Matched Pertussis cohort (N=314)	Matched Non-Pertussis cohort (N=1,256)	p-value
		Mean (SD) per patient	Mean (SD) per patient	
Primary care	GP consultations and nurse visits	631.39 (430.34)	406.08 (423.49)	<0.001
	Five most common prescribed products	13.87 (22.76)	12.00 (19.65)	0.114
	Five most common clinical values*	4.28 (5.26)	3.80 (4.81)	0.191
	Total of the above primary care costs	649.54 (442.05)	421.89 (432.80)	<0.001
Secondary care	A&E visits (all-cause)	80.09 (200.55)	50.68 (165.11)	<0.001
	Hospital inpatient admissions (all-cause)	682.58 (2,387.78)	568.31 (1,776.93)	0.285
	Outpatient specialist visits (all-cause)	413.18 (686.22)	363.41 (684.81)	0.015
	Total of the above secondary care costs	1,175.85 (2,850.57)	982.40 (2,224.76)	0.005
Total	Total of the above primary and secondary care costs	1,825.39 (3,109.89)	1,404.29 (2,429.28)	<0.001

B. 1 month before to 1 day before diagnosis date

		Matched Pertussis cohort (N=314)	Matched Non-Pertussis cohort (N=1,256)	p-value
		Mean (SD) per patient	Mean (SD) per patient	
Primary care	GP consultations and nurse visits	1,455.06 (1,093.58)	441.00 (692.43)	<0.001
	Five most common prescribed products	26.47 (36.84)	10.91 (25.39)	<0.001
	Five most common clinical values*	40.03 (67.77)	9.57 (37.58)	<0.001
	Total of the above primary care costs	1,521.56 (1,132.84)	461.49 (715.82)	<0.001
Secondary care	A&E visits (all-cause)	189.22 (639.85)	44.44 (305.93)	<0.001
	Hospital inpatient admissions (all-cause)	672.34 (5,065.36)	603.21 (5,864.92)	0.388
	Outpatient specialist visits (all-cause)	485.14 (1,087.61)	396.81 (1,022.80)	0.059
	Total of the above secondary care costs	1,346.69 (5,789.23)	1,044.46 (6,190.43)	<0.001
Total	Total of the above primary and secondary care costs	2,868.25 (6,017.21)	1,505.95 (6,399.17)	<0.001

\*Clinical values include laboratory tests and clinical assessments such as body mass index, blood pressure, pulse rate, alcohol consumption, etc.  
A&E, accident & emergency; GP, general practitioner; N, number of patients in the cohort; SD, standard deviation.

**Conclusions:** A pertussis episode among patients  $\geq 50$  years with asthma resulted in significant increases in HCRU and DMC around the pertussis event.

**Conflict of Interest Disclosure:** Marta Vicentini is employed by the GSK group of companies and hold shares in the GSK group of companies.

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ID# 17

### Lung Cavitation, Pneumothorax, Pneumomediastinum as Fatal Complications of COVID-19: Case Report

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Lucia Valdarchi<sup>2</sup>, Luca Triolo<sup>1</sup>

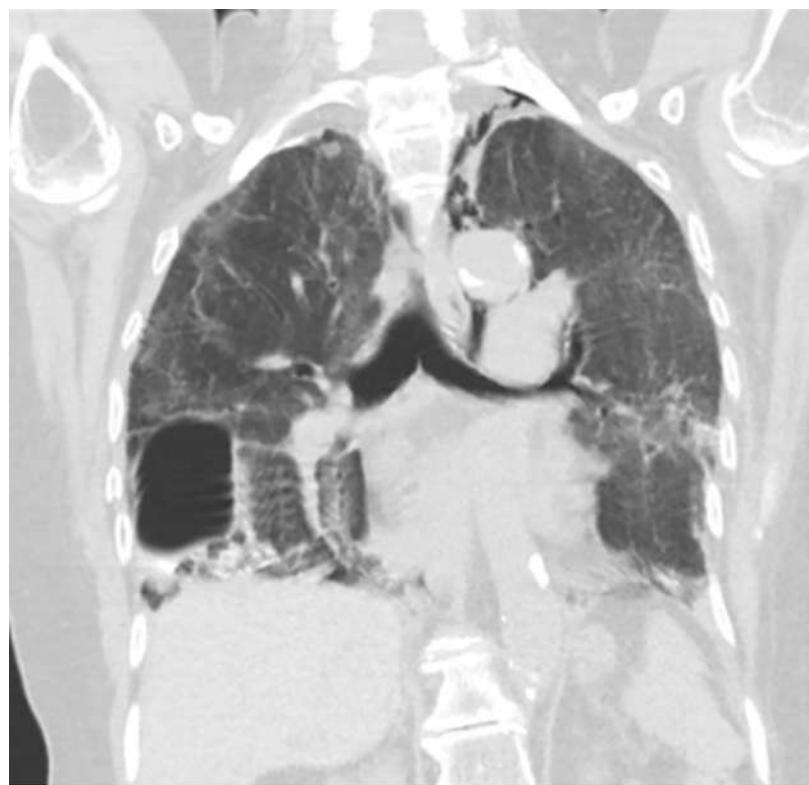
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Rehabilitation Unit, San Filippo Neri Hospital, Rome, Italy

**Introduction:** The coronavirus disease 2019 (COVID-19) is caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is associated with

several fatal cases worldwide. We report a clinical case of a patient with SARS-CoV-2 and rare complications: pneumomediastinum, pneumothorax and lung cavitation lesion characterized by chest computed tomography (CT).

**Case report:** An 81-year-old woman with a history of hypertension, cardiac arrhythmia, and hypercholesterolemia all pharmacologically controlled was admitted to the emergency department after 5 days of fever and dyspnea. A CT chest scan showed extensive ground-glass opacities involving both lung parenchymas. The genomic amplification test for SARS-CoV-2 was positive, and the patient was treated with azithromycin, methylprednisolone, and oxygen support with a reservoir mask at 15 l/min (FiO<sub>2</sub> of 90%). Due to SARS-CoV-2, she was admitted to the subintensive pulmonary care unit for non invasive mechanical ventilation. After two weeks, given the torpid evolution of the disease, it was decided to perform a chest CT with contrast medium, suspecting pulmonary thromboembolism. On the chest CT, left partial pneumothorax with pneumomediastinum were identified, as well as COVID-19 pulmonary involvement. A lung cavitation lesion with an air-fluid level was seen in the lower lobe of the right lung. The cavity with small air-fluid level was localized in the place of previously present area of rarefaction (Fig. 1). Nasal high flow oxygen therapy at 50 l/min, FiO<sub>2</sub> of 90% started. Follow-up, radiological controls showed reabsorption of the pneumomediastinum and pneumothorax. However, the patient clinically presented progressive deterioration with decreased renal and respiratory functions and hemodynamic instability. Despite the support measures



**Fig. 1.**

and the intra-hospital management, the patient developed multiple organ failure and died 40 days after the symptoms initiated.

**Conclusions:** The present case illustrates the severity of the disease associated with rare complications such as pneumothorax, pneumomediastinum and lung cavitation. These findings in patients with COVID-19 pneumonia confirmed the usefulness of chest CT to rule out thromboembolic complications or, in patients with progressive worsening of respiratory function, pneumothorax associated with pneumomediastinum. Given the fatal outcome, it cannot be excluded that the presence of pneumothorax and/or pneumomediastinum and/or lung cavitation may be associated with greater severity and worse outcomes. More studies are required to assess causality or association.

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ID# 18

### Radiological Findings of Pulmonary Fibrosis Post COVID-19: Lung Trasplantation is Only Option?

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**Introduction:** Infection with the novel coronavirus 2 (CoV-2) causes COVID-19 which can lead to pneumonia and severe acute respiratory syndrome (SARS-CoV-2). Clinical, radiographic, and autopsy reports of pulmonary fibrosis were commonplace following SARS and MERS, and current evidence suggests pulmonary fibrosis could complicate infection by SARS-CoV-2. We present a clinical case of patient developing SARS-CoV-2 and prolonged COVID-19 with chest computed tomography (CT) showing a

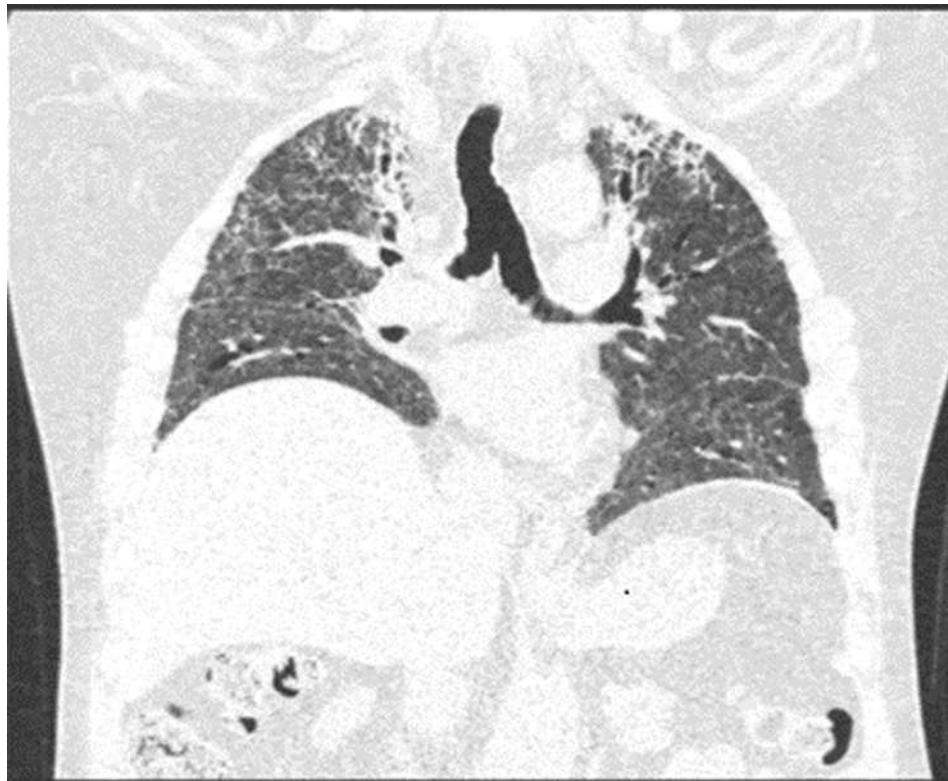
typical pulmonary fibrosis during the follow-up, while initial CT examination showed only GGO.

**Case report:** The patient was a 60-year-old man with no prior co-morbidities, who presented at the emergency department with short of breath and fever for the last one week. Reverse transcription polymerase chain reaction (RT-PCR) test from nasopharyngeal swab samples confirmed the diagnosis of COVID-19. Chest computed tomography (CT) scan documented extensive ground-glass opacifications involving both the lung parenchymas. Due to SARS-CoV-2, he was admitted into intensive care unit (ICU) for noninvasive mechanical ventilation. Intravenous piperacillina/tazobactam and desametasone were started empirically. In following days, the clinical condition of patient improved; prone position ventilation was discontinued for 3 hours or more. After two weeks, on the chest CT scan, right partial pneumothorax, pneumomediastinum and subcutaneous neck emphysema were identified, as well as pulmonary involvement by COVID-19. Nasal high flow oxygen therapy at 45l/min, FiO<sub>2</sub> of 80% started. His partial pressure of oxygen (PaO<sub>2</sub>)/FiO<sub>2</sub> ratio was < 150 persistently. Patient improved and the chest CT scan after 15 days showed resolution of pneumomediastinum and subcutaneous neck emphysema, but crazy-paving pattern interlobular septal thickening was seen. The patient was symptomatically improved but continued to have hypoxemia even after 3 months of treatment. He was transferred in Respiratory Diseases Unit. After 5 months, clinical conditions of patients improved as well his hypoxemia. CT chest showed persisting of crazy-paving patterns with peripheral cystic changes and interlobular septal thickening (typical 'honeycomb', appearances due to pulmonary fibrosis) with light improvement of these findings in lower pulmonary lobes (Fig.1). He discharged on home oxygen and corticosteroid oral therapy and enrolled trial for the subsequent follow up. Furthermore, lung transplantation hypothesis was considered.

**Conclusions:** We presented a previously healthy patient who developed a pulmonary fibrosis after receiving treatment for COVID-19. Lung transplantation can potentially be a life-saving treatment for patients with nonresolving COVID-19-associated respiratory failure and radiological findings suggestive of fibrotic lung disease. Alternatively low-dose corticosteroid oral therapy can improve pulmonary disease.

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**Fig. 1.**

ID# 19

### **Staphylococcus Aureus Coinfection on a COVID-19 Pneumonia: Percutaneous Transthoracic Drainage Use**

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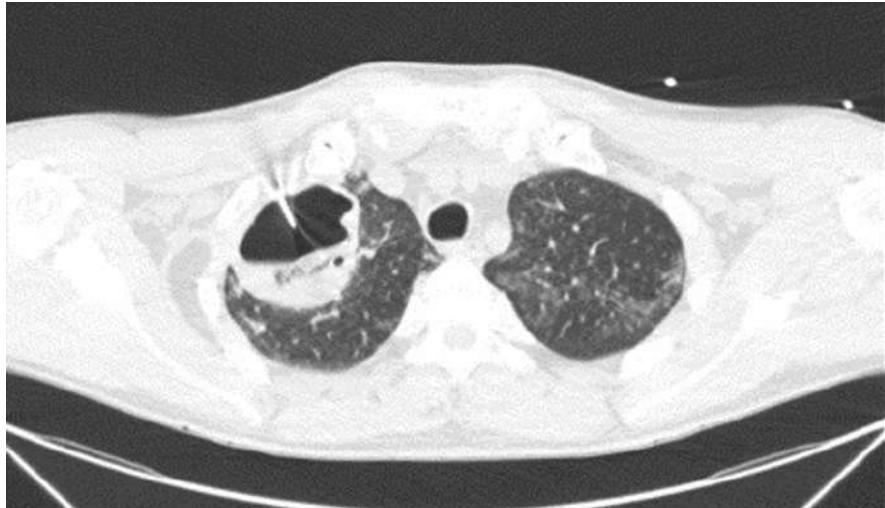
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**Introduction:** Coronavirus disease 19 (COVID-19) is known as a new viral infection. The risk of viral-bacterial co-infections is high, resulting in increased mortality rates. We present a clinical case of patient with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and lung cavitation lesion due to staphylococcus aureus coinfection.

**Case report:** The patient was a 53-year-old man with a history of hypertension, who presented at the emergency department with

short of breath and fever for the last one week. Chest computed tomography (CT) scan documented extensive ground-glass opacifications involving both the lung parenchymas and pulmonary embolism of main right pulmonary arteria. Reverse transcription polymerase chain reaction test from nasopharyngeal swab samples confirmed the diagnosis of COVID-19. Due to SARS-CoV-2, he was admitted into intensive care unit (ICU) for non invasive mechanical ventilation. Intravenous piperacillina/tazobactam and desametasone were started empirically. In the following days, the clinical condition of patient improved; prone position ventilation was discontinued for 3 hours or more. After one week, on the chest CT scan, right partial pneumothorax and pneumomediastinum were identified, as well as pulmonary involvement by COVID-19. Nasal high flow oxygen therapy at 45 l/min, FiO<sub>2</sub> of 80% started. Patient improved and transferred in Respiratory Disease Unit. The chest CT scan after 10 days showed resolution of pulmonary embolism and pneumomediastinum but a lung cavitation lesion with air-fluid level was seen in the upper lobe of the right lung. Staphylococcus aureus was isolated from endobronchial aspirate using flexible bronchoscopy. The patient started an antimicrobial treatment with linezolid 1.2 g/day, cefaloridina 1.8 g/day and capsofungin 70 mg/day. After two weeks, chest CT scan showed worsening of cavitation with air fluid level in the right lung. Antimicrobial therapy was modified based on vancomicina 2 g/day and meropenem 3 g/day. Furthermore, lung lesion was treated with CT-guided percutaneous transthoracic tube drainage (PTTD) (Fig 1). After



**Fig. 1.**

thoracentesis, bacteriological examination confirmed pus discharge with *Staphylococcus aureus* isolated. PTTD was efficacious tool for the management of refractory lung abscess. After 7 days, right lung cavitation decreased. No complications relating to the procedure occurred.

**Conclusions:** We presented a previously healthy patient who developed a lung abscess after receiving treatment for COVID-19. Lung cavitation due to COVID-19 pneumonia is uncommon. Causes of cavitary lung lesions must be investigated appropriately. Interventional radiologic procedure (PTTD) is a safe, simple and efficacious tool for the management of refractory lung abscess.

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**ID# 21**

### **Association Among Strength and Mechanical Ventilation in Prone COVID-19 Patients. Retrospective Study**

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**Introduction:** A significant proportion of subjects with COVID-19 develops the acute respiratory distress syndrome (ARDS) and requires invasive mechanical ventilation (IMV) and admission to an intensive care unit (ICU). Several studies evaluated an incidence of ICU-acquired weakness (ICUAW), as measured by means of a Medical Research Council (MRC)-graded manual muscle strength score <48 in patients receiving IMV at least 7 days. Maintaining prone position for a long time is associated with muscle deconditioning in COVID-19 patients, as well. Proximal muscle strength is significantly less than distal muscle strength in both upper and lower limbs in patients with ARDS. Identifying muscle strength in COVID-19 patients can benefit overall muscle health and minimize muscle deconditioning through a progressive rehabilitation program.

**Obiettivi/Object:** The first aim was to assess an association among MRC-score, time of IMV and prone position cycles in

COVID-19 patients. The secondary aims were to describe muscle strength in different muscle groups and evaluate different MRC-score between 2 groups of patients: IMV <7 days and ≥7 days respectively.

**Methods:** This was a retrospective study, including adult patients affected by COVID-19, who received IMV and were placed in prone position, evaluated by MRC scale. Good collaboration was required (with a score of the five standardized questions at least 3/5). Group differences in the continuous variables were assessed by Mann-Whitney U tests. The correlations between the included independent variables were analysed using Pearson's correlation coefficients. Simple linear regression analyses were performed to determine the associations between the included variables and MRC-score. A P value <0.05 was considered statistically significant.

**Results:** A total of 33 patients were included, 8 female, with a mean age at the test of 57 years, a standard deviation of 10.6. A significant correlation was found between MRC and IMV days ( $r=-0.681$ ,  $p<0.000$ ) and a moderate but significantly association between MRC-score and prone position cycles ( $r=-0.493$ ,  $p<0.003$ ). Proximal muscle strength was lower than distal muscle strength. However, there was a significantly difference only in upper limbs (lower limbs  $p<0.160$ ; upper limbs  $p<0.000$ ). In the 2 groups of patients, MRC-score was significantly lower in patients with IMV ≥7 days (mean 34.1 vs 49.4;  $p<0.002$ ).

**Conclusions:** In our study MRC-score was associated with IMV and prone position. MRC is lowest in patients with IMV ≥7 days. This condition could be an important aspect for a good physical function recovery in these patients, and it could leave a mark on resources and costs in pulmonary rehabilitation.

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### ID# 22

#### Atypical Pericarditis in COVID-19

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**Introduction:** Patients affected by coronavirus disease 2019 (COVID-19) may develop typical symptoms (fever, dry cough and muscle weakness) and common complications (such as pneumonia and acute respiratory distress syndrome), however, they might also present uncommon complications, which include neurological, dermatological, ophthalmic, cardiac and atypical respiratory manifestations.

**Objects:** Treatment of uncommon complications in COVID-19.

**Case report:** Herein we report the case of SE, a 27-year-old male patient who presented with fever, complained fatigue and dry cough for 10 days, vomiting and diarrhea for 2 days, and he had had multiple admissions to the emergency room in the last week. A nose-throat swab for SARS-CoV-2 research was positive, and the RX showed a bilateral interstitial lung disease and lung consolidation, without signs of pleural effusion. So we established corticosteroid therapy, thromboprophylaxis with Enoxaparin 4000 UI, and antiviral therapy with Remdesivir. The next day, further imaging investigations were made: the TC showed a bilateral pleural effusion at the base of the lungs (with maximum thickness at the right lower lobe of 5 mm) and pericardial effusion maximum thickness of 8 mm. The patient didn't show chest pain, ECG alterations or worsening of the respiratory manifestations. Within 24 hours an echocardiogram was performed, showing a marked reduction of the pericardial effusion (8mm → 2mm in diastole and 4mm in systole). Thus Anti-inflammatory therapy with Ibuprofen 600mg x 2 for 20 days was planned out, while the patient kept on his corticosteroid and thromboprophylaxis therapy.

**Results:** Acute pericarditis is usually self-limiting and the pleural and pericardial effusion didn't affect the patient's outcome, neither extended the length of hospitalization.

**Conclusions:** Pericarditis is commonly seen in viral infections, however is usually without any pericardial effusion. In COVID-19 pericarditis can have atypical presentation with non-respiratory symptoms and non ECG alterations, while pericardial effusion can be present.

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### ID# 24

#### Change of Pleural Artifacts During Thoracic Ultrasound in Respiratory Care of COVID-19 Patient

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**Introduction:** Chest ultrasound was used during the last pandemic for the evaluation of acute COVID-19 hospitalized patients.

**Objects:** The aim of the work was to see the modification in the pleural sonographic artifacts during the High flow O<sub>2</sub> therapy Vs Non Invasive Ventilation (NIV) in COVID-19 patient.

**Case report:** A COVID-19 male patient, born in 1948, was evaluated with a thoracic ultrasound scan during the the reservoir mask therapy (O<sub>2</sub> with 15 lt/m) and Non Invasive Mechanical Ventilation (NIV) with oronasal mask (O<sub>2</sub> with 6 lt/m). A Logic S8 ultrasound machine, set in abdominal way, has been used to study the artifacts' modification during the therapy. The convex probe, of 3-5 MHz, was used for the study of both the pleura (with focus

at 4/5 cm) and the pulmonary densification and diaphragm excursion (with focus at 15-20 cm). We used, to record, the points MAP of the Italian COVID-19 Lung US project of Trento University classification based on 14 points. We studied the change of pleural artifacts before and after one hour in supine position, during high-flow O<sub>2</sub> therapy with 15 lt/m (SpO<sub>2</sub> 98%) and during non-invasive ventilation with: O<sub>2</sub> at 6 lt/m, PS of 7 cmH<sub>2</sub>O, Peep of 5 cmH<sub>2</sub>O, FR 15, Inspiratory Trigger medium, Expiratory Trigger 25% (SpO<sub>2</sub> 97%).

**Results:** The A lines artifact that appeared during Sonography of NIV ventilation (SpO<sub>2</sub> 97% with O<sub>2</sub> at 6 lt/m) representing normal airway ventilation respect at B lines artifacts with the reservoir mask (SpO<sub>2</sub> 98% with O<sub>2</sub> at 15 lt/m).

**Conclusions:** Thoracic ultrasound can be a simple, safe and useful method, at bed side patient, to study the alteration of pleural artifacts. The change of pleural artifacts (from consolidation and B lines to A lines), during respiratory treatment, can guide the technician towards choosing the correct strategy of therapy.

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ID# 26

### "Artificial Intelligence-Driven Insights Analysis (AIDA)" Applied to Chronic Respiratory Diseases

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**Introduction:** Medical&scientific Insights are a fundamental tool to interpret medical environment and uncover current unmet

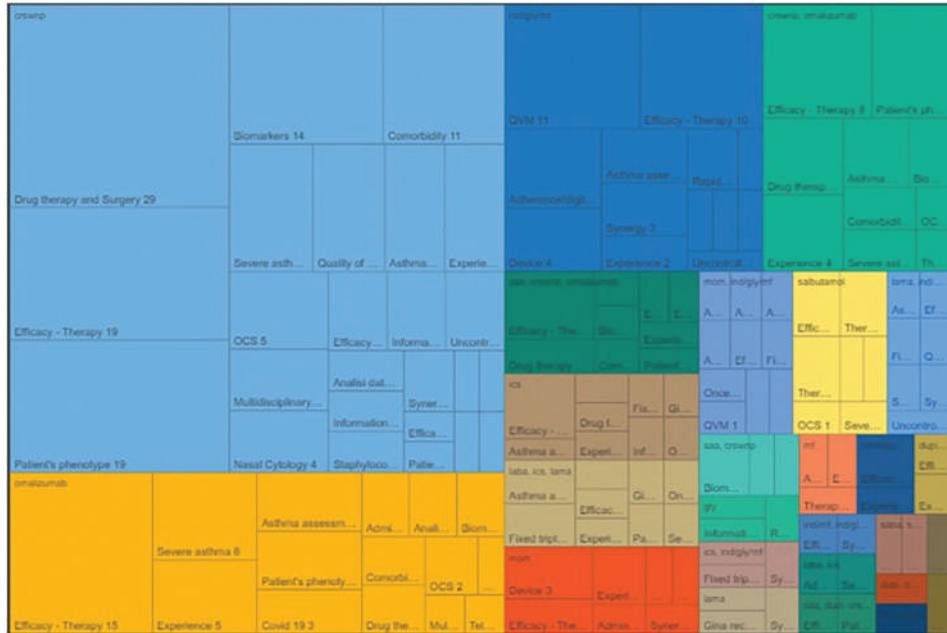
medical needs. Insights are the result of an acute and deep process of listening and comprehension of the medical context. Insights analysis may contribute to guide clinical drug development or to support any institution aiming to improve patient care within or in collaboration with the Health Care System in order to optimize access to the most appropriate therapies and finally improve patients' lives. To date, due to the amount of insights that is possible to be collected, conventional analysis is complex, potentially biased and unable to extract the greatest value from this data source.

**Objects:** To get unbiased and strategic information from the analysis of insights supported by artificial intelligence (AI), to guide the future drug development.

**Methods:** We applied Google AutoML-Machine Learning Natural Language Artificial Intelligence engine to analyze the insights text coupled with a contextual dictionary built by subject matter expert (Medical Science Liaisons - MSL) realizing a semi-supervised machine learning tool. We applied the model to insights collected by the Novartis MSLs in Italy from January 2020 to March 2021. As first step, the unsupervised machine learning model extracted key metadata and aggregated them in medical keywords. Moreover they were combined to identify relevant themes associated with the original insights. Human intelligence and expertise constantly reviewed metadata, keywords and themes, to make the process automatic and able to predict admissible behaviors and actions that scale-up the solution. A Sentiment Analysis Score, leveraging Google ML, was also associated to each input content. A graphic dashboard was created to allow an intuitive and effective visualization of the data.

**Results:** 260 insights were analyzed with "AIDA" tool. The recurrent themes of input and actions deriving from the analyzed insights were identified and clustered (Figure 1): efficacy of therapies, asthma assessment, experience in the use of a therapy and the need for exchange of information on therapies and diseases. They were therefore acknowledged as the most representative themes to guide the future medical strategy for drug development.

**Conclusions:** The "AIDA" insight exploitation for the chronic respiratory diseases in Italy allowed an objective and systematic analysis of key information for the setup of future clinical drug development and institution collaboration. The method will continue to be improved aiming for a wide spreading of the technology in a more vast area.



**Fig. 1.** Insights identification and clustering matrix

ID# 27

## Multiorgan Shock with Major Arrhythmia and Hepato-renal Injury in COVID-19: A Case Report

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**Introduction:** Many patients with Coronavirus Disease 2019 (COVID-19) have also an underlying cardiovascular (CV) disease. New or existing heart failure can be encountered at different stages in the course of a COVID-19 patient presentation, thus represents a challenge into understanding the interaction between heart failure and the infection. A careful investigation and treatment of the hemodynamic implications is essential for appropriate management of the patients

**Objects:** Respiratory and medical treatment in COVID-19 to improve and stabilize the hemodynamic profile in Congestive Heart Failure (CHF).

**Case report:** Herein we report the case of CP, a 87 year old male recently vaccinated against COVID-19, who showed up to emergency department with a complaint of angor and dyspnea. He was affected by coronary artery disease (CAD), CHF with left ventricular ejection fraction (LVEF) 46% (last check in 2020), chronic gastritis and peptic ulcer; he had previously had in 2009 an acute myocardial infarction (AMI) that underwent multiple

angioplasties with percutaneous transluminal coronary angioplasty (PTCA) + drug-eluting stent (DES) on common arterial trunk (CAT), coronary artery bypass grafting (CABG) in 2010. CP was admitted a cardiogenic shock diagnosis, ventricular sustained tachycardia (VST), LVEF 20% treated with cardioverter defibrillator shock and vasoactive amines. During the hospital stay he developed rapid atrial flutter (RAF) and Luciani-Wenckebach periodicity (LW), also severe anemia occurred and AST/ALT ratio in serum raised as well serum creatinine (Scr), suggesting an underlying hepato-renal damage. Hepatitis screening resulted negative, abdominal investigations showed no organomegaly and abnormalities. A nose-throat swab for SARS-CoV-2 research was made resulting positive and the imagings showed a bilateral interstitial pneumonia. Thus we established low flows oxygen therapy, blood transfusions, antibiotics, antiarrhythmic, corticosteroid and thromboprophylaxis therapy.

**Results:** Severe anemia and the hepato-renal injury were completely tackled by medical therapy with restitutio ad integrum. The patient was discharged as the ante-quo status, the electrocardiogram didn't show any abnormalities, while the ecocardiography showed an improvement of LVEF (51%), with no need of additional hemodynamic investigations.

**Conclusions:** Cardiogenic shock with low cardiac output and major arrhythmia could be related to acute lung damage and acute distress respiratory syndrome (ARDS) in COVID-19 pneumonia as the result of hypoxaemia and hypoperfusion.

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ID# 28

## A Diagnostic Algorithm in COVID-19 Pulmonary Outcomes

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**Introduction:** Pulmonary involvement from COVID-19 is almost constant, even in many patients recovered from the acute phase (interstitial pneumonia) respiratory symptoms and signs persist (dyspnoea, cough, desaturation, respiratory insufficiency) and pneumonia leads to interstitial disease (ground-glass) and hence to pulmonary fibrosis (honeycomb lung). A diagnostic algorithm can be a simple and practical way not to exclude differential diagnoses with pulmonary embolism and other acute events and to set up therapies in a systematic way.

**Objects:** Propose a simple and easy diagnostic algorithm with implementation. It is of particular importance to identify and distinguish the various phases of post-COVID-19 with chest ultrasound or with chest CT scan, excluding pulmonary embolism in high dimer-D patients, suggestive gait test and compatible objectivity.

**Methods:** Prescription of: blood tests (complete blood count, PCR, LDH, AST, ALT, pt, appt, dimer-D, retinoblastoma, azotemia, ferritin, interleukin-6, electrolytes) radiological (CT chest CMC or High Resolution), respiratory physiopathology (Walking test, Global spirometry, Plethysmography, DL<sub>CO</sub>). Set drug therapies with blood coagulation (NAO/TAO) in case of pulmonary

embolism, oral steroid (OCS) in case of extensive interstitial disease, long-acting beta 2 agonist bronchodilators (LABA), antimuscarinics (LAMA), inhaled steroids (ICS). In the case of fibrosis and a honeycomb pattern, treatment with dipalmitoyl ethanolamine (PEA).

**Results:** 258 outpatient patients, average age 60.68 years, 115 women, 143 men, who arrived with an urgent request from the general practitioner, for a pneumological visit and treated on an outpatient basis. 1 patient died during treatment, 4 patients were diagnosed with pulmonary embolism. 4 patients required a prescription for oxygen therapy. 228 patients presented ground-glass, 30 patients showed normal chest CT. 36 patients show pulmonary fibrosis, with honeycomb.

**Conclusions:** Monitoring with DL<sub>CO</sub> shows progressive improvement in values after ICS treatment. Small pathway deficiency evidenced by spirometry can be treated with LABA-LAMA especially in patients with a previous history of cigarette smoking or COPD. Plethysmography is important for the decrease in residual volume which is also evident in young patients without evident pulmonary fibrosis or interstitial disease. Patients who quickly develop a honeycomb fibrosis pattern can be treated with a cycle of oral, after inhaled steroid and PEA to avoid permanent damage.

## Reference

Piccole vie e terapia inalatoria triplice ICS-LABA-LAMA fad sincrona, Vernocchi 26.02.21

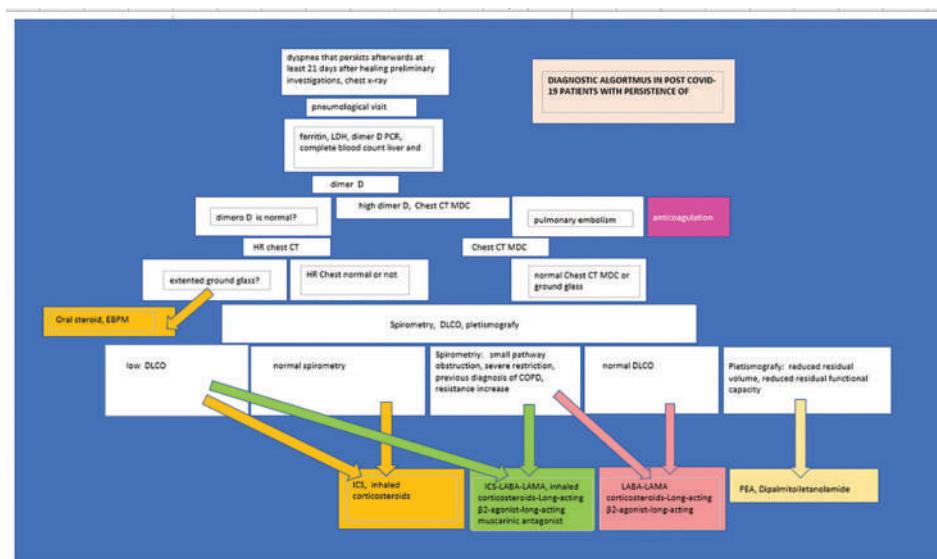


Fig. 1.

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ID# 29

## Intrapulmonary Percussive Ventilation in Intensive Unite Care: Case Report

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Tommaso Sinigaglio, Cecilia Defraia, Alessandra Colzi,  
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**Introduction:** Intrapulmonary percussive ventilation (IPV) (C) is a technique that, using high-frequency oscillatory ventilation with a device called "Percussionator", facilitates the removal of bronchial secretions and the resolution of atelectasis, improving efficiency and distribution of ventilation.

**Objects:** This device has been used for our clinical case with the aim of carrying out bronchial clearance and improving gas exchanges.

**Case report:** Patient B. D., aged 27, male, hospitalized at the intensive care "Neuroanesthesia e Rianimazione" of the hospital of Careggi Firenze, presented a traumatic brain injury. On the sixth day of hospitalization the patient developed pneumonia due to *Pseudomonas* and began antibiotic therapy. The patient was sedated and underwent tracheostomy procedure. He was bradipnoic, hypercarbic ( $\text{PCO}_2$  55), hypersecretive, ventilated in a controlled mode (SIMV, VT 580 ml, RR 18 a/m). Treatment with IPV was carried out for 6 consecutive days with a time of use of 9 minutes: 3 minutes in high frequency, 3 minutes in medium frequency, 3 minutes in low frequency,  $\text{FiO}_2$  50%. Arterial blood gas analysis

(ABG) was performed before and after the treatment and repeated every two hours during the day. During the treatment with IPV, a continuous monitoring of vital parameters is provided: heart rate, arterial blood pressure,  $\text{SpO}_2$ . After the treatment and later, when necessary, the patient was suctioned. A chest CT was performed before treatment with IPV and again after 6 days.

**Results:** ABG carried out immediately after the treatment shows a reduction of  $\text{PaO}_2$  of 40%. After two hours it shows an increase of 30% compared to the base value and this value is stable in the next ten hours. After 6 days of treatment the patient switched from controlled ventilation to supported ventilation (CPAP/PSV mode, 8+8). The CT of the chest (A) performed before the treatment with IPV shows a marked lung consolidation, basal pleural effusion flap, a limited atelectasis of the left-lower-lobe. The CT scan (B) 6 days after IPV treatment shows a reduction of the lung consolidation, the anterior and posterior-basal segments are more ventilated, and partial resolution of the multiple-consolidating of the upper right and left lower lobe.

**Conclusions:** As reported by many authors (1,2), IPV helps in the removal of a large amount of secretions and, as in our case, was considered an important help during the antibiotic therapy in bronchial clearance, in atelectasis resolution, weaning from invasive mechanical ventilation, without presenting any side effects, even though the patient was in SIMV.

## References

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2. Clini EM, et al. Intensive Care Med 2006;32:1994–2001.

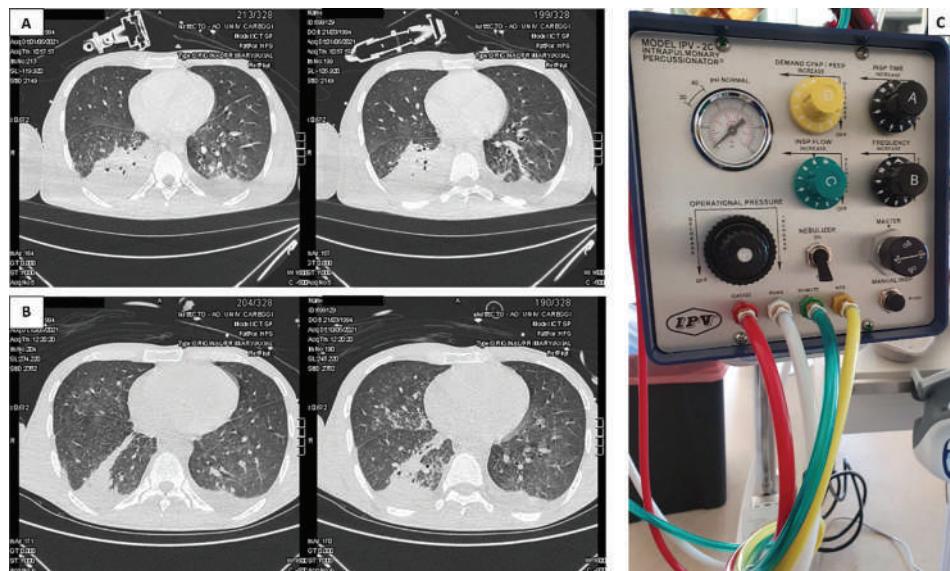


Fig. 1.

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**ID# 30**

## **Integrated Home Treatment of COVID-19 in 406 Families**

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**Introduction:** Not always hospital admission is in patients with SARS-CoV-2 pneumonia the best choice, if possible, being treated at home is better both for the patients, and for the health system that can dedicate resources for who really need hospitalization.

**Objects:** Safely avoid hospitalization and in any case guarantee high-level assistance, limit infections and unnecessary travel.

**Methods:** From 30.03.20 to 30.05.21 we followed 407 families with COVID-19, the following were essential identifiers for the patients to remain at home: 1.the presence of a family willing to meet recent criteria, providing support in contacting us in swabs, blood tests and prescriptions; 2.the suitability of the house with a room suitable for insulation, bathroom and heating; 3.the presence of care-giver; 4.the possession of a telephone with internet network to provide the doctor with clinical data and to receive and tutorials; 5.pulse oximeter and the ability to use it to monitor SPO<sub>2</sub>. The therapies were modulated in relation to the severity of the patient established both with the values of the resting SPO<sub>2</sub>, the walking test, the respiratory rate, the fever, and with the execution of the chest ultrasound interpreted according to the Soldati score. Prednisone 0.5-1 mg/kg/day for 5-10 days then tapering off, LMWH in prophylactic dosage according to weight, Azithromycin 500 mg for 6 days, supplement of vitamin D 50,000U/week and zinc 50 mg/day. All pts were invited to tutorials with diaphragmatic breathing and recoil and taught in the correctness of execution during the specialist home assessment. Absolutely avoiding bedtime, on mobilization even in case of fever, on abundant hydration and nutritional advice played an important part.

**Results:** 407 families were treated (about 3 positives on average for a total of 1197pts), only 4 hospitalized pts, 3 men of 44, 89, 57 years and a woman of 59 years, no one has been intubated. No deaths in followed families. No cases of pulmonary embolism. All patients with persistent respiratory symptoms after clinical recovery from COVID-19 were referred to the pulmonary clinic (258 patients with an average age of 60.68 years).

**Conclusions:** Integrated home treatment can be an alternative to sending to the emergency room and hospitalization where there is a specialist with minimal equipment (ultrasound), patients able to follow prescriptions provided via social media and send clinical data daily. Important was the network with pharmacies for oxygen

and drugs even on holidays and with the analysis laboratory for home blood sampling at a controlled cost.

## **Reference**

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**ID# 31**

## **Effects of Home Respiratory Rehabilitation Program in Patients with Post-COVID- Syndrome: Case Series**

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**Objects:** In the home rehabilitation COVID field, because of the heterogeneity of the symptoms present and the correlation of these to any pre-existing pathologies and age, it has not been possible to advance specific guidelines until today. This case series aims to describe the effects of a specific home rehabilitation program.

**Methods:** We evaluated 3 patients (58-68-76 years) with bilateral interstitial SARS-CoV-2 pneumonia undergoing treatment with non-invasive ventilation (helmet) discharged at home since two months. All patients had reduced exercise tolerance in activities of daily living (ADL), chest tightness, at 1 minute sit to stand test (1STST) mean desaturation >5%, they were able to climb 20 steps with mean dyspnea > 6 (modified Borg Scale) and increased heart rate by 30%. The rehabilitation program included calisthenics exercises and reconditioning to effort (cycle ergometer, walking, 10-step ladder). In addition to this: 2 daily sessions, 5 days/ week of PEP mask structured as follows: alternating inspiration and expiration resistors; inspiration and expiration pressure about 10-12 cmHO<sub>2</sub>; 5 repetitions x 2series insp, 5x2 esp, 5x2 inspiratory and expiratory resistors simultaneously; each cycle repeated on both side position and then seated. Two weekly physiotherapy sessions of mobilization of the shoulder girdles and rib cage, stretching of the intercostal, pectoral, transverse muscle, quadratus of the loins, psoas and diaphragm.

**Results:** After about 4 weeks from the start of treatment, all patients had a decrease in dyspnea during ADL, the disappearance of the sense of chest tightness, disappearance of episodes of mean desaturation >5% at 1STST, they doubled the number of steps climbed (about 40) before the appearance of dyspnea (borg 6) which, however, returns completely after one minute of recovery, with an increase in heart rate of about 15%. In the following month the progress is maintained, except for one patient (age 76), after 10 days of suspension of the specific respiratory treatment had an increase of dyspnea of about 30% in ADL. Upon resumption of treatment, he improved again in about a week

**Conclusions:** Some patients with SARS-CoV-2 discharged from the hospital and considered cured, still have symptoms and

RESULT OF 1 MINUTE SIT TO STAND TEST					
	age	n. repetition	FC	SO2%	BORGmax
<b>initial</b>					
Paz. A	76	15	84-110	96%-90%	>6
Paz.B	58	17	78-105	96%-89%	>6
Paz.C	68	15	82-105	94%-88%	>6
<b>final</b>					
Paz.A	76	15	85-94	95%-92%	4
Paz.B	58	18	80-90	95%-94%	4
Paz.C	68	15	84-92	94%-92%	4

functional limitations. We believe that an adequate home rehabilitation program controlled by personnel with adequate skills can favor functional improvement in ADL. Further studies on a greater number of patients will allow us to confirm the best methods of intervention.

## Reference

Carfi A, et al.; Gemelli Against COVID-19 Post-Acute Care Study Group. JAMA 2020;324:603-5.

### ID# 33

#### Pleural Epithelioid Hemangioendothelioma (PEH) with Pericardial Involvement: a Case Report

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**Introduction:** Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor that can affect any organ. The pulmonary subtype (pleural epithelioid hemangioendothelioma - PEH) is more aggressive and less frequent, with less than 200 cases reported in the literature, and the presence of pericardial metastases is particularly rare. Aspecific symptoms like chest pain, dyspnoea, cough and pleural effusion are often found at presentation. Due to the low prevalence and variable presentation, diagnosis can be difficult.

**Objects:** Description of a case report of PEH with pericardial metastasis referred to our department for unilateral pleural effusion and recurrent chest pain.

**Case report:** A 62-year-old non-smoker female was admitted to our hospital for left pleural effusion and repeated left-sided back

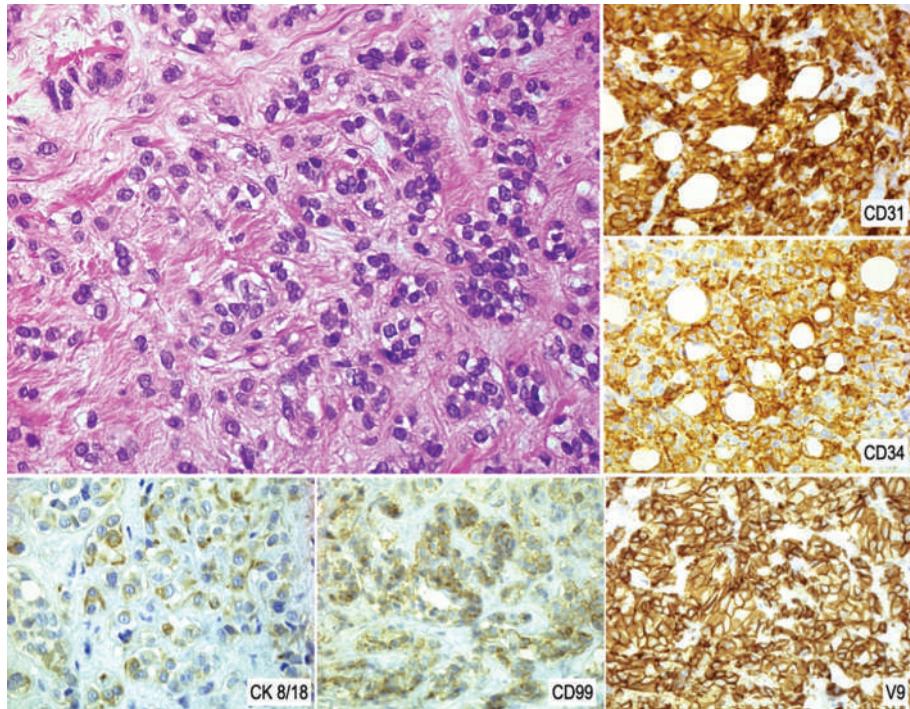
pain. She had a six-year history of bilateral pulmonary nodules, 16 located in the left lung and 23 in the right one, partially calcific and homogeneously spread, subjected to clinical and radiological follow-up. Cytological examination, cultural and BK research on pleural and bronchoalveolar fluid were negative. Chest CT showed significant left pleural effusion and parenchymal pulmonary nodules that hadn't increase in size since the last CT scan follow-up; the PET-CT highlighted glucose accumulation in the largest nodules, with weakly enhancing (SUV<sub>max</sub> = 1.4), thus fitting with both inflammatory and malignant process.

**Results:** Macroscopic examination during thoracoscopy revealed widespread involvement of the parietal pleura with many fibrous hyaline areas, and nodules on the pulmonary and pericardium surface, not discovered by the radiological imaging. Histological examination showed epithelioid cells arranged in cords and trabeculae with low-grade atypia, while immunohistochemistry was positive for CD31, CD34, vimentin V9, focal cytokeratin 8/18 and weak CD99 (Fig. 1) and allowed the diagnosis of PEH with metastatic pericardial localizations; the pulmonary parenchymal nodules were osteochondromas. The patient later began chemotherapy with monthly courses of Gemcitabine, still ongoing. During the treatment the patient underwent progressive weight loss, severe fatigue and persistence of the well-known back pain.

**Conclusions:** Epithelioid hemangioendothelioma is a rare malignancy that can involve several systems. Diagnosis can be complex, even when correct biopsy sampling is performed. The pleural variant is particularly rare and can be mistaken for various malignant thoracic diseases, including mesotheliomas, and infectious ones, such as tuberculous pleurisy. Especially, this case is noteworthy for the concurrent pericardium's involvement.

## References

Bahrami A, et al. Path Intern 2008;58:730-4.  
Yu L, et al. J Card Surg 2013;28:266-8.



**Fig. 1.**

ID# 35

### **Successful Sequential Treatment with Systemic and Inhaled Steroid to Resolve COVID-19 Pneumonia**

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**Introduction:** The current global Coronavirus disease (COVID-19) pandemic is characterized by an acute respiratory and systemic syndrome. There is great uncertainty about the possible pulmonary complications that patients with more severe manifestations may have in the longer term, such as fibrosis. The factors responsible for pulmonary fibrosis development are not clear; drug-induced pulmonary toxicity, non-protective mechanical ventilation, and hyperoxia-induced damage could be involved (1). We describe a young patient with severe bilateral COVID-19 pneumonia, treated sequentially with systemic and after with inhaled steroids/bronchodilators.

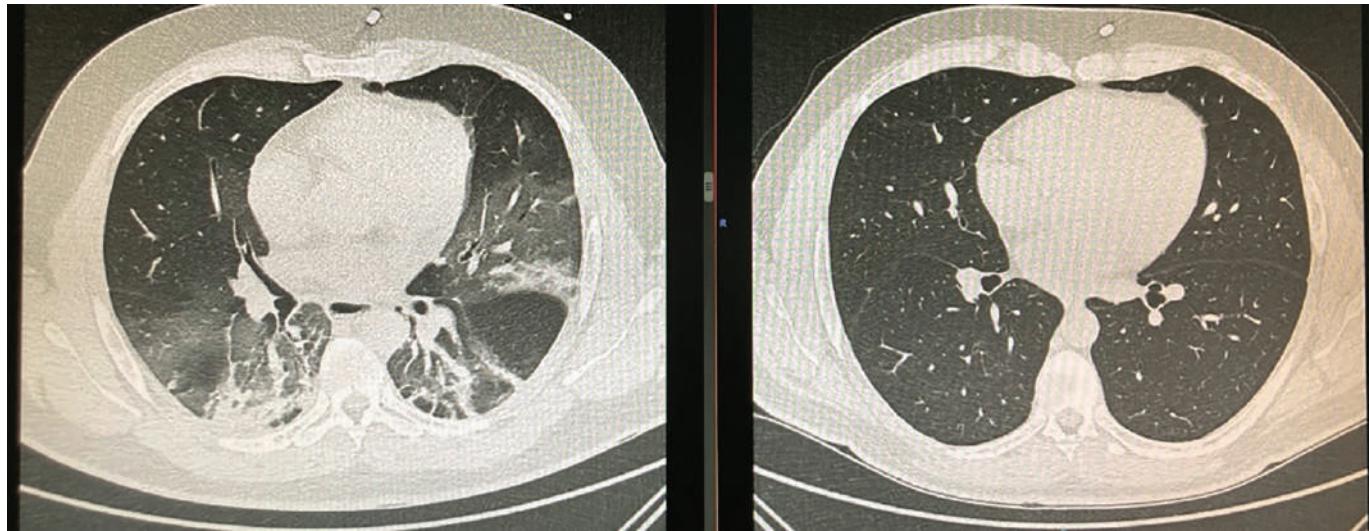
**Case report:** A 39-years-old male, non-smoker, without any underlying pneumological or autoimmune disorder, was diagnosed with COVID-19 pneumonia (figure 1) and mild hypoxemia at our Center. Treatment with low-molecular weight heparin (enoxaparin 6,000 U/daily), azithromycin 500 mg ev/daily, single shot low-dose subcutaneous tocilizumab (324 mg) remdesivir (day 1 loading dose: 200 mg IV than day 2 and thereafter: 100 mg IV for 5 days), intravenous dexamethasone (at a dose of 6 mg once daily) and oxygen therapy was started. During the first days of hospital stay he developed severe hypoxic respiratory failure non

responder to CPAP; he was subjected to oro-tracheal intubation and invasive mechanical ventilation. After 14 days the clinical condition progressively improve, and after invasive mechanical ventilation, he was de-escalated to HFNC. After 32 days of hospitalization he was discharged in room air, without support oxygen and with SARS-CoV-2 RT-PCR on a nasopharyngeal swab (NPW) tested negative from 15 days. Home treatment was started with beclomethasone dipropionate/formoterol 100/6 mcg bid for 3 months. After 30 days from negativization of NPW, he was subjected to pulmonary function testing (PFT): forced vital capacity (FVC) of 91 % predicted level, forced expiratory volume in one second (FEV<sub>1</sub>) of 98 % the predicted level and a diffusion capacity of carbon monoxide (DL<sub>CO</sub>) 66 % predicted level. After 3 months of treatment (Figure 1) a control high-resolution computed axial tomography (HRCT) (figure 2), that showed a resolution of the previous infiltrates (at T0) and PFT were repeated with improvement of DL<sub>CO</sub> (80% pred.).

**Conclusions:** Our case report showed benefits and normalization of HRCT features after treatment at home for 3 months with ICS/LABA. Inhaled corticosteroids are generally used for treating inflammatory conditions in the lung, such as asthma and chronic obstructive pulmonary disease. More evidence from clinical trial is necessary to establish the benefits of inhaled corticosteroids alone or with bronchodilators in people with pulmonary complications after COVID-19 disease.

### **Reference**

Spagnolo P, et al. Lancet Respir Med 2020;8:750–2.



**Fig. 1.**

**ID# 36**

### **Coronavirus Disease: Time Course of PaO<sub>2</sub>/FIO<sub>2</sub>**

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**Introduction:** The ratio between partial pressure of oxygen and fraction of inspired oxygen ( $\text{PaO}_2/\text{FIO}_2$ ) is used commonly for diagnosis of lung injury, for assessment of pulmonary disease course and therapy. During the severe acute respiratory syndrome due to the SARS-CoV-2 infection  $\text{PaO}_2/\text{FIO}_2$  ratio was used for risk stratification.

**Objects:** The objective of this study was to compare  $\text{PaO}_2/\text{FIO}_2$  in the very early phase of the disease [i.e. at the moment of admission in the emergency department (ED)] with the levels at the moment of discharge from acute setting, at respiratory rehabilitation discharge and after 12 months from the admission.

**Methods:** Between February and April 2020 we accepted 38 patients transferred from Emilia Romagna intensive and sub-intensive care units. Beside pharmacological therapy, patients underwent pulmonary rehabilitation, according to the Italian Position Paper multidisciplinary program.

**Results:** Patients admitted to our unit had suffered from long Los in acute care hospital, but they arrived weaned from mechanical ventilation; only 4 out 38 patients did not need oxygen supplementation. However,  $\text{PaO}_2/\text{FIO}_2$  showed a significant improvement ( $p < 0.001$ ) compared to the acute phase, even if still far from normal values. At hospital discharge  $\text{PaO}_2/\text{FIO}_2$  improved and was statistically different ( $p < 0.05$ ) from the admission values.  $\text{PaO}_2/\text{FIO}_2$  did not change during the check up after 12 months from patients' release, suggesting that the patients discharged had reached the best possible condition, at least from a respiratory point of view.

**Conclusions:** Pulmonary rehabilitation is possible and effective in patients recovering from COVID-19, as previously shown (1). Despite the small sample, no significant improvement is shown after 1 year respiratory rehabilitation discharge.

### **Reference**

- (1) Zampogna A, et al. Respiration 2021;100:416–22.

**Table 1.** Demographic and clinical characteristic of patients. Data are expressed as median, mean  $\pm$  SD and range. Los: lenght of stay; ED: emergency department

	median	range	mean $\pm$ SD	p-value
<u>Age (years)</u>	54	33-78		
<u>Los in acute hospital, days</u>	43.5	24-71	44.9 $\pm$ 10.8	
<u>Los in rehabilitation, days</u>	26	12-61	27.6 $\pm$ 9.4	
<u>ED admission:</u>				
PaO <sub>2</sub> , mmHg	52	44-60	51.9 $\pm$ 4.1	
PaO <sub>2</sub> /FIO <sub>2</sub>	247	209-290	246.9 $\pm$ 19.4	0.0008
<u>Rehabilitation admission:</u>				
PaO <sub>2</sub>	56	48-65	55.6 $\pm$ 4.6	
PaO <sub>2</sub> /FIO <sub>2</sub>	266	228-309	264.6 $\pm$ 22.1	0.007
<u>Rehabilitation discharge:</u>				
PaO <sub>2</sub>	77	64-91	76.7 $\pm$ 6.9	
PaO <sub>2</sub> /FIO <sub>2</sub>	366	304-433	365.1 $\pm$ 33.1	NS
<u>After 12 months:</u>				
PaO <sub>2</sub>	77.5	65-88	78.2 $\pm$ 5.7	
PaO <sub>2</sub> /FIO <sub>2</sub>	368.5	309-419	372.1 $\pm$ 27.5	

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ID# 37

## Audentes Fortuna Iuvat: Never Give Up on COVID Patients

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**Introduction:** The major morbidity and mortality from COVID-19 is largely due to acute viral pneumonia that evolves to acute respiratory distress syndrome (ARDS) with severe hypoxemia. The need for mechanical ventilation in critical ill is high ranging from 30 to 100 percent (1).

**Case report:** We report the case of a 62-year-old man, who went to the emergency room of our hospital for fever and ageusia, with positive swab for SARS-CoV-2 two days earlier, at the entrance P/F 290; Chest CT shown pulmonary emphysema with interstitial pneumonia, mediastinal mass of 14 cm and brachiocephalic stem thrombosis. He was recently hospitalized in thoracic surgery ward where he had undergone anterior mediastinotomy diagnosed with THYMOMA B with pleural metastases. For the worsening of respiratory exchanges, CPAP helmet treatment was started after trial failure with HFNC. Intensive care specialist, considering the oncological pathology, did not indicate IOT and invasive ventilation despite the worsening of the P/F index (80), peripheral oxygen saturation 88%, failure of pronation and the increase in respiratory rate. After a few days there was progressive worsening of the conditions: peripheral oxygen saturation 80%, tachypnoea, chest ultrasound documented ARDS. Therefore, therapy with morphine 4 fl/24h and NPT began. Critical conditions persisted for 18 days suddenly peripheral oxygen saturation went up to 96%. Gradual scaling of morphine therapy and weaning from the CPAP helmet then began to position HFNC approximately forty-five days after the onset of symptoms. After reduction of FiO<sub>2</sub> and Flow in HFNC was also suspended to switch to Venturi mask with subsequent transfer to the Medical Oncology Department.

**Conclusions:** Our case is intended as an encouragement not to give up even in the most difficult situations, in which everything seems to be lost, but only tenacity allows us to reach the goal.

## Reference

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ID# 38

## Involving the Voice of Patients with COPD in Health Management for the Co-Creation of Solutions

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<sup>1</sup>Medical Department, GlaxoSmithKline, Verona, Italy,

<sup>2</sup>Presidente, Associazione Italiana Pazienti BPCO Onlus,

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**Introduction:** Breathlessness and exacerbations are a huge burden in the life of patients with COPD, being the main cause for exercise limitation and health status impairment, particularly in patients with moderate-severe COPD who, despite the ongoing treatment, are still dyspnoic and/or exacerbated and may need an increase in therapy. New medicines have made it possible to improve the management of the disease, although adherence is still low and there may be difficulties in the inhaler use or in the acceptance of therapies because of adverse events.

**Objects:** In order to identify new opportunities for diagnosis, monitoring and treatment optimization, GSK has started a project, Paziente.net, involving patient with severe COPD on triple therapy, aimed at the analysis of patients' unmet needs through the acquisition of insights and at the co-creation of possible solutions.

**Methods:** COPD patients on triple therapy (ICS, LABA and LAMA) were selected by the referring specialist doctor for participation in the Patient.net project. A model of active listening was developed, to understand patients' unmet needs and expectations. The company's medical experts participated in the meetings in an exclusive listening mode. The insights were collected through guiding questions, analyzed, processed and shared with the medical specialists.

**Results:** A total of 16 Patient Insight Meetings were held, including 102 patients with moderate-to-severe COPD on triple therapy. Altogether, around 600 insights were collected, and main topics were identified, describing critical conditions related to the disease management. Up to 95% of patients reported late diagnosis of COPD, often after hospitalization for severe exacerbations or after investigations for other pathologies. Diagnosis was made almost exclusively by the pulmonologist. The impact of the disease was defined strong by all patients, with anxiety and fear for exacerbations. For most patients, transition to triple therapy brought further benefits, with improvement in their quality of life. Simplification of the therapy was also generally appreciated.

**Conclusions:** Patient.net is a key activity for understanding the real impact of COPD on patients' quality of life as well as their unmet needs and expectations. A diagnostic delay was still reported by the great majority of patients, suggesting the need for an increased focus on Primary Care for early detection, monitoring and treatment of the disease. The final goal of the project is to identify actions and co-create solutions with the medical specialists for

a correct management of COPD and its most difficult aspects, starting from the voice of the patient and his unsatisfied needs.

**Conflict of Interest Disclosure:** Carmen Stabile, Lara Bernardi, Miriam Vighini, Maria Sandra Magnoni, Elisa Form, Roberta Bodini and Roberta Tosatto are employed in GlaxoSmithKline.

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ID# 39

### A Case of Macrophage Activation Syndrome in a Patient with Severe SARS-CoV-2 Pneumonia

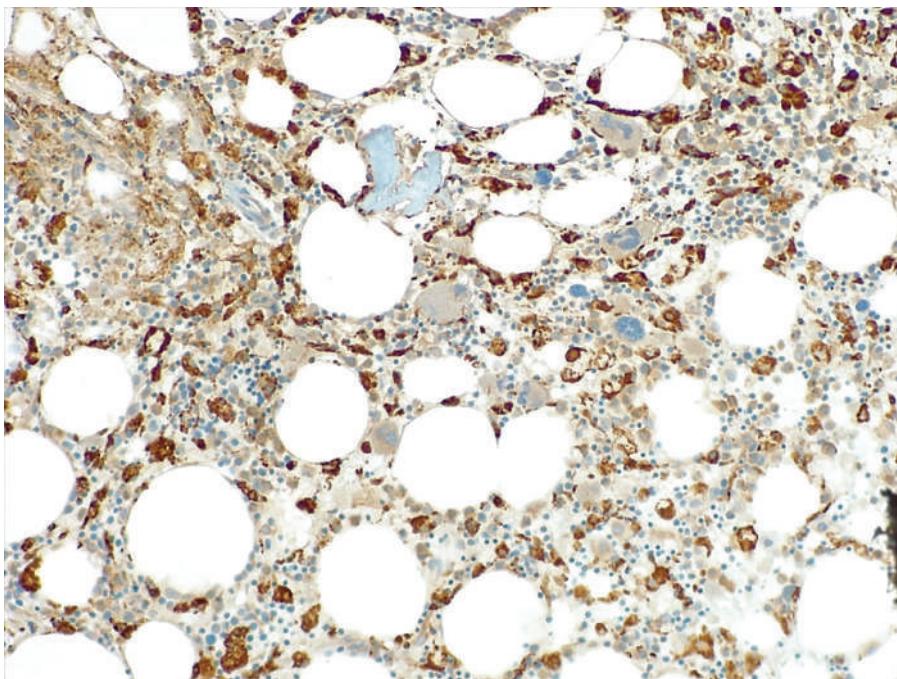
Valentina Conti<sup>1</sup>, Daniela Moruzzo<sup>2</sup>, Alessandro Pampana<sup>2</sup>, Beatrice Rosaia<sup>2</sup>, Guido Bianchini<sup>2</sup>, Alessandro Ginori<sup>3</sup>, Matteo Rotellini<sup>3</sup>, Anna Porcu<sup>4</sup>

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**Introduction:** Although SARS-CoV-2 lethality has been mainly associated with respiratory failure, it is now recognized the role of immune disregulation with macrophage activation and massive cytokine production (also known as “cytokine storm”), ultimately leading to multi-organ failure

**Case report:** Man, 85 year-old; Caucasian. Former smoker. Coexisting conditions: arterial hypertension, COPD, hypothyroidism. Good clinical conditions were reported, before hospital

admission. He was admitted to the Emergency Department (ER) for dyspnea; few days before he had tested positive for SARS-CoV-2 by nasopharyngeal swab (RT-PCR). At the ER, arterial blood gas analysis showed respiratory acidosis (pH 7.23, PaCO<sub>2</sub> 59 mmHg); blood tests showed leukocytosis (26'890/mcL, Neutrophils 23'280/mcL) with normal hemoglobin and platelet count; C-reactive protein was 14.8 mg/dL, serum creatinine was 1.28 mg/dL. A chest X-ray showed a right pneumothorax which required chest tube insertion before starting non invasive mechanical ventilation. The CT scan (performed before chest tube insertion), showed also bilateral ground glass opacities with some consolidations, and sparse, few cystic air spaces. In the following days, he developed kidney failure (creatinine max 4.14 mg/dL), and myositis (Myoglobin 7203 ng/mL, Ro52 positive, Uric Acids 19.3 mg/dL), despite progressive respiratory improvement which led to the discontinuation of mechanical ventilation and removal of the chest drain. Approximately ten days after admission, platelet count dropped (34'000/mcL). No clinical signs of new infection were present; blood culture were negative, procalcitonin was below normal limit; anti-platelets antibodies resulted not detectable; no evident bleeding was present, hemoglobin was stable; besides, respiratory conditions had improved in such a way that oxygen supplementation was discontinued. High dose steroids + Iv Immunoglobulins were started, with no improvement: platelet count kept dropping (16'000/mcL), whilst ferritin (1965 ng/mL) and IL6 (167 pg/mL) increased; in addition, total white cell count dropped (350/mcL). To reach a diagnosis, a bone marrow biopsy was then performed [image CD68 20X: hypoplasia and dysplasia affecting all three lineages; monocytes and macrophage infiltration, with foamy macrophages, is documented, leading to suspicion of hemophagocytosis]. Macrophage activation syndrome (also known as secondary hemophagocytic lymphohistiocytosis)



**Fig. 1.**

was diagnosed. Although steroid dosage was increased, general conditions worsened and few days later the patient died of multi-organ failure.

**Conclusions:** SARS-CoV-2 infection may cause a multi-organ involvement, urging the Respiratory Practitioner to consider all aspects of the disease when dealing with a patient with SARS-CoV-2 pneumonia.

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ID# 41

### An Updated Overview of Fatal Pneumothorax Case Series in COVID-19

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**Introduction:** Spontaneous pneumothorax was described as an uncommon COVID-19 complication.

**Objects:** We performed a retrospective review of 199 patients admitted to our COVID-19 semi-intensive care respiratory unit (SARS-CoV-2 infection confirmed by molecular testing) from October 2020 to March 2021.

**Methods:** Their mean age was 76, 53% males, 63.8% still alive at time of discharge. All of them underwent chest-X-rays, 47.2% with CT-scan. In 88.4% we observed bilateral lung consolidations, 7% having only the right lung involved at time of diagnosis. The 6% of our patients experienced spontaneous pneumothorax. 75% showed right pneumothorax, and 8% bilateral.

**Results:** 50% of pneumothorax patients were obese, 33.3% current or former smokers, 80% had a history of cognitive impairment, 80% had received non-invasive ventilation before pneumothorax. Blood chemistry showed 83.3% elevated LDH, 70% high ferritin, 75% high troponine, 91.7% high neutrophils/leukocyte rate, elevated CRP in 100%, high D-Dimer test (81.8%).

**Conclusions:** These findings are consistent with the possible mechanism of hyperinflammatory form associated with critical illness. The mean P/F of pneumothorax group at our unit admission was 132. Their mortality rose up to 83.3% ( $p < 0.001$ ). According to our experience, high-flow oxygen therapy may be a safer alternative to avoid the potential fatal occurrence of pneumothorax in COVID-19, but further researches are needed to lead to an early identification of risk factors for potentially fatal COVID-19 complications.

### Reference

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ID# 42

### Respiratory Rehabilitation Effectiveness in Idiopathic Pulmonary Fibrosis

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**Introduction:** In patients with Idiopathic Pulmonary Fibrosis (IPF), functional exercise tolerance and quality of life have been shown to be significantly decreased. Current IPF guidelines suggest only a weak recommendation for respiratory rehabilitation (1). However, to date, various studies have shown the effectiveness of rehabilitation programs in IPF patients.

**Objects:** The aim of this study is to evaluate this efficacy in terms of both strength tolerance and quality of life improvement.

**Methods:** The study population (15 patients, mean age  $77.6 \pm 9.7$ , 80% male, diagnosed with IPF for over 2 years, treated with antifibrotic medication) was divided into 2 homogeneous groups: the first underwent weekly rehabilitation treatment session for 2 months (case group-CaG), the second not (control group-CoG). Each patient of the 2 groups was subjected, both at the start and the end of study, to 6 Minutes Walking Test (6MWT), Dyspnea Borg scale, Fatigue Borg scale and spirometry. Only for CaG, Short Form36 Health Survey quality of life questionnaire (SF36) and clinical scales were proposed.

**Results:** A comparison of the 6MWTS, Borg scales and spirometry showed a significant improvement in CaG ( $p$ -value 0.04), instead CoG suffered a slight deterioration ( $p$ -value 0.01) at the end of study. The Borg scales did not report significant improvements, with the exception of Fatigue Borg scale in CaG ( $p$ -value 0.03). FEV<sub>1</sub> remained stable in CoG, while a statistically significant improvement ( $p$ -value 0.02) was seen in CaG. In the CaG, at the end of treatment, the SF36 questionnaire revealed physical/social activities and mental health improvements ( $p$ -value < 0.05), dyspnea amelioration in terms of mMRC ( $p$ -value 0.004) and BODE INDEX ( $p$ -value 0.03).

**Conclusions:** Through this study it has been seen that respiratory rehabilitation programs improve dyspnea and quality of life in IPF subjects, so it should not be considered as a last attempt in patients with severe respiratory impairment, but an essential part of IPF patient treatment.

### Reference

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ID# 43

## Idiopathic Pulmonary Fibrosis and Sleep Disordered Breathing

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**Introduction:** Sleep Disordered Breathing (SDB) represents an important comorbidity recognized by the ATS/ERS guidelines for the diagnosis and management of IPF. These disorders, often remain undiagnosed, are associated with reduced quality of life.

**Objects:** The aim of this study is to evaluate the incidence of SDB in IPF patients followed at our reference center.

**Methods:** 20 patients diagnosed with IPF for over 2 years, being treated with antifibrotic medication were included and underwent anamnesis collection, quality of life questionnaire (Short Form 36-item health survey, SF36) and polysomnography. The average age was  $70.4 \pm 5.9$  and 60% was men. The sample was stratified based on the presence and severity of SDB based on Apnoea/Hypopnoea Index (AHI) values.

**Results:** Through polysomnographic examination we obtained the following results (mean $\pm$ SD): Oxygen Desaturation Index (ODI)  $22.2 \pm 14.4$  events/hr, rate of sleep-time spent under 90% oxygen saturation (T90%)  $29.3 \pm 22.4$ , SpO<sub>2</sub> Nadir%  $74 \pm 10.9$ , mean SpO<sub>2</sub>%  $89.4 \pm 3.7$ , values of the Epworth scale (ESS) which measures daytime sleepiness  $5.6 \pm 5.1$ . In this study the presence of Obstructive Sleep Apnea (OSA) in subjects with IPF corresponds to 87.5%, of which 12.5% mild, 62.5% moderate and 12.5% severe. In addition, we found the presence of particular conformations of the face, expressed with the Mallampati Score, type III and IV in 87.5% of patients, which involves an approximately 2-fold increase in the risk of developing SDB. Physical limitations were observed through the SF36 questionnaire; the average scores of the 8 domains are quantitatively summarized as follows: physical functioning  $40 \pm 12.5$ , role limitations due to physical health  $37.5 \pm 14.4$ , pain  $47.8 \pm 16.7$ , general health  $33.5 \pm 11.1$ , fatigue  $64.4 \pm 22.2$ , social functioning  $53 \pm 19.4$ , emotional well-being  $65 \pm 17.4$  role limitations due to emotional problems  $49.9 \pm 13.9$  (maximum score for each domain equal to 100 in the absence of limitations or disabilities).

**Conclusions:** This study highlighted the importance of diagnosing and promptly treating sleep disturbances in patients with IPF to improve the symptoms and the quality of sleep and life, already partially compromised by the presence of a rare disease.

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ID# 44

## Pneumomediastinum and Spontaneous Retroperitoneal Bleeding in COVID-19: A Case Report

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**Introduction:** Coronavirus disease 2019 (COVID-19), caused by a new coronavirus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has resulted in a global pandemic. Patients usually present with respiratory symptoms and fever. However, two-third are asymptomatic and this has led to a management dilemma among physicians. As COVID-19 progresses, awareness of atypical complications of the disease increases. The study of COVID-19 uncommon complications is critical for the correct management of patients during hospitalization.

**Case report:** A 67-year-old man positive for SARS-CoV-2, with no significant comorbidities, non-smoker, and with no family history of bleeding and coagulation disorders presented to the Emergency Department of our institution with fever and dyspnea. The patient was admitted to the PNEUMO-COVID ward for hypoxemic respiratory failure. Chest x-ray demonstrated bilateral parenchymal consolidation. The patient was supported with a C-PAP helmet (PEEP 10 and FiO<sub>2</sub> 60%) and was treated with corticosteroids, antibiotics, and enoxaparin. Initial laboratory investigations revealed lymphocytopenia, increased neutrophils, lactate dehydrogenase, C reactive protein, D-Dimer, fibrinogen, all negative prognostic indices. On day 12 of hospitalization, the patient experienced worsening dyspnea accompanied by decreased PO<sub>2</sub> and elevated D-dimer. The chest CT angiogram examination excluded pulmonary embolism but reported pneumomediastinum. From this moment the patient was treated using 35% Venturi mask. The patient presented, also, a progressive decrease in hemoglobin, with a concomitant reduction in platelet count and an increase in white blood cells. Following sudden anemia and abdominal pain, the patient underwent an abdomen CT scan which showed an increase in the left psoas muscle volume due to the presence of a supplied hematoma that was in communication with another extensive hematoma with spreading of the contrast medium as from active bleeding. Another blood effusion layer was observed in the retro sacral area. The patient received radiological embolization of the left lumbar artery branch at the L3 level and the left inferior epigastric artery. Following embolization, the patient's hematological parameters improved, and the abdomen CT scan showed no active bleeding.

**Conclusions:** Handling cases with unusual presentation requires a careful approach. The study of uncommon clinical presentations of COVID-19 is of extreme importance, not only to ensure an accurate and early diagnosis but also for the correct and appropriate management of COVID-19 patients during hospitalization.

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**ID# 45**

### **Opportunistic Infection in COVID-19: Stafilococcus Aureus and Herpes Simplex**

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**Introduction:** In SARS-CoV-2 infection the presence of immunosuppression it's frequent (for the use of steroids and also for the disease itself) and so it's possible the onset of opportunistic infections.

**Case report:** Woman 45 years old, housewife, no smoker, without any prior disease. She reported the beginning of symptoms (fever, myalgia and rhinorrhea) the 2nd of December with positive molecular pharyngeal swab for SARS-CoV-2. Persistence of positive swab without symptoms after 21 days. Hospitalization 05th of february for herptic stomatitis with neck's soft tissues edema. Pharyngeal swab still positive for SARS-CoV-2. The Chest CT scan shown: "multiple nodules with widespread distribution, diameters range from few to 40 millimeters, most of that with reversed halo sign". The blood test shown an increase of inflammation indexes and lymphopenia (linf: 310). We started an empiric therapy with doxiciclin, piperacillin/tazobactam and diflucan and also an anti-viral therapy (acyclovir). We collected other specimen with the following results: - HIV: negative, - serum beta D glucan and galatctomannan (both negative), - blood culture (positive for S.aureus MSSA; the same bacterium was find in the sample

collected through bronchoscopy). After 15 days she had an improvement of symptoms and of lymphopenia (linf 990). The patient was transferred in the department of internal Medicine to continue therapy and diagnostic tests. The CT scan after 1month shown: reduction of edema of neck's tissues, reduction of number and diametres of nodules, basal fibrotic bands.

**Conclusions:** The possible onset of opportunistic infection in patients affected from COVID-19 should be take into account even after months. For this reason it's mandatory a follow-up in all patients, even those with mild symptoms.

### **Reference**

Cusumano JA, et al. Open Forum Infect Dis 2020;7:ofaa518.

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**ID# 46**

### **Long Coronavirus Disease 2019 and Remdesivir**

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**Introduction:** Long term Coronavirus disease-19 (COVID-19) is a syndrome, affecting 20% of Covid patients. The main symptoms, lasting more than 12 weeks after the onset of acute COVID-19,



**Fig. 1.**

are the following: fatigue, breath shortness, chest pain, arthralgia, myalgia, sleep disorders, hair loss, decline in memory, headache. Long COVID-19 is caused by inflammatory cellular damage, due to the infection and as a result of post-critical illness. Remdesivir is an antiviral medicine indicated for treatment of COVID-19. It is indicated in hospitalized patients (aged 12 or over and weighing at least 40 kg) with pneumonia requiring low flow oxygen at the start of treatment.

**Objects:** To verify the effect of Remdesivir in long COVID syndrome.

**Methods:** We evaluated 60 patients hospitalized because of COVID-19 pneumonia, in Venturi mask with FIO<sub>2</sub> averaging 40% (range 24%-60%). Their median age was 59 years (range 41-75), 60% were male, 70% had comorbidities (obesity, diabetes mellitus, ischemic heart disease, systemic arterial hypertension, fibrillation atrial). The median chest CT score was 12/20 (range 5-18). In the first group 30 patients received Remdesivir therapy (200 mg the first day and 100 mg per day for other 4 days), together with methylprednisolone, enoxaparin, N-acetylcysteine. In the second group 30 patients were treated with the same drugs except Remdesivir. We used a questionnaire to investigate the respiratory support on admission, the type of hospital therapy, the discharge from the hospital and post-covid symptoms (fatigue, fever, coughing, sleep disorders, chest pain, headache, diarrhea, lack of concentration, excessive sweating, lack of appetite, shortness of breath, myalgia, arthralgia, depression, skin rash, loss of weight, taste, smell and hair, decline in memory, tachycardia, conjunctivitis).

**Results:** All patients completed the therapy and healed. Most of them complained of a mild long COVID syndrome for some months. In the first group (treated with remdesivir) the symptoms were the following: 33% fatigue, dyspnea, 30% decline in memory, arthralgia, myalgia, 15% hair loss, 10% headache, sleep disorders. In the second group (treated without remdesivir) 33% of patients had fatigue, 25% dyspnea, decline in memory, 16% arthralgia, myalgia, 10% hair loss, headache, sleep disorders. People of both groups reported the same symptoms, without significant difference between the two groups. A study with a larger population sample would be required.

**Conclusions:** Remdesivir therapy is an effective treatment in patients with COVID-19 pneumoniae and is well tolerated, but in our experience there are not significant difference in long COVID syndrome in patients that received remdesivir therapy.

## Reference

Sisò-Almirall A, et al. Int J Environ Res Public Health 2021;18:4350

ID# 47

## A Pilot Study on Using SuperDimension when Performing Cryobiopsies

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**Introduction:** Transbronchial cryobiopsies has become increasingly important in the diagnostic workup for interstitial lung diseases. The rate of complications and mortality are low compared to surgical lung biopsies, but the diagnostic yield is not as high (75-85% vs. 90-98%). The reason for the lower diagnostic yield could in some cases be explained by biopsies taken too central or in less affected areas of the lungs. In this pilot study we wanted to examine the feasibility of using the electromagnetic navigation system, superDimension (SD), when performing cryobiopsies to increase the diagnostic yield.

**Objects:** In this pilot study we wanted to examine the feasibility of using the electromagnetic navigation system, superDimension (SD), when performing cryobiopsies to increase the diagnostic yield.

**Methods:** Electromagnetic navigation bronchoscopy and cryobiopsies were performed using SD system (ver.7.0, Medtronic Inc.) consisting of an electromagnetic board (Locatable BordTM, Medtronics, MN, USA) placed on the back of the patient and a position sensor at the tip of the navigational probe which is introduced into the airways through an extended working channel and guided by a real-time 3D reconstruction of previously acquired computer tomography images. The procedure was performed with the patients in general anesthesia using a rigid bronchoscope when performed in Careggi University Hospital, Florence, Italy and with a flexible bronchoscope trough an orotracheal tube when performed in Aarhus University Hospital, Aarhus, Denmark.

**Results:** In total, 11 patients were included (Florence: 5 patients, Aarhus: 6 patients). In addition, SD was not possible in three other patients due to severe fibrosis or mismatch between the navigation system and the bronchial tree. Disposable cryoprobes, size 1.7 mm, were used in Aarhus, and reusable cryoprobes, size 1.9 mm in Florence. Pneumothorax was detected in two of the 11 patients (18%). Mild hemorrhage was seen in one (9%) and moderate hemorrhage in five (45%). The biopsies contributed to the diagnosis in 9 of the 11 patients (82%). The final diagnoses were idiopathic pulmonary fibrosis: 2, hypersensitivity pneumonitis:2, smoking related interstitial lung disease: 2, scleroderma associated interstitial lung disease:1, middle lobe syndrome: 1, cryptogenic organizing pneumonia:1, fibrotic nonspecific interstitial pneumonia:1 and unclassifiable interstitial lung disease: 1.

**Conclusions:** Using superDimension when performing cryobiopsies is feasible. A larger randomized, controlled, single blinded trial is necessary to homogenize the technique between centres and to evaluate the diagnostic yield and complications.

**Table 1.**

Number of patients (F/M)	Aarhus 6 (2/4)	Florence 5 (2/5)	Total 11
<b>Age, median (range)</b>	67.5 (55-80)	65.8 (57-74)	65.8 (55-80)
<b>Number of biopsies</b>	3,5	3,8	3,6
<b>Site of biopsies</b>			
-Right upper lobe	2	0	2
-Right middle lobe	1	2	3
-Right lower lobe	2	3	5
-Left lower lobe	1	0	1
<b>Pneumothorax</b>	0	2 (40%)	2 (18%)
<b>Hemorrhage</b>			
-Mild	1 (17%)	1 (20%)	2 (18%)
-Moderate	4 (67%)	1 (20%)	5 (45%)
<b>Contribution to diagnosis (%)</b>	4 (67%)	5 (100%)	9 (82%)
<b>Diagnosis</b>			
- Idiopathic pulmonary fibrosis	0	2	2
- Hypersensitivity pneumonitis	2	0	2
- Smoking related ILD	1	1	2
- Cryptogenic organizing pneumonia	1	0	1
- Nonspecific interstitial pneumonia	1	0	1
- Middle lobe syndrom	0	1	1
- Scleroderma ILD	1	0	1
- unclassifiable ILD			

**ID# 48****Serum Levels of Surfactant Protein-B (SP-B) as biomarker in IPF and ILD-SSc**

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**Introduction:** ILDs are often accompanied by histopathological evidence of alterations in alveolar type 2 cells (AECsII) deputed to the production of surfactant. Surfactant is a phospho-lipo-protein surfactant complex that coats the alveoli. The protein component consists of 4 types of proteins SP-A,B,C and D that can be assayed.

**Abstracts**

**Objects:** The aim of the study is to analyze the possible association between the serum levels of SP-B in patients with Idiopathic Pulmonary Fibrosis (IPF) and Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD) and the severity of these diseases.

**Methods:** 34 patients were enrolled: 14 with diagnosis of IPF and 20 with diagnosis of SSc-ILD. 10 healthy subjects, smokers, were included as healthy controls. All patients underwent a blood samples collection for quantitative analysis of SP-B levels using specific ELISA kit, pulmonary function test, 6mwt, ABG, chest HRCT (We adopted the Visual score as severity index).

**Results:** SP-B values were significantly higher in the ILD group than in the control group, and significantly higher in the SSc group than in the IPF group. In the IPF group we observed a direct correlation between the SP-B levels and the values of pulmonary function tests. In particular, we showed that the higher the SP-B values, the more respiratory function was preserved. On the other hand, an inversely proportional correlation has been demonstrated between SP-B and the CPI, GAP index, and the Visual Score of fibrosis at chest HRCT: a higher degree of fibrosis corresponds to lower blood concentrations of SP-B.

**Conclusions:** We assume that SP-B may be a marker of alveolar damage but that serum levels are higher in the early stage of IPF, since the alveoli, in which it is produced, are not yet fibrotic and do not result devoid of AECs II. On the contrary, these levels are lower in the advanced stage of the disease, precisely because of the progressive damage of the alveolar epithelium and the consequent subversion of the lung parenchyma with reduced respiratory performance. In summary, in the advanced stages of disease, due to apoptosis, cellular senescence, EMT, bronchiolization, and metaplasia, there is a subversion of the lung parenchyma with fibrotic replacement, reduction in the number of AECs II, and then production of SP-B. In patients with ILD-SSc, SP-B levels are higher than in IPF but there is no correlation with respiratory function tests and radiological scores. This finding might reflect different mechanisms leading to a restrictive lung disease.

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Papaioannu AI, et al. PLoS One 2016;11:e0157789.

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ID# 49

## A Special Case of Bronchiectasies – the Mounier-Kuhn Syndrome

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**Introduction:** Mounier-Kuhn Syndrome or tracheobronchomegaly is characterized by enlarged trachea and principal bronchi and is present in clinical and prognostical variety, sometimes associated with connective tissue disease (Ehlers-Danlos, Marfan and Cutis Laxa). Cigarette smoking and air pollution may act as irritating factors. No prevalence is actually known. Symptoms vary from minor as cough, to major, with respiratory tract infections of variable severity and recurrent cough, probably as a result of stagnation of secretions in the bronchial tree due to atrophy of the inner part of trachea and main bronchi. Diagnosis is made by chest CT scan and bronchoscopy, complete Spirometry measurements are useful but not diagnostic. The radiodiagnostic criterion is a diameter of the trachea greater than 3 cm: this is usually measured 2 cm above the aortic arch and bronchial diameters of 24 mm (right), and 23 mm (left).

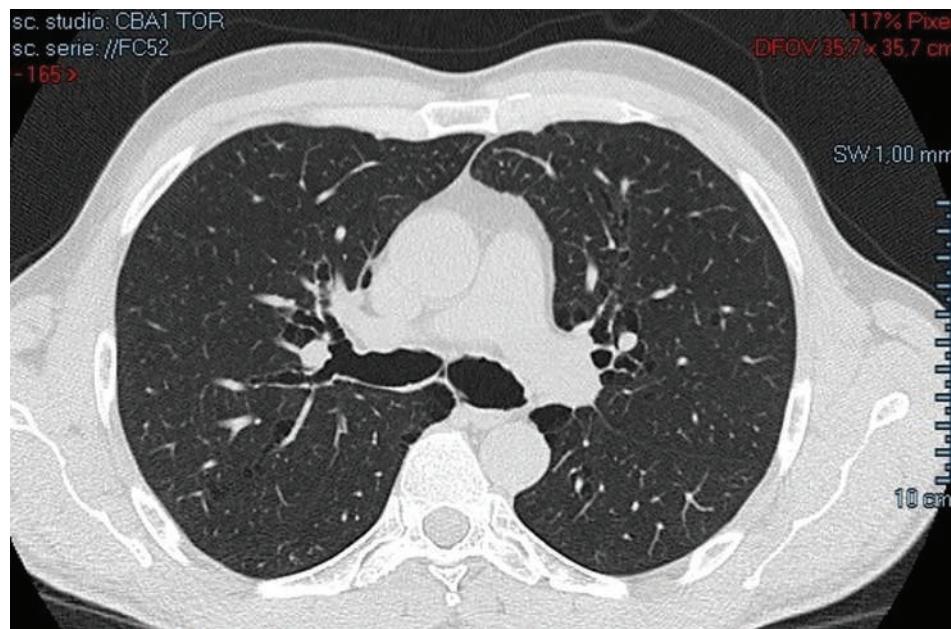
**Case Report:** A 52 year old man, familiarity for bronchial asthma. Former smoker (25 P/Y), no professional exposure. Frequent episodes of bronchitis since infancy, a recent left pneumonitis. Comorbidities: gastroesophageal reflux with hiatal herniation, chronic sinusitis and allergic rhinitis (grass sensitivity).

First presentation with fever, cough without expectoration, treated with broad spectrum antibiotics. The diagnostic Chest CT revealed paraseptal emphysema and bronchiectasis, as well as the characteristic radiological criteria (see above), with an indented aspect of the final tract of trachea and main bronchi. Spirometry revealed moderate obstruction (FEV<sub>1</sub> 66%), normal total lung capacity and mildly increased residual volume. The image shows a characteristic feature Bronchoscopy evidenced large and malacic bronchial walls with a rich net of submucosal capillaries, ectatic bilateral bronchi, but no microbiological significant secretions. Differential diagnosis were excluded (Ehlers-Danlos, Cutis Laxa, Meconium aspiration Syndrome and others). The patient was treated as well with physiokinetic exercises for lung clearance and bronchodilatation and is well since. Treatment recommendations include treatment of bronchial infection to prevent complications and frequent cycles of physiokinetic therapy, postural drainage. Acute exacerbations are treated with antibiotics. In rare cases, tracheal stenting has been used.

**Conclusions:** Since the Mounier-Kuhn Syndrome might easily be overlooked, diffusion of diagnostic aspects and standardisation of the radiologic criteria can help identify the pathogenesis, genetics and epigenetic contributions. The recognition of the syndrome will help individualize and evaluate the optimal treatment as well as the prevention of complications.

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**Fig. 1.**

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ID# 50

## Accuracy of Multidisciplinary Diagnosis of COVID-19 Using BAL as Gold Standard

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Carlo Nozzoli<sup>5</sup>, Loredana Poggesi<sup>5</sup>, Venerino Poletti<sup>6</sup>,  
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**Introduction:** The sensitivity of the nasal swabs is low and false-negative results may worsen both the spread of the outbreak, due to inappropriate allocation of patients, and the prognosis of patients, due to inappropriate and/or delayed treatment. To the best of our knowledge, to date no study has investigated the diagnostic accuracy of a multidisciplinary team (MDT, i.e. pulmonary physician and thoracic radiologist) diagnosis of COVID-19 in suspected cases with negative nasal swabs that underwent subsequent BAL.

**Objects:** The aim of this study was to evaluate the accuracy of the MDT diagnosis of COVID-19 in suspected cases not confirmed by nasal swabs, compared to BAL (that for the purpose of this study was considered the diagnostic gold standard).

**Methods:** Here we present the interim analysis of a study developed as a part of a wider international research project: the Dragon project (IMI2 - Call 21; Grant agreement number 101005122). This pilot study is a multi-center, retrospective, observational study, but interim analysis here presented is limited to a single center (Florence University Hospital). All consecutive patients admitted for suspected COVID-19 that resulted negative to two consecutive nasal swabs underwent BAL. MDTs with different expertise levels were asked to provide a provisional diagnosis (up to three choices allowed), confidence levels and management decision (patient allocation and treatment) after reviewing clinical, HRCT and BAL data in a stepwise fashion.

**Results:** We enrolled 86 patients, median age 63 years (range 19-90), 52 males (60.5%), 50 (60%) current or former smokers. 83 (95%) patients had one or more comorbidities (median 3, range 1-10; Charlson CI 4.6, 0-11). BMI 24.3 (14.3-24.5), P/F 295 (76-547). Only 7 cases were found positive on BAL (8.4%). For the MDT1 sensitivity, specificity, positive and negative predictive value were respectively: 28% (2/7), 60% (48/79), 6% (2/33), 90% (48/53). For the MDT2 (younger) sensitivity, specificity, positive and negative predictive value were respectively: 57% (4/7), 81% (64/79), 21% (4/19), 95% (64/67). The concordance between the two MDTs was poor: 60% of cases, with a kappa of 0.09 (SE 0.1).

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## Abstracts

**Conclusions:** The negative predictive value of a MDT diagnosis of COVID-19 is high irrespective of expertise level of the MDTs. However the sensitivity and the positive predictive value are miserable and the inter-observer variability is strikingly high. Therefore, BAL has a relevant role in confirming COVID-19 infections even if the proportion of positive cases is very small.

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ID# 51

## A Multicenter Study of Post-COVID-19 Interstitial Lung Syndrome

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**Introduction:** Available data indicate that a large minority of patients with COVID-19 develop ARDS, and pulmonary fibrosis is a recognized sequela of ARDS. However, the long-term pulmonary consequences of COVID-19 remain speculative.

**Objects:** The aim of this study is to evaluate risk factors, prevalence and characteristics of POST-COVID-19 interstitial lung changes, with the unique opportunity to evaluate radiologic and pathologic correlations using HRCT and transbronchial lung cryobiopsy specimens.

**Methods:** Here we present the preliminary data on HRCT features of POST-COVID-19 ILD. Data were collected at the time of the first interim analysis (28/11/2020) of the PCOILS trial: a prospective, multicenter national study involving 12 Italian centers (Fig 1). We collected data of consecutively hospitalized patients at baseline and then at 6 (+/-) months after hospital discharge. HRCT changes at 6 months involving more than 5% of the total

lung volume were considered significant. Patients with significant HRCT changes will undergo BAL and/or cryobiopsy and a subsequent follow-up with HRCT and lung function evaluation at 12(+/-1) and 18 (+/-1) months.

**Results:** At the time of the present interim analysis, 524 patients from 9 centers were enrolled (enrollment is still ongoing and will end on January 31st, 2021). Median age was 67 years (range 18-87), 330 were males (62.9%). HRCT changes were detected in 333 participants (63.5%), and in 219 (41.7%) were considered significant. 118 cases (22.5%) showed fibrotic changes including the following HRCT patterns: 7 (1.3%) probable UIP, 45 (8.5%) NSIP (with or without OP), 38 (7.2%) indeterminate, 28 (5.3%) fibrotic consolidations. Among the remaining 101 (19.2%) non fibrotic cases the radiologists described: 11 (2%) NSIP-OP, 15 (2.8%) indeterminate, 67 (12.7%) pure ground glass, 8 (1.5%) consolidations all suspected for lung cancer.

**Conclusions:** This preliminary analysis confirms that after COVID-19 infection a large minority of patients develops interstitial lung changes mostly with NSIPOP, indeterminate features or ground glass. The hypothesis that post-COVID-19 interstitial changes and interstitial lung diseases may share common risk factors, pathogenetic mechanisms and disease behaviour warrants further evaluations.

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ID# 52

## Lung Cancer and Pulmonary Langerhans Cell Histiocytosis: A Case Report

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**Introduction:** Pulmonary Langerhans cell histiocytosis (PLCH) is a diffuse lung disease that usually affects young adult smokers (1). The prognosis is usually good, and smoking cessation is the main therapeutic measure. Lung adenocarcinoma is the most common lung cancer, with an often poor prognosis, particularly in advanced forms (2). For both of these diseases, diagnostic certainty is histological. In this report we describe the case of a patient with lung adenocarcinoma (stage IVb) with associated pulmonary Langerhans' cell histiocytosis.

**Case report:** Patient aged 60 years, male, previous moderate smoker, owner of a knitting company. No known allergies, no family history of pulmonary disease. In home therapy with cardioaspirin for left carotid stenosis. Patient in good general condition until January 2021 when, due to the onset of dyspnoea and coughing, he underwent radiological investigations. A CT scan of the chest showed diffuse cystic formations of irregular morphology, thickened walls, associated with solid nodular opacities as well as the presence of solid neoformation at the right hilar site infiltrating the upper and lower right bronchial branches with atelectasis of the middle lobe parenchyma. The patient then completed radiological diagnostics with CT scans of the brain and abdomen. At encephalic level, lesions compatible with metastasis were found. Respiratory



**Fig. 1.**

function tests showed mild restrictive deficit and a moderate reduction in alveolar-capillary diffusion. The patient was evaluated in the interventional pneumology outpatient department of Careggi Hospital in Florence. A diagnostic bronchoscopic procedure was planned. Bronchoscopic inspection showed a sleeve-like stenosis of the right middle and upper lobar bronchus. Bronchoalveolar lavage was performed to the right lung lower lobe for cytological, microbiological and immunological samples. Subsequently, transbronchial biopsies were taken from the anterior segment of the right upper lobe and cryobiopsies from the lateral segment of the right lower lobe.

**Conclusions:** Histological results confirmed the suspicion of pulmonary Langerhans cell histiocytosis and detected the presence of lung adenocarcinoma with 70% PDL-1 expression.

## References

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### ID# 53

#### **COVID-19 Related ARDS: Helmet CPAP Treatment in RICU**

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**Introduction:** The SARS-CoV-2 outbreak spread in Lombardy Region (Italy) rapidly saturating intensive care unit beds, forcing the application of noninvasive respiratory support in respiratory intermediate care unit (RICU).

**Objects:** We aimed to analyze the effects of helmet continuous positive airway pressure in COVID-19-related acute respiratory distress syndrome in RICU. The primary outcome was CPAP failure, defined as the occurrence of either intubation or death due to any cause during RICU stay; the secondary one was the identification of factors related to patients' prognosis.

**Methods:** 150 consecutive patients with acute respiratory distress syndrome due to COVID-19 and referred to Vimercate Hospital (MB) between March and May 2020 were enrolled. All patients were treated with helmet continuous positive airway pressure. Demographics, clinical and laboratory tests and blood gas analysis were collected.

**Results:** Patients in the study had a mean (SD) age of 62 ( $\pm$  11) years. The worst  $\text{PaO}_2/\text{FiO}_2$  ratio during continuous positive airway pressure stratified the subjects in mild (26/150), moderate (39/150) and severe (85/150) acute respiratory distress syndrome.

Most of patients were treated with systemic corticosteroids (79%). 93 patients (62%) were successfully treated while 57 (38%) failed; of the latter, 32 patients were transferred in the intensive care unit to receive invasive mechanical ventilation. Dimer test and ferritin at admission, use of steroids, P/F in oxygen at admission and age were independently associated with CPAP failure. The severity of acute respiratory distress syndrome and the use of steroids strongly correlate with clinical outcomes. Mortality rate in our cohort of patients was 28%.

**Conclusions:** The application of helmet continuous positive airway pressure in RICU and the administration of corticosteroids in COVID19-related ARDS are associated with satisfactory clinical outcomes.

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### ID# 54

#### **Morphological Aspects of Pulmonary Nocardiosis**

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**Introduction:** Nocardia is an opportunistic pathogen that most frequently affects the lungs. Pulmonary nocardiosis (PN) is an uncommon but potentially life-threatening infection. PN typically occurs in patients with cell-mediated immunosuppressive conditions, but infection may occasionally develop in immunocompetent patients as well. The pathological manifestations of nocardiosis are described as pyogenic or necrotic changes, and the typical pathological feature is suppurative necrosis with abscess formation; therefore, low density areas or cavities often appear in the lung.

**Objects:** The aim of this study was to describe the pathologic features of pulmonary nocardiosis, focusing on possible novel or under reported features.

**Methods:** Retrospective revision (2014–2021) of pathological specimen from lung biopsies, along with clinical and radiological evaluation of PN patients seen at 2 referral university hospitals in Italy (Florence and Forlì).

**Results:** Seven patients were included in this study, 4 women and 3 men, median age 59 years. Nocardia was detected in 2 cases by CT-guided needle biopsy, in 4 cases by transbronchial lung cryobiopsy and in 1 case by bronchoalveolar lavage. In 4 cases, BAL was negative, and subsequent biopsy positive. Major risk factors

**Table 1.**

	Age	Sex	Cent er	smoking status, P/Y	Comorbidity	PFT	BAL, microbiology	Nocardia Species	Biopsy	Anatomy Pathological
1	58	M	FO	Non smoker	None	FEV1 96%, FVC 91%, DLCO 61%	Positive	Abscessus	CR	OP
2	48	F	FO	Former smoker	Tuberculosis	FVC 81%, FEV1 78%, DLCO 37%	Not performed	Abscessus	CT guided Biopsy	OP
3	70	F	FO	Former smoker	None	FVC 105%, FEV1 86%, DLCO 51%	Positive	Abscessus	CR	bronchiolitis
4	69	F	FO	Non smoker	None	Not performed	Positive	Abscessus	Not performed	Not performed
5	77	M	FO	Former smoker	Diabetes mellitus 2	Not performed	Positive	Abscessus	CR	OP
6	72	M	FO	Former smoker	Tuberculosis	Not performed	Not performed	Beijingensis	CT guided Biopsy	OP
7	42	F	FL	Non smoker	None	FEV 121%, FVC 100%, DLCO 100%	negative	Not specified	TBB	peribronchial lymphoid infiltrate.

CR: cryobiopsy; F: female; FO: Forlì; FL: Florence; M: male; OP: organizing pneumonia

PFT: pulmonary function test S : former smoker; TBB : transbronchial biopsy

for PN were smoking and previous tuberculosis; all patients were apparently immunocompetent (as defined by normal WBC, Ig tests, no immunosuppressive drug). The most common species found was Nocardia abscessus (5 cases of 7, 71%), 1 case of Nocardia beijingensis and in 1 case is not specified. The most frequent anatomopathological pattern was organizing pneumonia (4 cases of 6, 66%), 1 bronchiolitis (mixed fibrotic and cellular) and e 1 peribronchial lymphoid infiltrate.

**Conclusions:** Our findings on the pathological aspects of pulmonary nocardiosis differ significantly from the literature, in fact we found in 66% of cases organizing pneumonia and other features suggestive of a possible underlying immune-mediated mechanisms not yet identified.

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### ID# 55

#### Our Experience with Lung Ultrasound in the Evaluation at Home of SARS-CoV-2 Pneumonia

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**Introduction:** Lung ultrasound (LUS) is a non-invasive bedside technique that is used to diagnose interstitial lung syndrome. In the last months it has rapidly become a tool for assessment of patients affected by COVID-19. LUS could be useful, being performed at several time points from clinical diagnosis, in

determining early lung involvement during the paucisymptomatic and to monitoring and follow up (1). In fact, thanks to its capability to provide information in real time and its portability, safety, and wide availability, LUS has been suggested to be a valuable tool in a wide variety of settings.

**Objects:** We aimed at evaluating presence of lung injury through the use of LUS in a population with paucisymptomatic COVID-19 infection (fever, cough, shortness of breath or difficulty breathing, tachypnoea) at home, in the early days of infection (within 10 days of positivity of the nasal swab).

**Methods:** We synthesized categorical variables as mean and standard deviation (SD). To study linear relation between the variables it is used the Pearson's correlation coefficient. The subjects considered positive to LUS were those with non-coalescent B-lines in > 3 in each area, those with coalescent B-lines as well as those with subpleural consolidations (2). The parameters analysed at home were: respiratory rates (RR), pulse oximeter ( $\text{SpO}_2$ ), national early warning score (NEWS), and nadir of  $\text{SpO}_2$  during 6 min walking test (6' WT).

**Results:** 55 patients were studied (33 females): mean age was  $55.36 \pm 6.2$  yrs, mean RR was  $16.6 \pm 1.5$  mean  $\text{SpO}_2$  was  $97.6 \pm 1.18$ , NEWS was 0-1, mean nadir of  $\text{SpO}_2$  during 6 min was  $94.1 \pm 1.29$ . 65% had LUS signs of pulmonary injury and the mean of point is  $4.2 \pm 4.6$  (normal value < 1); there was no significant correlation between mean  $\text{SpO}_2$  or nadir of  $\text{SpO}_2$  during 6'WT and LUS score instead exists a significant correlation between RR and LUS signs (p value 0.001).

**Conclusions:** LUS is powerful tool for diagnosis and is an excellent modality to complement the quality of traditional physical examination. In our study, the use of LUS has helped us in clinical evaluation and it allowed us to diagnose early and at patient's home the pneumonia during infectious of COVID-19.

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**ID# 56**

## Dipalmitoylethanolamide Treatment in COVID-19 Pulmonary Fibrosis

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**Introduction:** Pulmonary involvement from COVID-19 is almost constant; also in many patients recovered from the acute phase (interstitial pneumonia) respiratory symptoms and signs persist (dyspnoea, cough, desaturation, respiratory insufficiency) and pneumonia leads to interstitial disease (ground-glass) and from here to pulmonary fibrosis (honey comb).

**Objects:** Propose a therapy for symptomatic pulmonary fibrosis after COVID-19: dyspnea on exertion and at rest during supine recumbency. In these patients there is a decrease in the residual volume on plethysmographic tests and persistence of low DL<sub>CO</sub> values. Chest CT scan shows the evolution of interstitial disease from ground glass to pulmonary fibrosis, with honeycomb pictures, bronchiectasis and fibrotic shoots in areas of previous major activity. In these we proposed a cycle with dipalmitoylethanolamide (PEA) in addition to the steroid.

**Methods:** All outpatients referred by the treating clinicians for urgent pulmonological evaluation underwent HR chest CT, with evidence of pulmonary fibrosis. Respiratory function study with global spirometry, DL<sub>CO</sub> and plethysmography. In addition to pharmacological therapies in case of reduction of small pathways, long-acting beta 2 agonist bronchodilators (LABA), antimuscarinics (LAMA) are proposed in former smokers and with known COPD, in case of reduction of DL<sub>CO</sub> inhaled steroids (ICS). In case of fibrosis and honeycomb treatment, treatment with PEA: 600 mg BD for 10 days then continue with 600 mg day for another 30 days.

**Results:** 265 outpatients, average age 62.2 years, 121 women, 144 men, who arrived with an urgent request from the general practitioner, for a pneumological visit and treated on an outpatient basis. Of these 15 were placed on PEA therapy. Of these 15, 6 women and 9 men aged 65, 68: completed the cycle with PEA, the pre-treatment DL<sub>CO</sub> values 64% and post-treatment 83%. Pulmonary lesions on chest CT showed no changes.

**Conclusions:** Monitoring with DL<sub>CO</sub> shows progressive improvement of the values after treatment with PEA, also the values of Interleukin 6 showed normalization. Treatment with PEA associated with ICS and/or LABA/LAMA improves diffusion capacity and therefore respiratory function in COVID-19 post-interstiopathy pulmonary fibrosis. All patients showed subjective improvement with disappearance of dyspnea. PEA may reduce the

mastocyte activity of the lung interstitium, If this data were confirmed, it could be used already in the early stages of the cytokine response.

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**ID# 57**

## Co-Infections Identified by Broncho-Alveolar Lavage (BAL) in COVID-19 Patients

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**Introduction:** This is a substudy of a prospective multicenter study European project DRAGON: The RapiD and SecuRe AI enhAnced DiaGnosis, Precision Medicine and Patient Empwerment Centered Decision Support System for Coronavirus PaNdemics. This is multicenter observational study which objective is to improve the diagnosis of COVID-19 in patients at risk.

**Objects:** Identify coinfections and treat them with target therapy to improve patient outcomes.

**Methods:** The study involves hospitalized patients at Careggi University Hospital. All patients admitted for confirmed COVID-19 by nasal swabs RT-PCR underwent microbiological analysis and immunophenotyping on bronchoalveolar lavage, prior execution to Chest HRCT (High Resolution Computed Tomography).

**Table 1.**

	Age	Gender	P/F	Microbiological Agent 1	Copies	Microbiological Agent 2	Copies
1	89	M	<100	E. Coli	60000	Proteus Mirabilis	30000
2	45	M	200-300	S.Aureus	>10000 0		
3	54	M	200-300	S.Aureus	50000		
4	61	F	200-300	K. Pneumoniae	30000		
5	51	M	200-300	P. Jirovecii	40000		
6	80	M	200-300	A.Baumanii	>10000 0		
7	71	M	100-200	K. Pneumoniae	60000		
8	82	M	<100	HSV1	90000	Candida Albicans	40000
9	68	M	>300	H. Influenzae	>10000 0		

**Results:** Within this study, 41 BAL of patients admitted to COVID-19 wards were performed. The cohort of patients analyzed consisted of a median age of 56 years, 33 men and 8 women; with heterogeneous severity indices 2 with  $\text{PaO}_2/\text{FiO}_2$  (P/F) <100, 6 with P/F 100-200, 17 with P/F 200-300, 13 with P/F >300). Co-infection was detected in 9 of 41 patients (22%), in 2 cases of the 9 with two different microbial agents (Table 1. case 1 and case 8). The most frequent coinfections were Haemophilus Influenzae (2 of 9 cases) and Klebsiella Pneumoniae (2 of 9 cases). One case of Herpes Simplex reactivation. Analysis of patient immunophenotyping are still ongoing. Moreover, we observed that 7 of the 41 patients with initial positive nasal swabs, tested negative at repeated nasal swabs at the time of bronchoscopy, but positive on BAL.

**Conclusions:** According to literature our study confirms the presence of bacterial coinfections in a significant minority of COVID-19 patients.

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### ID# 60

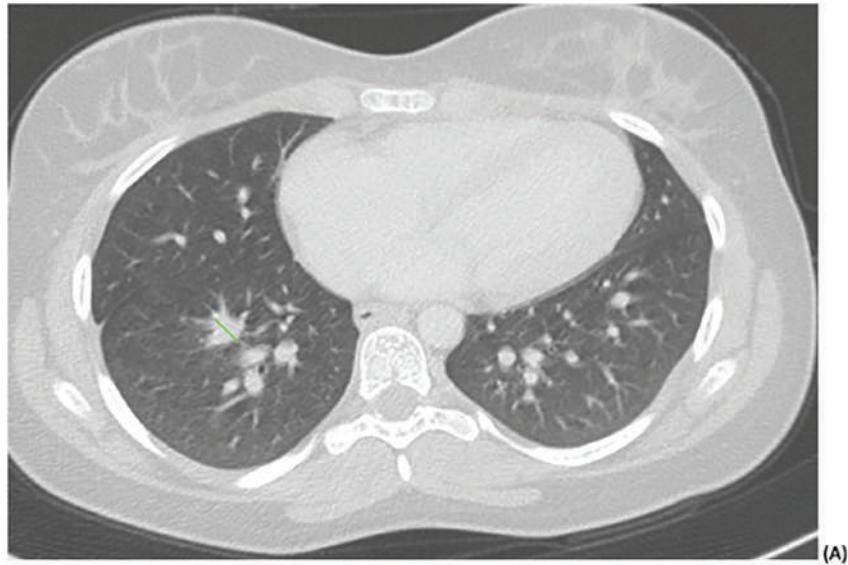
## Combination of Ultrathin Bronchoscope, EBUS and Cryobiopsy 1.1mm for Rare Lung Tumor's Diagnosis

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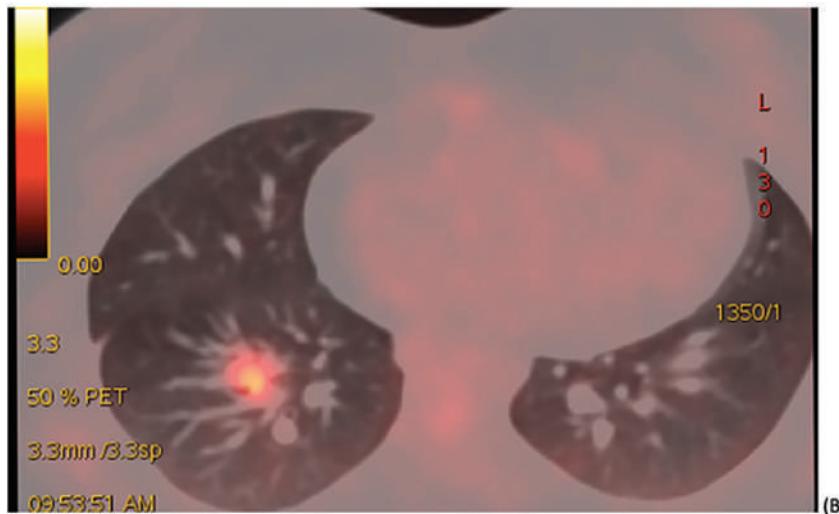
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**Introduction:** Diagnosis of a rare Inflammatory Myofibroblastic Lung Tumor in a pediatric patient through innovative technique combined with Olympus ultrathin bronchoscope (3 mm), Olympus radial EBUS (Endo Bronchial Ultra Sound) mini-probe, and cryobiopsy 1.1 mm.

**Case report:** Patient (f) aged 14 with mute past medical history. For about 1 year, iron deficiency anemia, treated with martial therapy. In this context FOBT (Faecal Occult Blood Test) research, Helicobacter pilory antigen, screening for celiac disease, and functionality thyroid are performed with negative results. Repeated episodes of haemoptoe. Chest CT (Computed Tomography) scan (Image A) shows a nodule, 18x13 mm, with spiculated contours in the antero-basal segment of the RLB (Right Lower Lobe) and an adjacent large "ground-glass" area and nodules ground-glass satellites; two nodules in the dorsal segment of the right upper lobe, 8 mm and 5 mm each; a 6 mm nodule subpleural in the right lower lobe. At fluorodeoxyglucose-PET (Positron Emission Tomography) (Image B) the hyperaccumulation of the tracer in the known nodule in the anterior-baseline segment of the RLB documents an increased metabolic activity there. After a previous non-diagnostic fibrobronchoscopy, the patient underwent rigid bronchoscopy



(A)



(B)

**Fig. 1.**

(Storz 14 tracheoscope) with Olympus ultrathin bronchoscope (3 mm). The lesion on which needle-aspirates, transbronchial biopsy and cryobiopsy 1.1 mm are performed, is identified with the aid of an Olympus radial EBUS mini-probe and fluoroscopic guide.

**Results:** Histology: neoplasm consisting of spindle cell elements and round/epitheliomorphic mixed with lymphohistioid inflammatory cellularity (positive immunohistochemistry for

Actin 1A4, HHF35, ALK-D5F3 and Vimentin). Diagnosis of inflammatory myofibroblastic tumor later confirmed by the subsequent right lower lobectomy.

**Conclusions:** The combination of Olympus ultrathin bronchoscope (3mm), mini-probe Olympus radial EBUS and cryobiopsy 1.1 mm made possible the diagnosis of this rare form of lung cancer in pediatric patient without complications.

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**ID# 61**

## **Characteristics of a Cohort of Patients Affected by Motor Neuron Disease: Experience from our Center**

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**Introduction:** Motor neuron disease is a rare neurodegenerative disorder causing progressive muscle weakness. Respiratory muscles are affected as well, leading to progressive respiratory failure; hence the importance of an interplay between the Neurologist and the Respiratory Practitioner.

**Objects:** We aim to describe the characteristics of a cohort of patients attending our clinic inside the Respiratory Unit of the Cardiothoracic Department, University Hospital of Pisa.

**Methods:** Data were derived from a database used for clinical purposes. We included all patients referred to our clinic by a neurologist from May 2010 to May 2021, with a diagnosis of motor neuron disease, not already mechanically ventilated at the time of the first. Data were collected in regard to: age, time of symptom onset, arterial blood gas analysis at first visit, start of noninvasive mechanical ventilation, time of death. SPSS Statistics was used to perform Student's t-test, Mann-Whitney U test (MWW), Pearson correlation, linear regression.

**Results:** We identified a total of 165 patients, 73 males (44.2%) and 92 females (55.8%). 44 patients (26.7%) had bulbar onset of the disease (dysphagia, dysarthria), of whom the majority (n=33, 75%) were females; 121 patients (73.3%) had spinal onset (impairment of walking, gripping) with only a slight prevalence of males (n=62, 51.2%) over females. Mean age at symptom onset (n=165) was  $64.4 \pm 10.6$  years, with no differences between spinal and bulbar patients ( $p=0.11$ , CI95% [-6.619; 0.689], t-test) or between males and females ( $p=0.83$ , CI 95% [-3.64;+2.92], t-test). Median time between symptom onset and start of noninvasive mechanical ventilation (n=104) was 27 months (7; 183), with bulbar patients starting earlier compared to spinal patients (median 19 and 33.5 months respectively;  $p=0.003$  MWW) while gender differences didn't reach statistical significance ( $p=0.055$ , MWW). Median time between symptom onset and death (n=33) was 38 months (11; 141), with no differences between spinal and bulbar patients ( $p=0.176$ , MWW) or males and females ( $p=0.123$ , MWW); patients who were older at symptom onset usually required mechanical ventilation earlier (linear regression, n=104,  $p<0.001$ , CI 95% [-1.75;-0.51]), although there was no significant correlation between age at symptom onset and time to death (Pearson,  $r=-0.188$ , n=33,  $p=0.152$ ). Spinal patients who needed ventilation earlier also died earlier (Pearson,  $r=0.927$ , n=25,  $p<0.001$ ). Values of  $\text{HCO}_3^-$  higher than 25 mmol/L at first visit were associated with a shorter survival (21.52 vs 38.25 months, n=33,  $p=0.041$  t test), especially among spinal patients.

**Conclusions:** The Respiratory Practitioner has an essential role in the management of motor neuron disease, especially during last stages.

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**ID# 62**

## **Unmet Needs in Asthma During Pregnancy: Results from a Doctor/Patient Survey**

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**Introduction:** Bronchial asthma is the chronic respiratory disease that most frequently can complicate the natural course of pregnancy; however, its optimal management during pregnancy and a woman's reproductive age remains uncertain.

**Objects:** This study proposes to assess the level of awareness, the limits and difficulties of asthma management in women during their pregnancy and reproductive age, from both patient and doctor perspective.

**Methods:** This study was carried out as an anonymous online survey for a month length. The main research networks and patients associations were involved.

**Results:** 76 doctors and 54 patients completed the survey. Table 1 report patients' and doctors' answers regarding: 1) asthma severity during pregnancy; 2) most common practice for women with asthma starting a pregnancy; 3) main asthma related-fears about starting a pregnancy. 98% of patients think it would be useful to talk with their doctor about their asthma before getting pregnant. Doctors look for a collaboration with the gynaecologist and the general practitioner because of uncertainty about the safety profile of anti-asthmatic agents during pregnancy, especially biologic therapies for severe asthma. Most doctors think women will fear that anti-asthmatic drugs will cause pregnancy complications or harm their babies. The 80% of patients feel comfortable enough to keep using their asthma medications for a safe pregnancy; besides, the same patients say they already received satisfying information about the pregnancy safety profile of drugs they assume for other coexisting conditions besides asthma. Doctors think that future pregnancy isn't considered when starting an asthma treatment; 55% of women admit never talking about this topic with their doctor.

**Conclusions:** Doctors ask for more evidence regarding the safety profile of asthma medications in pregnancy; both doctors and patients feel the need for a multidisciplinary approach involving both gynaecologist and medical practitioner. The general view is that of little attention to asthma management in the woman of reproductive age.

**Table 1.**

1	Asthma severity during pregnancy	Doctor	Mild 50%	Moderate 35%	Severe 10%
		Patient	Mild 28%	Moderate 50%	Severe 19%
2	Most common practice for women with asthma starting a pregnancy	Doctor (main answer)	I will refer my pregnant patient with asthma to a specialist (allergology/respiratory) only in case of asthma worsening		
		Patient (main answer)	My gynecologist will ask for a referral (allergology/respiratory) about my asthma at the beginning of my pregnancy		
3	Main asthma related-fears about starting a pregnancy	Doctor (main answer)	I fear complications for the pregnant woman / the baby she's carrying		
		Patient (main answer)	I fear my asthma will worsen		

ID# 63

### Clinical Diagnosis, Aspect and Treatment of Cardiac Sarcoidosis: a Case Report

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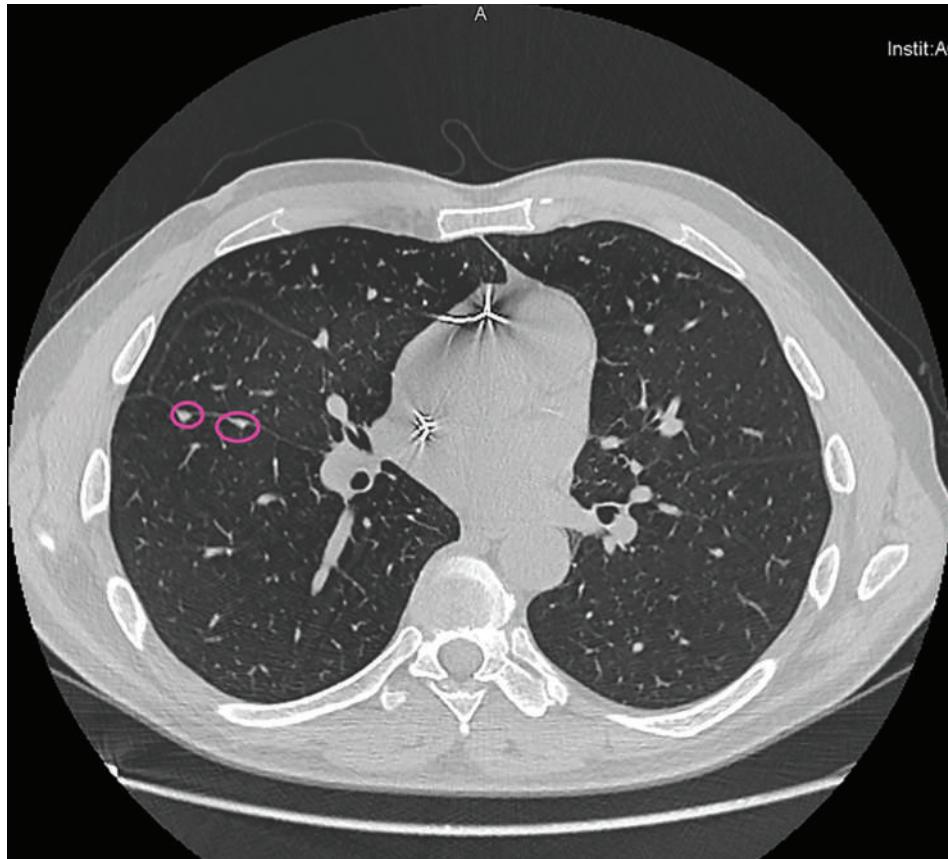
**Introduction:** Sarcoidosis is a granulomatous disease of unknown aetiology, which, however, in the 5÷25% of cases, can be associated with a cardiac manifestation.

**Objects:** Our objective is to understand how bronchoscopy with cryobiopsy is important in arriving to a diagnosis of a Sarcoidosis.

**Case report:** The patient is a 52-year-old man. He suffered of blood hypertension treated with Ramipril 2.5 mg and Bisoprolol 2.5 mg die. His occupational and environmental exposure isn't relevant, nor his family history. In his past medical history there were a supraventricular ectopic brads and atrioventricular block grade I (April 2018) and a radiofrequency ablation for supraventricular tachyarrhythmias with right bundle branch morphology (July

2018). During a football game in October 2020, he suffered of a cardio-respiratory arrest (ACC). He was defibrillated and treated with 3 vials of amiodaron. When arrived at Emergency Department, the results of the performed electrocardiogram (ECG) and echocardiogram were found altered. Then a cardiac magnetic resonance (RMN cardiac) was performed and resulted in a diffuse hypokinesia of the left ventricular segment, FE reduction and multiple alterations in several segments with non-coronary distribution and non-ischemic appearance associated with edema at the level of the lower wall. This clinical picture was the first clue of a possible presence of Sarcoidosis. At the physical examination normal breath sound was noted all over the chest, not pathological and eupnoeic in ambient air. The following pulmonary function test reported FVC 102%, FEV<sub>1</sub> 87%, TLC 107%, DL<sub>CO</sub> 78%. Additionally, the high resolution TC (HRTC) highlighted very tiny micro nodules with a modest tendency to merge in a "pseudo-plaque" form, while the PET/TC describes a tissue with high hypermetabolism compatible with inflammation in the retrosternal cavity and lymph node pertinence. Therefore an indication was given to perform a bronchoscopy with cryobiopsy. The immunophenotypic examination performed on alveolus bronchial washing shows a reduced cellularity with a prevalence of mononuclear cells. The pathological examination of the cryobiotic sample highlighted the "presence of non-necrotizing sarcoid granulomas mainly located in the subpleural area and in the pulmonary interstitice". The patient was treated with prednisone 50 mg/day and methotrexate 15 mg for one week. At the six month follow up, the patient showed improved echocardiographic picture and respiratory functions.

**Conclusions:** In this case report, notwithstanding the atypical radiological appearance and tiny extension, cryobiopsy was diagnostic. This approach made it possible to perform a rapid and accurate diagnosis to set up an adequate treatment.



**Fig. 1.**

ID# 64

### A Case Report of Cysitic Lung Disease (LAM) with Lung and Abdomen Involvement

*Ilaria Pulzato<sup>1</sup>, Francesco Balbi<sup>2</sup>, Alberto Bordo<sup>2</sup>, Patrizia Zoccali<sup>2</sup>, Antonella Serafini<sup>2</sup>*

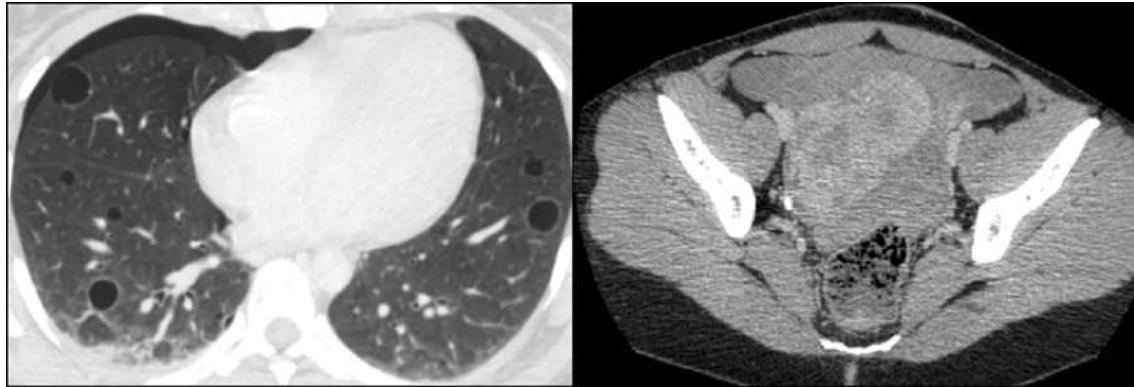
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**Introduction:** Different lung diseases may present cysts as the main abnormality, albeit lymphangioleiomyomatosis (LAM) and Langerhans cell histiocytosis (LCH) are the most common to present with diffuse lung cysts. The knowledge of these conditions and the distinguishing CT imaging features may lead the diagnosis and management.

**Case report:** A 36 years-old woman was admitted to our ER department for abdominal and pelvic pain. Upon clinical presentation, her oxygen saturation was above 95% on room air without respiratory distress. Abdominal computer tomography (CT) showed a homogenous well-defined pelvic mass originating from the left ovary with abundant abdominal free fluid. The CT scan at the level of the lung bases demonstrated a right sided

pneumothorax. A chest X-ray confirmed the large sided pneumothorax and a subsequent chest CT revealed bilateral diffuse bullous disease with multiple thin-walled cysts ranging from 0.4 mm to 20 mm with random distribution. The patient underwent pelvic surgery with the histologic diagnosis of Pecoma. LAM is a rare disease which often affects lungs, the majority of the patients die from respiratory failure. It is often misdiagnosed: the most common presentations are dyspnoea and cough whereas chylothorax and spontaneous pneumothoraces may be seen in advanced cases. Albeit rare extrapulmonary LAM has been described in some series with renal angiomyomas and abdominal lymphadenopathies. Pelvic and retroperitoneal masses are very rare and require laparotomy. Our patient represents a classical presentation of pulmonary LAM in a childbearing age with a rare extra-pulmonary manifestation treated with abdominal surgery. At three months follow up her pulmonary function test (PFT) showed normal vital capacity and forced expiratory volume in one second ( $FEV_1$ ), a tiny residual pneumothorax without respiratory distress.

**Conclusions:** The differential diagnosis of diffuse cystic lung disease should be organized on the basis of clinical history, serologic evaluation, and the HRCT cysts features and ancillary findings: lymphangioleiomyomatosis and LCH are the most frequently encountered causes of thin-walled cysts at HRCT.



**Fig. 1.**

ID# 65

### Uncovering the Mystery of Post-COVID ILD: Ground Glass Abnormalities are not Inflammatory

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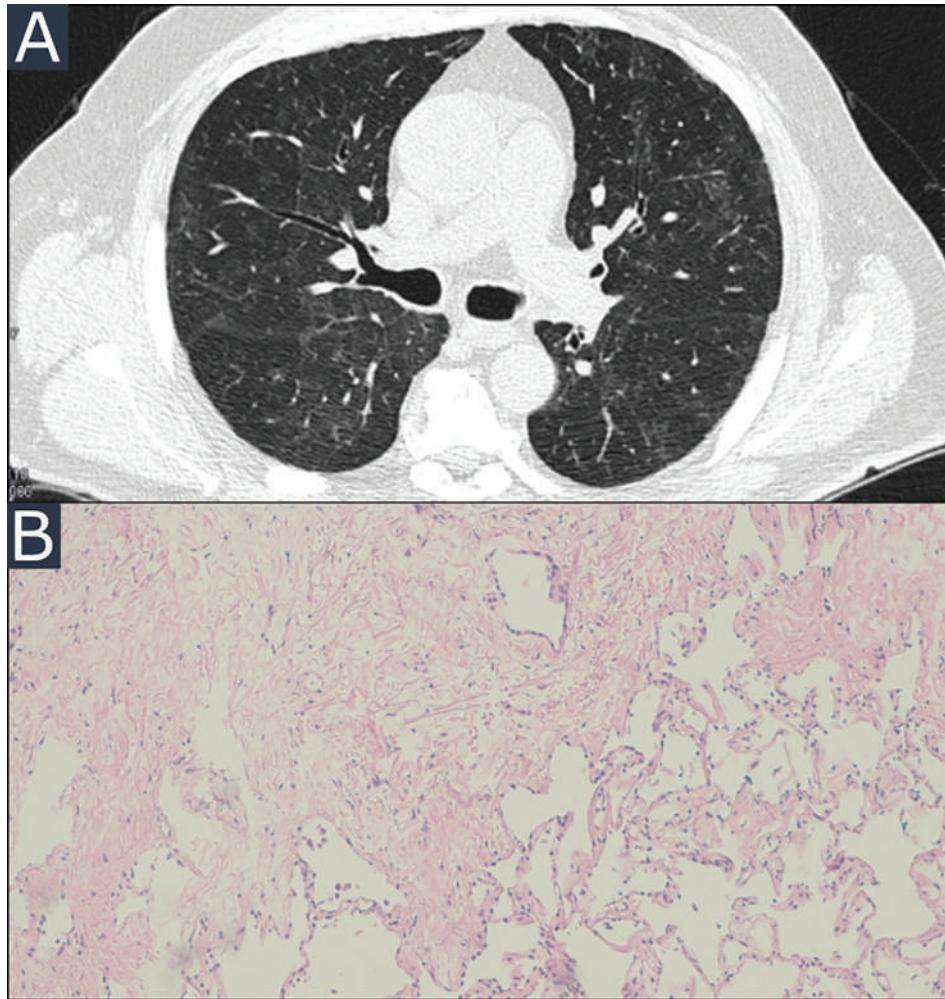
**Introduction:** We present a case of a middle-aged white male with no previous medical history that had long term persistence of ground glass abnormalities after SARS-CoV-2 infection. These radiological findings are not residual inflammation as it is currently hypothesized, but profound fibrotic histological changes as we confirmed via cryobiopsy. This clinical case is part of the PCOILS National trial that investigates post-COVID interstitial lung changes. We present a case of Interstitial Lung Disease after SARS-CoV-2 infection, evaluated with HRCT and transbronchial lung cryobiopsy.

**Case report:** 56 y.o. caucasian male bus driver with no remarkable medical history or familiarity for ILD in particular. He was admitted at Careggi University Hospital in March'20 for

respiratory failure due to SARS-CoV-2 pneumonia. He underwent CPAP treatment, antiviral therapy (lopinar/ritonavir) and immunomodulatory treatment (hydroxychloroquine, single-dose tocilizumab and systemic corticosteroids). He was discharged at home after 20 days of hospitalization without the need of supplemental oxygen and no apparent sequelae. Patient was enrolled in the PCOILS National trial and followed up with HRCT at 6 and 12 months that showed persistence of mild diffuse ground glass opacities at 6 months after discharge, increased in extension at 12 months (Fig. A). Patient reported stable mMRC 1 exertional dyspnea, all pulmonary function tests and cardiologic examinations were normal. The serology tests, including autoantibodies and immunophenotype, also showed no abnormal findings with the exception of a mildly elevated RCP, D-dimer and ferritin. According to PCOILS protocol, he underwent bronchoscopy, cryobiopsy and BAL.

**Results:** BAL showed normal cellularity and negative microbiology. At histological examination we found a dominant fibrotic pattern characterized by diffuse early fibrosis with areas of dense, “patchy” fibrosis alternating with normal lung tissue, with peribronchial and sub-pleural distribution (Fig. B). Inflammatory lymphoid infiltrate was moderate.

**Conclusions:** Here we describe for the first time a case of long COVID ILD characterized by extensive fibrotic histologic changes that on HRCT appears as mild ground glass opacities. Contrarily to current belief ground glass is not residual inflammation and criobiopsy may become useful in the correct evaluation of post-COVID changes with major implications for patient's treatment (anti-fibrotic or immunomodulatory therapies) and management decisions.



**Fig. 1.**

ID# 68

### **Spontaneous Ilio-Psoas Haematoma in COVID-19 Patients: Antitrombotic Prophylaxis is Really Safe?**

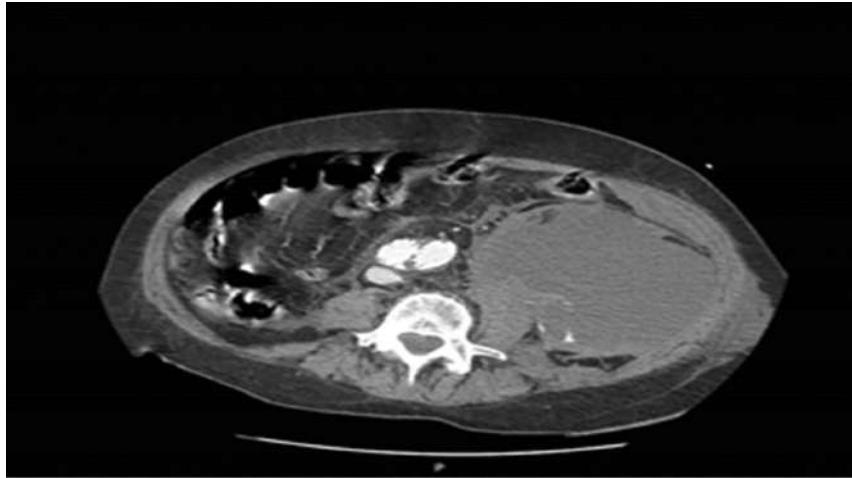
*Livia De Pietro, Angela Di Giorgio, Luca Longobardi, Carlo Gaudiosi, Antonietta Sorrentino, Gennaro Gravino, Diana Radicella, Alessandro Cirillo, Matilde Boccia, Samuel Scuotto, Alessandro Panico, Raffaele Cobuccio, Adriano Gesuele, Francesco Stefanelli*

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**Introduction:** An increasing number of studies indicate that COVID-19 (COronaVIrus Disease-19) is not only a respiratory disease. In some recently published studies it has been documented that the use of antithrombotic prophylaxis in patients hospitalized

for COVID-19 is associated with a higher chance of survival. A significant proportion of patients with SARS-CoV-2 infection suffer from coagulopathy which is associated with alterations in coagulation tests, microthrombosis and a high risk of thromboembolism that make the clinical picture more complex and cause adverse outcome. To this regard an initial elevation of D-dimers, a marker of coagulation activation and fibrinolysis, is indicative of a poor prognosis (1, 2). However, new scientific evidence points to an increased risk of bleeding complications in such patients, raising concerns about the widespread use of heparins, which have become part of the treatment of hospitalized patients for COVID-19, despite the data on the right prophylactic dose and on the duration of treatment are still rather limited.

**Case report:** We report a case series of eight subjects with SARS-CoV-2 pneumonia complicated by ilio-psoas haematomas (IPHs) at our COVID-19 Sub-intensive Respiratory Unit. In the last 8 months 280 subjects with confirmed SARS-CoV-2 infection were admitted to our unit. Among them, we found eight



**Fig. 1.**

spontaneous IPHs with an incidence of 3 cases per 100 hospitalizations. All the reported cases had severe clinical manifestations of COVID-19 pneumonia, with at least one comorbidity and were on treatment with prophylactic low weight molecular heparin. Six of the eight patients were treated with conservative measures; we discontinued heparin and introduced blood transfusions and volume resuscitation. Two haemodynamically unstable patients underwent arterial embolization. After a median of 7 days, in 7 of the 8 patients the symptoms relieved, the hemoglobin levels returned to normal and the size of retroperitoneal haematoma reduced. Unfortunately one patient died due to the worsening of respiratory conditions.

**Conclusions:** In view of the current indications for prescribing anticoagulant therapy in COVID-19 patients and the lack of solid evidence on optimal dose and duration, it is necessary to know the existence of potentially fatal complications such as iliopsoas haematoma in order to be able to detect them promptly. Further studies are needed to establish indications, posology and duration of antithrombotic prophylaxis to avoid the possible occurrence of potentially fatal bleeding.

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**ID# 69**

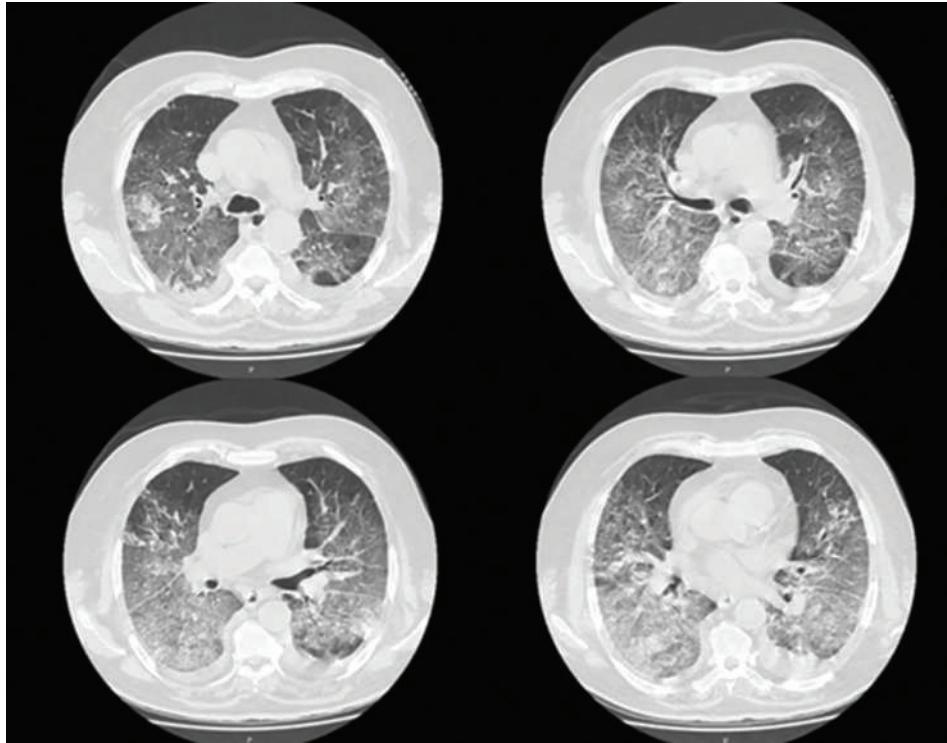
## **Severe SARS-CoV-2 Pneumonia in Vaccinated Patients**

*Livia De Pietro, Diana Radicella, Luca Longobardi, Angela Di Giorgio, Carlo Gaudiosi, Antonietta Sorrentino, Gennaro Gravino, Alessandro Cirillo, Matilde Boccia, Samuel Scuotto, Alessandro Panico, Adriano Gesuele, Raffaele Cobuccio, Francesco Stefanelli*

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**Introduction:** Three of the four COVID-19 vaccines currently approved require two doses, administered after a few weeks. In view of the difficulties in vaccine distribution capacity, the severe wave of COVID-19 (COronaVIrus Disease-19) in the last months and the emergence of new dangerous variants, the possibility of delaying the second administration to vaccinate more individuals with the first dose was considered as an alternative strategy. However, there was no clear advantage of delaying the second dose in reducing the transmission of infection.

**Case report:** We report seven cases of vaccinated patients admitted to our COVID-19 sub-intensive respiratory unit with



**Fig. 1.**

severe SARS-CoV-2 pneumonia. 5 of the 7 patients received the first dose of the vaccine and were subsequently hospitalized after a median of 12 days from administration; 2 of the 7 patients also received the second dose and were hospitalized 12 days and 60 days after administration, respectively. All the reported cases had severe COVID-19 pneumonia, documented by HRCT, with secondary respiratory failure requiring mechanical ventilation with high FiO<sub>2</sub> (fraction of inspired oxygen); these patients had at least one comorbidity and the duration of hospitalization was comparable to that previously recorded for unvaccinated patients.

**Conclusions:** Single-dose vaccination campaigns can help to contain the SARS-CoV-2 pandemic very quickly, but our experience suggests the importance of quantifying the effectiveness of vaccine-induced protection after the first dose in order to determine the optimal interval between the two doses. For all reported patients, genomic sequencing was started to understand the reasons behind the ineffectiveness of the vaccines, in particular in the two cases who received both doses.

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**ID# 71**

## Use of Helmet CPAP in COVID-19 Related ARDS in RICU in Three Waves: Preliminary Results

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**Introduction:** The three waves of SARS-CoV-2 pandemic between March 2020 and May 2021 in Lombardy Region (Italy) have rapidly led to an increase in hospitalization, forcing the application of non-invasive respiratory support in respiratory intermediate care unit (RICU) to patients with COVID-19 related acute respiratory distress syndrome (ARDS).

**Objects:** We aimed to analyze the effects of helmet continuous positive airway pressure in COVID-19 related ARDS (bilateral pulmonary infiltrates and P/F ≤300 in helmet CPAP with PEEP ≥5 cmH<sub>2</sub>O) in RICU. Patients' course, and in particular the CPAP failure, were valued and defined as the occurrence of either intubation or death due to any cause during RICU stay, in the three different waves. At the end of the analysis, factors that define different patients' courses among the three waves will be identified.

**Methods:** Prospective observational study on 517 patients with acute respiratory distress syndrome due to COVID-19, out of a total of 712 patients, aged less than 80 and referred to RICU in Vimercate Hospital (MB), between March 2020 and May 2021. All patients with ARDS were treated with helmet continuous positive airway pressure, managed by respiratory physicians.

**Results:** During the first wave (March – May 2020) 38% failed; among them 31 patients were transferred to intensive care unit with survival rate of 48%, total mortality was 28%, of which 21 DNI (14%). During the second wave (October – December 2020) 28% failed; among them 37 patients were transferred to intensive care unit with survival rate of 46%, total mortality was 19%, of which 13 DNI (7%). During the third wave (February – April 2021) 23% failed; among them 32 patients were transferred to intensive care unit with 59% survival rate, total mortality was 12%, of which 7 DNI (3.7%).

**Conclusions:** Results highlight the fundamental role of RICU in the management and treatment of patients affected by COVID-19 related ARDS. All patients were treated with helmet CPAP. The results have progressively improved during subsequent waves thanks to optimized targeted protocols and better territorial management, in particular the increased availability of beds in ICU has allowed to significantly reduce the number of “DNI” patients. It was hypothesized a determinant role of treatment with systemic corticosteroids, helmet CPAP and pronation in the prognosis of these patients.

who were admitted between 12 Oct 2020 and 31 May 2021, 103 patients with severe Covid pneumonia and respiratory failure with  $\text{SaO}_2/\text{FiO}_2$  index < 315 were included. Patients were divided into two cohorts. The first comprised patients who received remdesivir and SCT, consisting of dexamethasone 6 mg daily for up to 10 days or until hospital discharge. The second comprised patients who received combination therapy with remdesivir and HDMPT, consisting of methylprednisolone 250 mg i.v. for three days, followed by methylprednisolone 40 mg on days 4-8 and then followed by slow tapering every three days of dose of steroids. All patients were followed to death, intensive care unit (ICU) admission, or discharge from the hospital. The severity of hypoxemia was assessed by peripheral oxygen saturation  $\text{SO}_2/\text{FiO}_2$  index.

**Results:** Of 103 patients, 56 (54.4%) received remdesivir plus HDMPT and 47 (45.6%) received remdesivir plus SCT. Mortality at 30 days was significantly lower among patients who received HDMPT (4/56, 7.1%) compared to those who did not (15/46, 32.6%). Among patients who received HDMPT, 4/56 (7.1%) required invasive mechanical ventilation and ICU admission and 20/56 (35.7%) non-invasive ventilation vs respectively 14/46 (30.4%) and 29/46 (63.0%) among those treated with SCT.  $\text{SaO}_2/\text{FiO}_2$  index at day five and day 10 was significantly higher among patients who received HDMPT as compared to patients who received SCT ( $\text{SaO}_2/\text{FiO}_2$  day 5 - HDMPT: M=315.47, SD=1119.68; SCT: M=244.68, SD=105.51, p<.001;  $\text{SaO}_2/\text{FiO}_2$  day 10 - HDMPT: M=390.47, SD=114.59, SCT: M=295.23, SD= 143.61, p<.001).

**Conclusions:** Our results suggest that early combination treatment with methylprednisolone pulse and remdesivir reduced in-hospital mortality, need for ICU admission and induced a faster improvement of  $\text{SaO}_2/\text{FiO}_2$  index in patients with severe COVID-19 pneumonia.

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## ID# 72

### Combination Treatment with Methylprednisolone Pulse and Remdesivir for Severe COVID-19 Pneumonia

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**Introduction:** Remdesivir and steroids are two robust evidence-based therapies that are widely used in patients with COVID-19 pneumonia. However, optimal dose and timing of the steroids in patients with severe COVID-19 are still unclear, and the impact of corticosteroid therapy on outcomes of COVID-19 is highly controversial. Limited evidence suggests that early steroid pulse may have relevant survival benefits avoiding the progression of COVID-19 to a critical stage and improve clinical outcomes.

**Objects:** We evaluated the clinical outcomes of patients with severe COVID-19 pneumonia treated with remdesivir plus high dose methylprednisolone pulse therapy (HDMPT) compared to patients treated with remdesivir plus standard steroid treatment (SCT).

**Methods:** Observational, single center prospective study. Of 359 consecutive patients with a clinical diagnosis of COVID-19,

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## ID# 73

### Gender Medicine: Our Clinical Experience with Coronavirus Disease 2019

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**Introduction:** In literature the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection seems to have greater severity in the male sex. Different mechanisms could be at the basis of different severity of disease in men compared to women. Male sex has an higher expression of angiotensin-converting enzyme 2 (ACE2), entry door of virus. Several studies attribute to testosterone a role in pathogenesis of thromboembolic phenomena involved in lethality from coronavirus disease 2019 (COVID-19). Moreover, TMPRSS is a serine-dependent protease, involved in the penetration of the virus inside the cell, which depends on testosterone.

**Objects:** To verify, among our patients, the correlation between sex and comorbidities, lethality and severity of

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## Abstracts

COVID-19 pneumonia based on HRCT Chung score and type of respiratory support received.

**Methods:** We evaluated 200 patients with COVID-19 pneumonia hospitalized in Monaldi Hospital in Naples, 43, 5% of them were females and 56, 5% were males. 87 females have been recruited (mean age 68.5 years), the average HRCT Chung score was 13/20. 53, 5% of these patients needed CPAP therapy while the remaining 46,5% received high flow oxygen therapy (HFNC). 2% of women had pulmonary thromboembolism during hospitalization. Comorbidities: arterial hypertension (55.5%), type 2 diabetes mellitus (21%), atrial fibrillation (5%) ischemic heart disease (2.8%), stroke (1%), dementia (3.7%), COPD (5.6%), cancer (5.5%), obesity (22%), chronic liver disease (0.93%), kidney failure (3%), asthma (5%). Lethality rate was 32%. 113 males were enrolled (mean age 64.5 years) with a mean HRCT Chung score of 13.5/20. 55% of these patients needed CPAP therapy while the remaining 45% received HFNC. 2% of them had pulmonary thromboembolism during hospitalization. Comorbidities: arterial hypertension (41%), type 2 diabetes mellitus (16.5%), ischemic heart disease (13%), COPD (12.5%), cancer (5%), obesity (8%), chronic liver disease (1%), kidney failure (1%). Lethality rate was 30%.

**Results:** In our experience SARS-CoV-2 pneumonia affected especially males. Comorbidities affected mainly women, but people of both groups reported the same lethality rate and the same severity of disease without significant differences between males and females. Studies based on a larger population sample would be required.

**Conclusions:** Patients hospitalized with COVID-19 pneumonia were mainly males but females had more comorbidities on admission. In our experience there are not significant differences in severity and lethality of COVID-19 pneumonia between males and females.

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### ID# 75

## Respiratory Pathophysiology in Patients with COVID-19 Outcomes

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**Introduction:** Pulmonary involvement from COVID-19 is almost constant. In many patients after recovery from the acute phase respiratory symptoms and signs persist and lead to

interstitial disease and from there to pulmonary fibrosis. Respiratory pathophysiology can be a non-invasive, reproducible and low-cost way to follow its course, try to alleviate symptoms and modulate therapy. In some patients, pulmonary fibrosis occurs in a very short time therefore it is useful to set up a therapy at the first signs.

**Objects:** Evaluate the symptomatic post COVID-19 outpatient patients, to be prompt in the therapeutic choice. The patients recruited are all negative for swabs after at least 8 weeks of healing, excluding chest CATscan and pulmonary embolism examinations. Chest CATscan with HR method and oximetry monitoring were used to complete the diagnostics.

**Methods:** Use DL<sub>CO</sub> respiratory pathophysiology, global spirometry and plethysmography in symptomatic patients after COVID-19, to monitor healing and customize therapeutic choices in case of alterations (reduction of DL<sub>CO</sub>, reduction of residual volume, increase of resistance with plethysmography, reduction of small ways with spirometry). In the case of a reduction in the small pathways of long-acting beta 2 agonist bronchodilators, antimuscarinics in former smokers and with known COPD, in the case of a reduction in DL<sub>CO</sub> inhaled steroids.

**Results:** 265 outpatients, average age 62.2 years, 121 women, 144 men, who arrived with an urgent request from the general practitioner, for a pneumological visit and treated on an outpatient basis. Out of 265 patients 131 showed DL<sub>CO</sub> deficiency, with average values of 3%, 104 showed a normal picture with average values of 83%. Of 265 patients, 35 resulted in COPD, with FEV<sub>1</sub> less than 55%, increased resistance. Out of 265 as many as 80 showed deficits in the small pathways with FEF values of 25-75% of 41% even with FEV<sub>1</sub> still within limits. Of 265 patients, 31 were carriers of restrictive syndrome. 265 patients showed a decrease in the isolated residual volume, with normal lung volumes. The study serialized with global spirometry, plethysmography and DL<sub>CO</sub> every 2 months in patients with alterations.

**Conclusions:** Monitoring DL<sub>CO</sub> shows progressive improvement of values after ICS treatment. Small pathway deficiency evidenced by spirometry can be treated with LABA-LAMA especially in patients with a previous history of cigarette smoking or COPD. The significance of the progressive worsening of residual volume in patients with normal spirometry and DL<sub>CO</sub>, perhaps an expression of progressive and persistent fibrosis despite therapies, remains to be evaluated.

ID# 76

## Prognostic Value of ROX Index in COVID-19 Patients Treated with Continuous Positive Airway Pressure

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**Introduction:** Timing of intubation in patients affected with COVID-19 and acute hypoxaemic respiratory failure is challenging, since delaying intubation until the patient is acutely decompen-sated is potentially harmful. P/F ratio ( $\text{PaO}_2/\text{FiO}_2$ ) was normally used as a predictor of intubation and disease severity during this pandemic. ROX index, defined as the ratio of oxygen saturation as measured by pulse oximetry/FiO<sub>2</sub> to respiratory rate, has been validated only for patients with acute respiratory failure treated with high-flow nasal cannula.

**Objects:** The aim of our study was to evaluate the accuracy of ROX index as a prognostic predictor in COVID-19 patients treated with continuous positive airway pressure (CPAP), and to compare it with P/F ratio. Need for intubation and mortality were considered as outcome variables.

**Methods:** This was a retrospective observational study including 25 patients affected with COVID-19 and acute respiratory distress syndrome, who were treated with CPAP. ROX index and P/F ratio values were measured in selected patients at two specific time

points: at the beginning of CPAP (t0) and after 24 hours of treatment (t1). ROC curves were performed to detect the best cutoff values to predict risk of intubation and mortality. Further analysis was performed through  $\chi^2$  test and odds ratio. A p value < 0.05 was considered as significant.

**Results:** At t0, a P/F ratio of 152.5 and a ROX index of 8.86 were identified as the best cutoff values in predicting the need for intubation (with 83% sensitivity and 94% specificity for the first, 83% sensitivity and 47% specificity for the latter); the area under the curve (AUC) was 0.87 for P/F ratio, 0.57 for ROX index. At t1 a P/F ratio of 219 was identified as the best cutoff for predicting mortality (with 100% sensitivity and 76% specificity); a ROX index of 8.86 measured at t0 was detected as the best cutoff value to predict mortality (100% sensitivity and 53% specificity). The AUC was 0.88 for P/F ratio at t1, 0.70 for ROX index at t0.

**Conclusions:** This study confirms the prognostic power of P/F ratio in COVID-19 patients with acute hypoxaemic respiratory failure treated with CPAP. The ROX index showed a lower diagnostic accuracy than P/F ratio in predicting mortality and need for intubation. Since the ROX index is a non-invasive method and can be easily measured, integrating P/F ratio and ROX index measurements could be useful in clinical monitoring.

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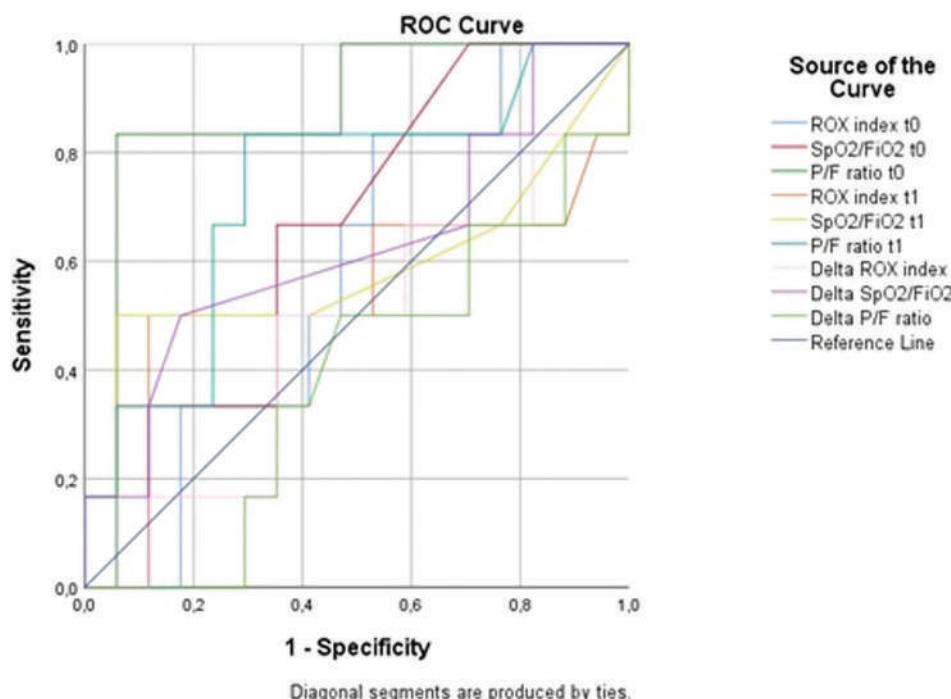


Fig. 1.

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**ID# 78**

## **Rehabilitation Model in Long Coronavirus Disease 2019 Syndrome**

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**Introduction:** Long term Coronavirus disease-19 (COVID-19) is a syndrome, affecting 20% of COVID patients. The main symptoms, lasting > 12 weeks of the onset of acute COVID-19, are the following: fatigue, dyspnea, chest pain, arthralgia, myalgia, cognitive dysfunction and decline in quality of life. Long COVID-19 is caused by inflammatory cellular damage due to the infection and as a result of post-critical illness.

**Objects:** To verify the efficiency of a rehabilitation model in order to facilitate the long COVID-19 management.

**Methods:** We have proposed a prospective intervention model for the rehabilitation of patients recovered for COVID-19 pneumonia from October 2020 to May 2021, at the Intensive Respiratory Care Unit, Monaldi Hospital in Naples. Patients at discharge were assessed by a field test (six-minute walk test or sit-to-stand test) and the same test was repeated during follow-up. Borg scale cr10 and visual analogic scale were used to assess dyspnea and fatigue. Before leaving patients received detailed instructions about exercise session set up and execution at home. The type of activity best suited to their recovery needs was agreed with doctors, taking into account each and everyone's needs in order to comply with their home therapy. During hospitalization they were trained to measure physical exertion during exercise by monitoring heart rate and dyspnea (Borg cr10 scale or Talk Test for quick self-assessment). A physical activity protocol consisting of breathing exercises (such as the active cycle of breathing techniques) and an endurance exercise activity (cycling, walking, nordic walking or other similar activity).

**Results:** Treated patients were able to self-manage exercise while maintaining heart rate in a range between 50% - 80% of heart rate reserve (Karvonen) and dyspnea assessed at level 3 of the talk test (ability to speak with some difficulties) during the prescribed exercise. The exercise was performed starting from a minimum of twenty minutes up to a maximum of one hour a day for 6 days a week. Patients used oximetry monitoring only in the first few exercise sessions to ensure that they did not reach values below 90% of SpO<sub>2</sub> during rehabilitation.

**Conclusions:** The rehabilitation is vital for post-covid infected individuals because improves breathing, mobility and mental health by reducing anxiety, depression and improving self-esteem.

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**ID# 79**

## **Bilateral Spontaneous Pneumothorax as Uncommon Complication of COVID-19 Pneumonia**

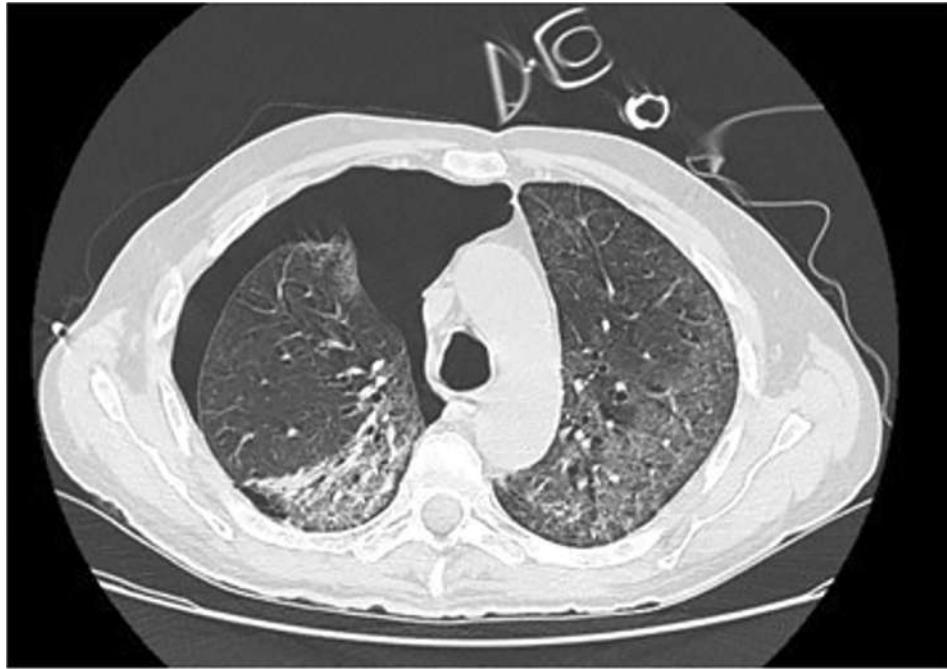
*Diana Radicella, Matilde Boccia, Alessandro Cirillo,  
Livia De Pietro, Angela Di Giorgio, Carlo Gaudiosi,  
Gennaro Gravino, Luca Longobardi, Samuel Scuotto,  
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**Introduction:** SARS-CoV-2 is a novel human coronavirus responsible for the Coronavirus disease 2019 (COVID-19) pandemic. Pneumonia and acute respiratory distress syndrome are the major complications and the most common symptoms are fever, dry cough and shortness of breath. While most people develop only mild or uncomplicated illness, many others develop a severe disease that requires hospitalization and oxygen support. For hypoxic respiratory failure, the frontline treatment is supplemental oxygen. The high-flow nasal cannula (HFNC) therapy gained attention as an alternative means of respiratory support for patients who were critically ill. The HFNC system is less invasive and decreases breathing frequency and work of breathing. Recent evidence suggested that some complications can occur in the context of COVID-19 pneumonia, such as spontaneous pneumothorax (1). Computerized tomography (CT) has an important role in the initial evaluation and follow-up of this disease (2).

**Case report:** A 62 years old man with COVID-19 was admitted to the hospital. He appeared short of breath but no fever. He was a nonsmoker, with no chronic pathology in the anamnesis. His CRP was high 4.38 mg/dl and the procalcitonin and d-dimero's values were normal. The blood pressure was 145/90 mmHg and pulse was 110 bpm. His respiratory rate was 35 and the oxygen saturation (SpO<sub>2</sub>) was 75%, improving to 95% on HFNOT 60 L/min FiO<sub>2</sub> 85%. CT demonstrated "Extended pneumothorax on the right. Diffuse pulmonary interstitium thickening associated a ground-glass opacities..." A chest tube was placed without clinical improvement (SpO<sub>2</sub> 93% on HFNO). So we put an aspiration on right drainage and the clinical presentation was SpO<sub>2</sub> 96.4% on HFNOT with flow 35 l/min FiO<sub>2</sub> 60%. After 14 days he presented chest pain and severe desaturation so we had requested a chest X-ray that showed a significant left-sided pneumothorax and another pleural drainage was inserted with aspiration. Post-procedure chest X-ray showed an improvement of the pneumothorax in the left and adequate right lung expansion. CT chest doesn't show multiple bilateral bullae in the lungs and we had analyzed the alpha-1-antitrypsin that resulted normal. He had not ever required invasive or noninvasive positive pressure ventilation.

**Conclusions:** Pneumothorax is a rare complication associated with COVID-19 pneumonia. In our case the pneumothorax is spontaneous and bilateral, a very rare condition. Unfortunately, the mechanisms are not fully elucidated, although it is probably



**Fig. 1.**

because of the rupture of the alveolar wall due to the increasing pressure difference between the alveolus and the pulmonary interstitium.

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### ID# 80

## Airways Remodeling in Asthma: Have we to Change the Paradigm?

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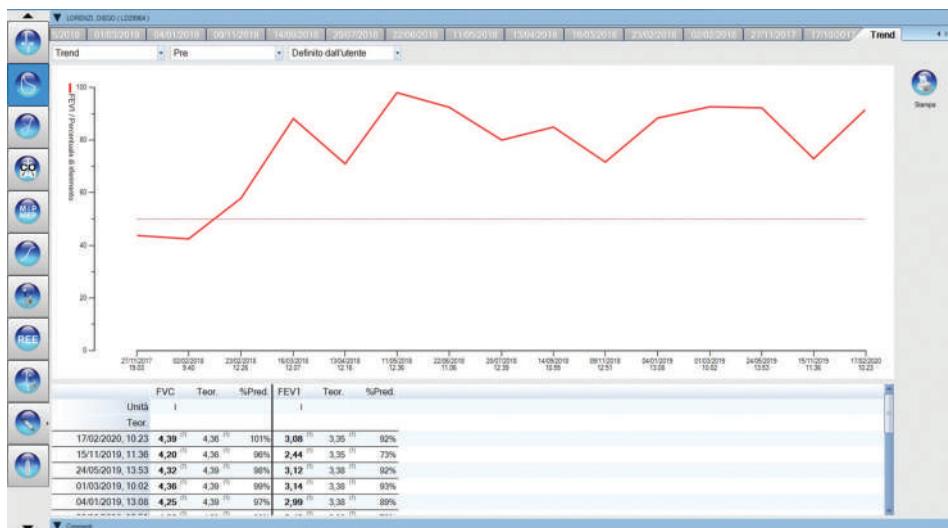
**Introduction:** For a long time, observing the lack of beta<sub>2</sub>-response in chronic asthmatic patients we have sustained the item of STRUCTURAL REMODELING of bronchial tree. All we thought that the structural modifications (increased smooth

muscle mass, gland enlargement, neovascularization, loss integrity of epithelial barrier, subepithelial fibrosis) occurring in airways of patients suffering of bad stages asthma, in particular in not young patients, could determinate a definitive low response to antiasthmatic therapies. Therefore with a very small outcome in terms of quality of life for the patients, and the persistent deteriorations of pulmonary function tests.

**Methods:** Biological therapies (in our practice: Omalizumab, Mepolizumab, Benralizumab, Dupilumab), if not ever, surely in many cases, allow to reach a very good therapeutical response, sometimes unespected, in a large number of patients.

**Results:** For many patients, it has two consequences: A) it means a “radical change of my life”; B) in the functional test station it allows a marked gain in Pulmonary function after biological agent. In figure 1 we can observe the gain in term of FEV<sub>1</sub>: before/after biologic therapy. Sometimes also reaching the quite normalizations of a pulmonary function tests, also in patients previously resulted not beta<sub>2</sub>-responsive, also in not young people.

**Conclusions:** As in other many scientific papers, reporting functional improvement in functional status of asthmatic patients treated with biological therapies, it could be suggestive that the item of REMODELING of bronchial tree, even if present in bad stages of asthma, has not to be considered IRREVERSIBLE, at least in cases of good response to biological treatments.



**Fig. 1.**

ID# 81

## Tracheal Cannula Removal in Severe Acquired Cerebral Injury: Role of Pulmonary Rehabilitation

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**Introduction:** Decannulation is one of major outcomes in the rehabilitation of patients suffering from severe Acquired Cerebral Injury (sABI) and who are carriers of a tracheostomy cannula positioned to allow mechanical ventilation and airways protection from inhalation or secretion retention.

**Objects:** To evaluate a tracheostomy weaning protocol requiring the competence of pulmonary specialists and respiratory therapists, for interventions such as control of gas exchange, management of cough, prevention of inhalation and respiratory infections and endoscopy evaluation.

**Methods:** Retrospective data analysis of a cohort from a local Tracheostomy Register, including pts affected by sABI over 15 years of age and having tracheostomy tube in place at admission. Setting and Participants: all patients admitted to our pulmonary and neurorehabilitation units in a 12 year period. Personal and clinical data were collected for each patient, including aetiology, infectious and obstructive complications pre- and post-decannulation, removal of the canula, and the severity of the neurological clinical picture according to the Glasgow Outcome Scale (GOS) at admission and discharge. The Decannulation Prediction Tool (DecaPreT) was applied to identify patients with sABI who to be

safely decannulated (1). Pulmonary rehabilitation was focused mainly on procedures of bronchial secretion management and lung expansion. All patients underwent bronchoscopy.

**Results:** 359 subjects were studied, mean age 51.5 years (range 15-75): 162 admitted for cerebrovascular disease (45.1%), mainly cerebral haemorrhage; 120 for severe head injury (33.4%); 25 for post-anoxic encephalopathy (7.0%); 52 (14.5%) for other disorders (neoplastic, infectious, inflammatory). Ten of them died. Decannulation was obtained in 278 subjects (79.6%). The decannulation took place on average at 79 days from the acute event (range 21-461 days). The probability of decannulation was significantly dependent upon the nature of the encephalopathy, the severity of the clinical conditions according to the GOS at the moment of discharge, and the pre-decannulation infectious and obstructive complications. In 14 cases (19% of failed weaning) endoscopy was a main criterion in preventing decannulation (obstruction or stenosis or vocal cord palsy). No significant associations were recorded between decannulation and duration of hospitalisation, gender or age of the patient, or clinical picture at admission. 5 out of 278 patients (2%), had to be repositioned with a tracheal cannula. In the group of decannulated patients, the probability of respiratory tract infections dropped significantly from 23% (95% CI: 18-28%) to 4% (95%CI: 2-6%) ( $p<0.000$ ).

**Conclusions:** Pulmonary rehabilitation is a fundamental component in the long term multidisciplinary management of patients with sABI undergoing protocols for removal of tracheostomy.

## Reference

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ID# 83

## Chest CT Crazy Paving Pattern Revealed Monolateral Pulmonary B Cell MALT Lymphoma

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**Case report:** A 48 years old mild smoker woman, with no comorbidities, presented in our outpatient with breathlessness, mild exert dyspnoea, fever and fatigue. Chest CT revealed monolateral pulmonary opacities, consolidation and crazy paving pattern. Blood exams revealed increased lymphocyte count and PCR elevation. Further studies revealed serum IgA elevation (2270 mg/dL), kappa chain elevation (10.30 g/L), electrophoretic Gamma peak (34.2%) and increased FDG metabolism of the lesion stated by PET. The patient underwent bronchoscopy with transbronchial biopsy performed in the lower right bronchus; also Agobiopsy of the right lower lobe consolidation was needed to histological characterization. Conclusive diagnosis was Polmuniary Non Hogdkin B cell Lymphoma – MALT Type.

**Conclusions:** Despite of its rarity, Polmuniary MaLT Lymphoma must be taken into account when approaching to CT presentation of alveolar opacities and Crazy Paving pattern since it has a favourable prognosis and many treatment strategies are available. Crazy paving pattern is mostly represented in ARDS, Polmuniary

infections and diffuse alveolar disease (such as Alveolar Proteinosis). Primary Pulmonary Lymphoma is a rare condition (only 1% of Lung Neoplasia – 3-4% of extranodal LNHS) but MALT Lymphoma represent over 80% of all lymphomas involving lungs. There is no ascertained relationship with common risk factors (smoke, sex, age, infections...) and only a moderate relationship with autoimmune stimulation of bronchial MALT (e.g. Sjogren) resulting in increased risk, 6.5-fold, of Lymphoma. Clinical manifestations are not specific. At Chest TC study MALT Lymphomas are more frequently bilateral (<60%) consolidations (55%); less frequently have a double pattern (<20%), GGO and septal thickening are less frequently represented (10-25%). Diagnosis includes exclusion of inflammatory and infectious conditions. Histological analysis of pulmonary specimens is necessary and is obtained with Bronchoscopy and Agobiopsy (positive diagnosis rates is 86-88% with a single biopsy). Immunohistochemistry is mandatory to confirm the diagnosis and assess a specific therapy. A correct diagnosis can be really challenging since clinical manifestation and anamnesis are not specific for this condition and radiological presentation of alveolar opacity matches with many, more common, etiologies.

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**Fig. 1.**

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**ID# 84**

## **Resolution of Insomnia by Means of Respiratory Rehabilitation and Diaphragm Manipulation**

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**Introduction:** Sleep is an active phenomenon of fundamental importance for the life of each individual, as it allows the restoration of somatic and mental functions that are spent throughout the day. A reduction in the quality, duration or cycles of sleep, compromising the body's ability to rest, can cause distinct disorders in insomnia, dysomnia and parasomnia. These disorders can be caused, or be the cause, by phenomena such as anxiety and stress. Stress represents a drive to act on various stimuli, which are considered as excessive, leading to a state of uneasiness; can make it difficult to fall asleep and disturb sleep itself, this is because stress activates hormonal mechanisms that compromise the natural lowering of cortisol levels in the evening, which keeps the body in a constant state of "arousal" and does not allow falling asleep.

**Objects:** The study aimed to demonstrate the influence of both breathing and anatomical structure (eg diaphragm mobility) on sleeping disorder with a particular focus on subjects in a chronic stress situation. The study didn't aim to only restore the normal biomechanics and physiology of the examined structures but, since recurrent stressors can determine the alteration of sleep, also evaluate the organism's ability to adapt to stressors during sleep.

**Case report:** One patient (female, white, 54 yo) was investigated before, during and after the treatment. Investigation was carried out by means of a questionnaire about sleep quality, number of awakenings during night, time necessary to fall asleep etc. The treatment consisted in manual HVLA techniques on metamers C3-C4-C5 (where the frenic nerve originates) + T11-T12-L1-L2 (insertions of the pillars of the diaphragm) + respiratory exercises teaching the patient to breathe using the diaphragm rather than the auxiliary muscle.

**Results:** At the end of the treatment (which consisted in 10 sessions) the hours of sleep increased from 6 hours per night to 8/9 hours per night. The time necessary to fall asleep decreased from 25/30 minutes to about 10 minutes and the number of awakenings during the night decreased from 6-7 to 2-3.

**Conclusions:** The study demonstrate that there is a strong connection between breathing and sleep. Sometimes in order to rebalance a patient's sleep (both in quality and quantity) we could decide to work with a physical and non pharmacological approach in order to restore the proper physiology of the structures which control the breathing processes and, in this way, bring the patient to an optimal situation during sleep.

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**ID# 85**

## **A Case of Hypersensitivity Pneumonitis Associated to Tobacco Snorting**

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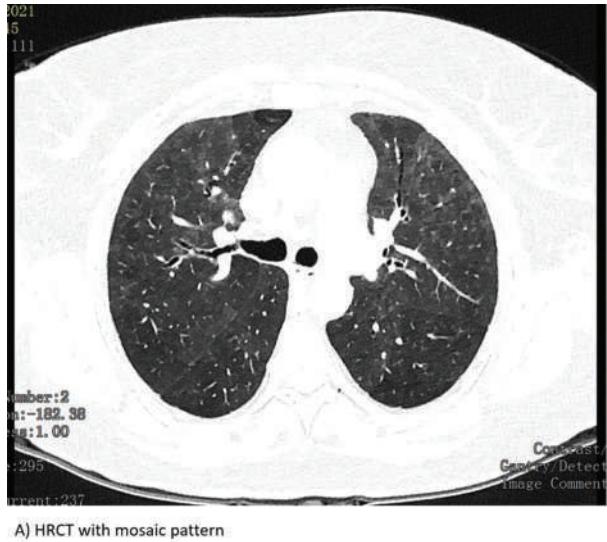
**Introduction:** Hypersensitivity pneumonitis (HP) are interstitial lung diseases determined by an immunologic reaction to an inhaled antigen following a chronic exposure. The most common organism leading to HP are thermophilic actinomycetes like *Micropolyspora faeni*, *Thermoactinomyces vulgaris*, and fungi like *Aspergillus*. Aetiology varies greatly from region to region. HP is underdiagnosed also because of geographical conditions, season, local customs, and proximity to industrial exposure. Generally, there is a higher prevalence of respiratory symptoms among farmers during non-dry climates in an indoor setting. The prevalence of farmer's lung seems to be higher in Asian countries than in Europe. The treatment of HP includes antigen avoidance and systemic steroids (1,2).

**Case report:** We describe the case of a 52-years-old woman, with a history of interstitial pneumonia in 2009, depression with personality disorder, obesity (BMI 34). Not smoker, takes care of farm animals. Refers usual tobacco snorting. Hospital admission in November-December 2020 for adverse event to paracetamol, associated with COVID-19 positivity. Precipitins titers were negative. The thorax HRCT showed an involvement of lung parenchyma with mosaic pattern, mostly at the upper lobes. The control-CT of March 2021 was unchanged (Figure 1A). Lung function was impaired with a restrictive pattern (FVC 67%, FEV<sub>1</sub> 60%) (Figure 1B). The patient underwent bronchoscopy with transbronchial biopsy (TBB) and bronchoalveolar lavage (BAL). BAL showed 45% Lymphocyte (CD8 67%, CD4), TBB Histology was consistent with the diagnostic Hypothesis of HP. The patient was prescribed to stop tobacco inhalation and initiated oral steroid therapy.

**Conclusions:** We would like to underline the importance of an accurate anamnesis to identify exposures responsible of HP development, in order to teach the patient the correction of bad habits and prescribe appropriate protection measures where antigen avoidance was not possible (2).

## **References**

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A) HRCT with mosaic pattern

	Theor	Best Pre	% (B/P)
FVC	3.07	2.05	67
FEV 1	2.62	1.57	60
FEV 1% FVC	79.22	76.27	96
MPEF 75/25	3.21	1.23	38
FEF 25	5.61	5.65	101
FEF 50	3.90	1.95	50
FEF 75	1.54	0.35	22
PEF	6.41	5.86	91
PIF		4.30	
FI/ F1		1.68	
FVC IN	3.16	1.68	53
VC IN	3.16	2.07	65
Data livello	07/04/21		
Ora livello	14:15		

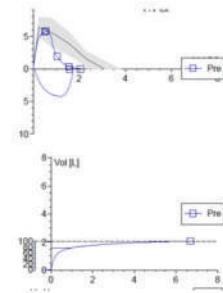


Fig. 1.

ID# 86

### Pulmonary Rehabilitation in COVID-19 Patients Admitted for Weaning from Ventilation and Tracheostomy

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**Introduction:** Patients with very severe forms of SARS-coronavirus-2 disease 19 (COVID-19) may need prolonged invasive mechanical ventilation (MV) through tracheostomy.

**Objects:** The aim of this study was to evaluate in a real-life setting the effectiveness of pulmonary rehabilitation (PR) in the weaning process from ventilation and tracheostomy.

**Methods:** Retrospective data analysis of patients with respiratory failure from COVID-19, consecutively admitted to a pulmonary rehabilitation weaning center in 12 months (March 2020–February 2021). Standard therapist-driven protocols of weaning were applied. Primary outcomes were weaning from mechanical ventilation and tracheostomy. Secondary outcomes were improvement of ADL (daily life activities), BIM (modified Barthel index), and rehabilitation complexity scale (RCS) scores. Weaning time was compared with our historical series of patients.

**Results:** Data of 51 patients were analyzed, mean age 66 yrs (range 23–81), M/F 39/12. Charlson comorbidity index varied from 0 to 5, mean 2. Mean length of stay (LoS) in semi-intensive care unit was 27 days (range 10–63), global LoS was 39 days (range 8–119). 6 pts died. 28 patients were weaned from MV in a mean time of 19 days (range 1–87). Weaning time of our historical series was 29 days (median, IQR 22–43) for polytrauma patients and 54 days (27–57) for other acute causes. In 41 patients tracheal cannula was removed after a mean time of 36 days (range 4–113); 10 patients

were discharged with tracheal cannula due to local complications, to be re-evaluated after 2–4 months. After rehabilitation, improvement in all secondary outcomes were registered (admission versus discharge): ADL 0,44 (0–6) vs 3,42 (0–6), BIM 6,7 (0–96) vs 51,2 (0–100), RCS 15,7 (7–18) vs 5,8 (1–16), mean(range), p < 0,01 for alla comparisons (paired t-test).

**Conclusions:** Pulmonary rehabilitation units with expertise in weaning from MV may have a significant role in the management of COVID-19 patients with a prolonged dependence from MV allowing acute units to accelerate turn over in a pandemic context of huge requirement of intensive care beds. PR impacted favourably on individual outcome measures in the large majority of patients.

ID# 89

### Changing Microbiological Epidemiology During and Before COVID-19 in a Tertiary Hospital ICUs

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**Introduction:** Severe acute respiratory syndrome 2 pandemic has had a heavy impact on national health system, especially in the first wave and principally in the Intensive Care Units (ICUs) occupancy. The large number of patients requiring hospitalization in

ICUs lead to a complete upheaval of intensive wards. The increase in bed, the fewer number of nurses per patient, the constant use of personal protective equipment, the new antimicrobial surveillance protocols could have had deeply effects on microbiological flora of these wards. Moreover, the overconsumption of antimicrobial therapy in COVID-19 patients, like several studies report, could have impact of this aspect.

**Objects:** To evaluate the changing pattern of microbiological epidemiology during and before COVID-19 pandemic in a tertiary hospital ICUs.

**Methods:** A retrospective, observational study was conducted in ICUs of "ASST Papa Giovanni XXIII" in Bergamo, a large tertiary referral hospital in Northern Italy. We collected the microbiological data from Bronchoalveolar lavage and Tracheal aspirate of patients hospitalized in ICUs from February 22 to May 31, 2020 (Period 1) and from February 22 to May 31, 2019 (Period 2). We calculated the odds ratio (OD) with 95% confidence interval (CI) to evaluate the difference of the prevalence of bacterial and fungal species and the resistant pathogens in the two study periods.

**Results:** A total of 194 COVID-19 patients were admitted to ICU in period 1 (65% of patients admitted to ICU), compared to 176 patients in period 2. 736 respiratory samples (3.8 per patient) and 392 (2.2 per patient) were collected during period 1 and 2, respectively. The proportion of positive respiratory specimens (for at least 1 pathogen) was 48% and 47.7% in period 1 and 2, respectively. In both periods, the most frequent bacterial isolates were *Pseudomonas* spp. and *Enterobacteriales*. The prevalence of *Pseudomonas* spp. shows a statistically significant increase from period 2 to 1, as well as the prevalence of *Enterococcus* spp. On the contrary, the prevalence of Gram negative non fermenting bacteria (GN-NFB), *Haemophilus influenzae* and *Streptococcus pneumoniae* showed a significant reduction between two periods. There was a statistically significant increase in resistance of *Pseudomonas* spp. to carbapenems and piperacillin/tazobactam and *Enterobacteriales* spp. for piperacillin/tazobactam, in period 1 compared to period 2, respectively.

**Conclusions:** A changing pattern in prevalence and resistance profiles of bacterial and fungal species was observed during COVID-19 pandemic. The longer ICU stay for COVID-19 patients and the antibiotic pressure could represent important risk factors for bacteria colonization and/or infection.

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## ID# 91

### Chest CT Signs of Aging Lung: Incidence and Impact on Mortality

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**Introduction:** As a result of an increasingly life expectancy and the widespread use of CT scans in daily clinical practice, incidental findings of pulmonary alterations in elderly have become more common.

**Objects:** The aim of the present study was to evaluate the incidence of the main signs of lung aging in a population of asymptomatic elderly subjects without known cardiopulmonary pathologies and to value their possible impact on mortality.

**Methods:** 151 consecutive subjects who had not a known history of cardio-pulmonary disease nor any respiratory symptoms and 40 patients with a diagnosis of IPF were enrolled in the study (133 males and 58 females, aged between 75 and 90 years). The 151 asymptomatic patients were checked at CT scan for signs of lung aging. Survival rate among the IPF patients and those with and without sign of aging lung was recorded.

**Results:** A relatively high proportion (78%) of asymptomatic old individuals presented signs of lung aging, including senile hyperinsufflation (14%), mosaic attenuation (36%), gravitational ground glass opacity (12%), increased bronchoarterial ratio (11%), pulmonary cysts (10%), peri-osteophyte ground glass (11%), apical pleural cap (19%), subpleural nodules (13%) and subpleural reticulation (9%). 42% of patients showed more than one sign of lung aging. With the only exception for senile emphysema/hyperinflation, we observed no correlation with a previous smoking history. Subject with signs of aging lung presented a higher mortality compared to those without alterations ( $p=0.04$ ), as aspect IPF patients showed the higher mortality rate ( $p<0.01$ ) than other groups.

**Conclusions:** Despite incidental Chest CT findings in a aged population may be part of the normal spectrum of senescent lung, they may imply a condition of greater frailty. In order to protect the health of the elderly person, therefore, physician should reinforce specific lung health advice, including avoid smoke, carry out the flu and pneumococcal vaccination, eat well, exercise and maintain a robust social network to stave off loneliness.

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## ID# 92

### Lactate Dehydrogenase and Therapeutic Strategy in COVID-19 Pneumonia

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**Introduction:** Inflammatory cytokine storm play a central role in disease progression of COVID-19. Many laboratory markers have been associated to an adverse outcome in COVID-19 patients. Lactate dehydrogenase enzyme (LDH) is a sensitive indicator of the cellular metabolic state, aerobic or anaerobic direction of glycolysis and cell injury. High lactate dehydrogenase level was significantly associated with severe COVID-19 pneumonia on admission.

**Objects:** To investigate if LDH, an easy laboratory test, could define the severity of COVID-19 pneumonia and guide physicians in their choice of therapeutic strategy.

**Methods:** We analyzed laboratory tests to identify tissue damage and inflammatory status in 102 COVID-19 patients (61 males and 41 females) admitted to Pneumology Department of Monaldi Hospital (Naples) from November 2020 to May 2021. We investigated the relationship between LDH values (normal range 80–300 U/L) and the type of therapeutic strategy (low and high flow oxygen therapy and non-invasive ventilation).

**Results:** Patients had a mean age of 71.75 years. Serum level of LDH was > 300 U/L in 64.38% of patients (first group) and <300 U/L in 35.62% of patients (second group). In the first group 65.5% of patients needed non invasive ventilation (CPAP/NIV), 29.76% needed high flow nasal cannulae oxygen therapy (HFNC) and 4.7% needed low flow oxygen therapy. In the second group 21% of patients needed CPAP/NIV, 51.32% needed HFNC and 27.68% needed low flow oxygen therapy.

**Conclusions:** LDH seems to be related to severity of COVID-19 pneumonia and to the type of therapeutic strategy. Moreover LDH value could guide physicians in the choice of respiratory support such as non-invasive ventilation.

## Reference

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### ID# 93

#### A Woman with a Diagnosis of Asthma and Multiple Pulmonary Nodules - a Case Report

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**Introduction:** Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) syndrome is a rare disorder that is characterized by the presence of respiratory symptoms, airflow obstruction, and constrictive bronchiolitis with nodular proliferation of the neuroendocrine cells with or without tumorlets/carcinoid tumors on histology. We describe the case of a woman with dyspnea and wheezing and multiple pulmonary nodules, suspecting DIPNECH.

**Case report:** A 55-year-old woman with a history of asthma from childhood came for worsening synthsms. She is a school-teacher with no history of exposure to chemicals or inhalants. She had no smoking history, no history of connective tissue disease, and no family history of lung disease. She had a history of allergies to parietaria and dermatophagoides. She was evaluated 7 years ago by another pulmonologist for shortness of breath, with a diagnosis of severe obstructive ventilatory defect. At FPT, there was a severe obstructive defect ( $FEV_1$  1.29 L, 54%pred), with air trapping (RV 2.53 L, 139%pred). At blood exams, there were many eosinophils (550 cells/mm $_3$ ), with a little increase of IgE. She underwent a chest

CT, with evidence of areas of mosaic perfusion to be attributed to air trapping, multiple pulmonary nodules in the lower left and right lobe (maximum diameter 5 mm). She underwent a PET scan, which did not show any significant uptake, and a diagnostic bronchoscopy was not informative. Due to the patient's refusal to undergo surgical lung biopsy, it was decided to carry out a careful clinical radiological follow-up of the pulmonary nodules. After 2 years, on the control chest CT the nodules are unchanged. These small nodules were predominantly present in areas of air trapping, often located along the centrilobular bronchovascular bundles. Due to the stability of the lesions and their radiological characteristics, we suspect DIPNECH in a patient with a history of asthma.

**Conclusions:** DIPNECH is an under-recognized disease characterized by proliferation of neuroendocrine cells in the bronchial wall, which preferentially affects middle-aged women. Patients are either asymptomatic or present with long-standing dyspnea due to obstructive syndrome that can be mistaken for asthma.

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### ID# 94

#### Post-Radiotherapy Eosinophilic Pneumonia: a Rare Case

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**Introduction:** A rare infiltrative syndrome similar to idiopathic chronic eosinophilic pneumonia (CEP) can develop up to 10 months after radiotherapy for breast cancer. Most of the patients have a history of asthma or allergy, presumably with a Th2-oriented lymphocyte response. Progressive onset of cough, dyspnea, and chest pain with systemic symptoms such as fever, asthenia, weight loss, fatigue are typical. Chest X-ray opacities are often misdiagnosed and may be unilateral (irradiated lung) or bilateral, with air-bronchogram and/or ground glass pattern, migrating and with upper/peripheral predominance. Peripheral blood and bronchoalveolar lavage eosinophilia is significant; rapid involvement is obtained with corticosteroid and relapses after treatment withdrawal are frequent. Because its clinical presentation is similar to bronchial asthma it is important to differentiate this two entities since their etiopathogenesis and management is different.

**Case report:** A former-smoker, 45 year old woman was admitted for dyspnea, wheezing and cough since 6 month. Past medical history included chronic nasal polyposis and right breast adenocarcinoma requiring infero-lateral quadrantectomy followed by radiotherapy (50GY) 18 months before. At chest examination bilateral wheezes and at blood tests elevated levels of eosinophils (700 mCL-12%), Tot-IgE (322 IU/ml), RAST+ dermatopagoides pt were observed, while chest X-Ray was normal. Pulmonary functional tests show severe obstructive pattern responsive to



**Fig. 1.**

salbutamol 400 mcg and reduction in  $DL_{CO}$ . So, diagnosis of severe allergic/eosinophilic bronchial asthma was made and beclomethasone/formoterol 200/6 mcg twice daily associated with omalizumab 450 mg subcutaneously monthly was prescribed. Five-months after, she was admitted again for worsening with fever, dry-cough, dyspnea, expiratory-wheezing. Blood tests show mild respiratory failure, C-Reactive Protein 10 mg/dl, eosinophils 2000mcL (20%), fibrinogen 520 mg/dl while chest HRCT-scan highlighted bilateral ground glass attenuation and consolidation predominantly in the upper lobes with septal-line tickening (Fig. 1). Diagnosis of CEP follow radiotherapy was confirmed at broncho-alveolar lavage showing elevated eosinophils (45%) and transbronchial biopsy of middle lobe with a pattern of interstitial and alveolar eosinophils, multinucleated giant cells and histiocytes while microbiological tests were negative. Prednisone 0.5 mg/kg/day was administered with slow tapering over 6 month and omalizumab was stopped, so patient underwent a rapid clinical- radiological improvement without any relapse.

**Conclusions:** This case report highlights the importance of differential diagnosis and phenotyping between similar respiratory diseases such as bronchial asthma and other forms of pulmonary eosinophilia.

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**ID# 95**

## Comparison of Lung Ultrasound and Chest Computed Tomography in the Evaluation of Severe Asthma

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**Introduction:** Transthoracic ultrasound (TUS) is an accepted complementary tool in the diagnosis of many pleuro-pulmonary diseases. However, its use in conditions in which the lungs are still aerated is debated and ultrasound findings are not specific.

**Objects:** The purpose of our study was to compare TUS and chest computed tomography (CT) scan in patients with severe uncontrolled asthma. In addition, ultrasound findings were correlated with pulmonary function.

**Methods:** 72 consecutive subjects with a diagnosis of severe uncontrolled asthma (Asthma Control Test score < 20) despite a treatment with high doses of ICS/LABA plus a LAMA, according to step 5 of GINA guidelines, were enrolled in the study (51 females and 21 males, aged between  $60 \pm 9$  years). A complete TUS exam

was performed to evaluate “gliding sign”, pleural thickening and subpleural nodules. Patients also underwent a CT scan in order to check signs of hyperinflation and parenchymal or bronchial abnormalities.

**Results:** In TUS imaging the main sign observed was the lack or reduction of the gliding sign in medial posterior and anterior thoracic scan. Patients showing absence of gliding sign, confirmed by a “Barcode” sign in M-mode, also showed signs of hyperinsufflation on CT scan and the highest TLC% ( $110.4 \pm 8.7$  vs  $86.8 \pm 8.9$ ,  $p < 0.0001$ ) and VR% ( $145.4 \pm 25.2$  vs  $90.1 \pm 20.3$ ,  $p = 0.0008$ ) values on plethysmography. In addition, we noticed that an irregular thickening of the hyperechoic pleural line ( $3.4 \pm 0.5$  mm) and subpleural nodules correlated with subpleural areas marked by distal airways inflammation (e.g. ground glass opacities, bronchiectasis, bronchial thickening).

**Conclusions:** A condition of hyperinflation in severe asthma patients may mimic ultrasound findings of pneumothorax (absence of gliding sign, Barcode in M-mode). To know this information is important especially in an emergency setting where an erroneous management due to a misdiagnosis based on ultrasound pattern only can lead to fatal consequences (e.g. the insertion of a chest tube in hyperinflated lungs). Furthermore, as peripheral airways have been recognized as a predominant site of inflammation, airflow obstruction and remodeling in severe asthmatics, performing a TUS in these patients could provide useful information on the state of the peripheral lung that could be used in the follow-up and which has a correspondence with CT imaging.

patients and 60% of those admitted to intensive care units survive. A more subacute or chronic stage of disease is however increasingly being reported in a portion of COVID-19 survivors that created a new syndrome named post-COVID (defined as presence of symptoms  $>3$  weeks from onset of COVID-19 symptoms) or Long or Chronic COVID (defined as presence of symptoms  $>12$  weeks). Telemedicine is a useful tool in mitigating the issues as well as providing a modality for continued care in not-hospitalized COVID-19 patients using during the infection period several electronic methods to deliver health information from a distance and give therapeutic changes.

**Objects:** To evaluate the impact of COVID-19 in a cohort of past-infected COVID-19 not-hospitalized patients treated during the infection at home with a telemedicine program and their conditions one month later from the negativity

**Methods:** We have evaluated during the period from 1 June to 1 July 2021 a cohort of 116 COVID-19 patients, stratified into 3 groups of severity (mild, moderate and severe) of COVID infection based on NIH criteria. Each patient was studied simultaneously using telemonitoring of vital parameters ( $\text{SaO}_2$ ; HR, RR and TC) and by telephone interview and scoring several items: dyspnoea (using mMRC scale); Fatigue (borg scale); QoL questionnaire (EuroQol 5-dimensional-5 levels, EQ-5D-5L, questionnaire); Neurological impairment (headache – vertigo/dizziness – Anosmia/ageusia – insomnia – Memory – brain fog). The monitoring was made in two different times (T0 and T1, from the day of the second nasopharyngeal swab negative test and after 4 week respectively). Lung ultrasonography will be performed at the T0 and T1 times for a small amount of patients of subgroup of COVID-19 severity.

**Results:** The results are showed in table 1.

**Conclusions:** This is the first study on a large cohort of post infection COVID-19 not hospitalized patients monitored and treated by telemedicine. Data suggest the pivotal role of a program of telemedicine on the monitoring of the vital parameters in patients during the infection and during one month after the negativity.

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## ID# 96

### Evaluation of the Past COVID-19 Infection in Not-Hospitalized Patients Monitored by Telemedicine

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**Introduction:** SARS-CoV-2 has spread rapidly with devastating consequences worldwide. Although mortality from acute COVID-19 rivals or exceeds that of influenza, 80% of hospitalized

**Table 1.**

	LIEVE (n=59)		MODERATA (n=25)		SEVERA (n=32)	
	T0	T1	T0	T1	T0	T1
<b>Età (anni)</b>	$40.7 \pm 19.6$		$45.9 \pm 13.7$		$61.1 \pm 16.1$	
<b>Δ-Infezione (gg)</b>	$14.2 \pm 5.3$		$14.6 \pm 6.7$		$19.2 \pm 11.4$	
<b>Nadir SaO<sub>2</sub> (%)</b>	96.1 ± 1.68	98.1 ± 1.14	95.1 ± 1.96	97.5 ± 1.46	91.4 ± 1.3	96.4 ± 2.5 *
<b>mMRC</b>	0.25 ± 0.59	0.05 ± 0.22 *	1.0 ± 1.1	1.11 ± 1.05	1.23 ± 1.42	1.18 ± 0.98
<b>Borg</b>	1.35 ± 2.42	0.82 ± 1.77	3.14 ± 2.56	3.67 ± 3.12	3.5 ± 2.73	3.09 ± 2.51
<b>EuroQol - Mobilità</b>	1.08 ± 0.34	1.09 ± 0.45	1.14 ± 0.36	1.33 ± 0.50	1.65 ± 1.96	1.18 ± 0.40 *
<b>EuroQol - Cura della persona</b>	1.06 ± 0.31	1.09 ± 0.45	1.05 ± 0.22	1.00 ± 0.1	1.23 ± 0.43	1.09 ± 0.30
<b>EuroQol - Attività quotidiane</b>	1.12 ± 0.38	1.09 ± 0.45	1.33 ± 0.48	1.56 ± 0.73	1.35 ± 0.49	1.27 ± 0.65
<b>EuroQol - Dolore/Discomfort</b>	1.16 ± 0.46	1.09 ± 0.45	1.29 ± 0.46	1.22 ± 0.44	1.27 ± 0.53	1.27 ± 0.65
<b>EuroQol - Ansia/Depressione</b>	1.34 ± 0.56	1.14 ± 0.49	1.42 ± 0.51	1.56 ± 0.44	1.27 ± 0.45	1.09 ± 0.30
<b>Ecografia polmonare (score)</b>	1.3	0.5	5.2	2.7	9.4	5.0

\*p &lt;0.05

**Tabella 1:** distribuzione dei parametri raccolti mediante telemedicina in una coorte di 116 pazienti COVID-19 con pregressa infezione in due differenti tempi (T0: alla negativizzazione – T1: dopo 4 settimane dalla negatività). Ai pazienti è stato somministrato telefonicamente un questionario sulla Qualità della vita (EuroQoL) multiparametrico. A tutti i pazienti è stata valutata a distanza la saturimetria e l'impatto della dispnea e della fatica muscolare.

**ID# 97****The Role of Radiological Phenotypes in the Management of the Hospitalised COVID-19**

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**Introduction:** COVID-19 pneumonia causes ARDS-like manifestations that can result in significant lung damage and death.

**Objects:** We have tried to identify radiological phenotypes that could help us understand this disease and the best treatment approaches.

**Methods:** This retrospective study was conducted on COVID-19 hospitalised patients admitted to our Units from March to December 2020. All patients who had undergone a chest CT scan

were enrolled and classified into one of three phenotypes (PH1, PH2 and PH3) according to the agreement between two blinded pulmonologists. Several parameters at admission and clinical outcome at 28-days were collected from each patient.

**Results:** One-hundred-twenty patients (age  $62.9 \pm 14.79$  yrs, 69.2% male) were enrolled and underwent chest CT scans. Inter-reader agreement of phenotype classification was excellent ( $k > 0.81$ ) for each phenotype. Clinical and laboratory data showed D-dimer levels higher in PH2 than each other phenotype, at all measurements. Most of PH3 patients needed support ventilation (72%, 28/39), vs. 60% (18/30) of PH2, and 51% (26/51) of PH1 during hospitalization. Analysing the mortality at 28-days, PH1 had a favourable outcome, while the majority of deaths (10/18) were observed in PH3-assigned patients.

**Conclusions:** Evaluating clinical and laboratory data of each CT phenotype, we found a more favourable outcome in PH1, higher mortality in PH3 and D-dimer levels three times higher than the others in PH2 with no differences in time to clinical deterioration and CT scans. Therefore, we could hypothesise that the three radiological phenotypes found in our patients might be independent and not one the evolution of the other.

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**ID# 98**

## **Radiological Phenotypes and Clinical Efficacy of Pronation in COVID-19 Pneumonia**

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**Introduction:** COVID-19 pneumonia has a large spectrum of clinical severity. A significant proportion of patients develop severe acute respiratory failure (ARF) that needs mechanical ventilation. The anomalies observed on chest CT scan allow to identify specific radiological phenotypes to diversify treatments and ventilator settings. Prone positioning is effective in reducing mortality in invasively ventilated ARDS patients, so it has also been proposed for COVID-19 pneumonia.

**Objects:** The aims of the study were a) to correlate radiological phenotypes with clinical severity outcomes and b) to compare the phenotypes in terms of survival and response to pronation in COVID-19 patients admitted to our hospital.

**Methods:** 61 patients were evaluated (42 M), aged 63.3 + ( $\pm 12.82$ ) admitted to our Covid Hospital between November 2020 and April 2021. All patients were assessed with Severity Score index, blood gas analysis, blood chemistry tests, chest x-ray, chest HRTC. Prone position was indicated whenever patients had a  $\text{PaO}_2/\text{FiO}_2$  (P/F) ratio lower than 200.

**Results:** There are no statistically significant differences between the phenotypes in terms of age, BMI, blood chemistry tests, days of hospitalization and mortality during the admission. There were significant differences in terms of a) P/F ratio: phenotype 1 is on average > 200, decrease to 154 and 162 for phenotype 2 and 3 ( $p = 0.04$ ), and b) response to pronation: P/F ratio increased significantly in 50% of patients in phenotype 1, in 84% of patients in phenotype 2, and in 65% of patients in phenotype 3. There were no differences in terms of days of hospitalization (on average  $21.45 \pm 7.821$ ) and mortality between phenotypes.

**Conclusions:** Patients with COVID-19 pneumonia can be divided into three different radiological phenotypes with different characteristics in terms of clinical features and response to prone position. Prone positioning has the main purpose of improving oxygenation and preventing tracheal intubation, so an early individuation of responders to pronation could be very important.

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**ID# 99**

## **Vocal Re-Education in a Group of Women with Osteovox and Osteopathic Techniques**

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**Introduction:** Vocal re-education is a growing field that deserves further study, multidisciplinary techniques require transversal skills.

**Objects:** In a group of 5 female singers, who arrived for gastroesophageal reflux cough, with dysphonia, never smokers, never drinkers, with no history of asthma or COPD, no acute events in progress. We proposed a re-education cycle with vocal, osteopathic and spirotiger techniques with the MvM Italy instrument. All women, aged between 18 and 50, on average 34.4, were of normal weight, had 4 out of 5 anxiety disorders.

**Methods:** The treatment lasted 3 sessions, made use of respiratory gymnastics with Spirotiger with respiratory rate 13 acts per minute, 3 liters maximum volume. Exercises to lengthen the anterior muscle chain, diaphragmatic breathing and training with Vocal Coach singing with arpeggios on ascending scales, lip trill, osteopathic diaphragmatic mobilization techniques and cycles with spirotiger.

**Results:** The disturbances regressed, the patients were able to sing a higher semitone and the dyspnea was eliminated, the voice had more volume, elasticity, timbre and agility.

**Conclusions:** In all women the sound tension has improved, the strong emotionality has decreased, the tremor in the voice has regressed, the voice from "angular and metallic" has become deep and emotional, with the voice I am able to communicate emotions, in the spoken voice the articulation, the phonatory pauses and the dynamics improve, the voice becomes soft and harmonious and effortless.

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**ID# 101****Is Outpatient Rehabilitation Effective in Severe COPD Elderly Patients? The Answer from the Real Life**

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**Introduction:** Pulmonary rehabilitation is well known to be effective in chronic obstructive pulmonary disease (COPD) and other pneumopathies. However, its effectiveness is often questioned in elderly patients, especially in those who suffers from severe disease and other comorbidities.

**Objects:** The aim of the study was to evaluate the functional effects of a supervised respiratory rehabilitation program conducted by a multidisciplinary team (medical staff and physiotherapists) in an outpatient setting in a cohort of elderly subjects with severe and very severe COPD according to the GOLD guidelines.

**Methods:** The cohort was made of 60 subjects (50% men, 50% women) with a mean age of 72 +/- 9.5 years suffering from severe and very severe COPD in stable conditions. 16 subjects were on long term domiciliary oxygen. All patients were assessed upon entry into the facility (T0) and at discharge (T1) based on the modified MRC (Medical Research Council), CAT (COPD Assessment Test) and 6MWT (6 Minutes Walking Test) values. The rehabilitation program was made of 18 individual sessions with a frequency of two sessions per week. We focused on drug and oxygen therapy optimization, self-care educational interventions, bronchial clearance and respiratory re-education techniques, retraining the upper limbs to effort through crank ergometer and lower limbs through mobile platform.

**Results:** Mean initial values were mMRC 2 +/- 0.79; CAT 17 +/- 6.49; 6MWT 249 +/- 106.27 metres. Training intensity was 60-70% of the maximum functional exercise capacity. Data statistical analysis was carried out using the student's t test. Statistical significance was considered when p value was <0.001. Mean final values were mMRC 1 +/- 0.9 (p<0.00001); CAT 12 +/- 5.99 (p<0.00001); 6MWT 330 +/- 121.44 (p<0.00001) with a median percentage increase of 75.16. There was no statistically significant difference based on gender.

**Conclusions:** Outpatient respiratory rehabilitation managed by a multidisciplinary team proved to be significantly effective in improving symptoms, exercise tolerance and quality of life in a cohort of elderly subjects with severe and very severe COPD regardless of gender.

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**ID# 102****Pulmonary Embolism and SARS-CoV-2 Pneumonia: a Possible Predictive Role of Serum IgG?**

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**Introduction:** Pulmonary embolism (PE) is one of the most significant complications in patients with acute respiratory failure due to SARS-CoV-2 pneumonia. Its development seems to be linked to cytokine storm mediated by pro-inflammatory interleukins and systemic inflammatory response. The incidence of thromboembolic events, and their predictive factors, are still unclear (1).

**Objects:** To evaluate the incidence of PE in patients with SARS-CoV-2 pneumonia and to investigate possible associated biomarkers.

**Methods:** We consecutively enrolled patients with SARS-CoV-2 pneumonia, between November 2020 and January 2021, who performed a computerized tomography chest angiography (CTA) in the emergency department or during hospitalization based on clinical suspicion for PE. All patients were treated with thrombosis prophylaxis before performing CTA. Data are expressed as mean +/- standard deviation (SD) for normally distributed variables and median [IQR] for non-normally distributed variables. Differences between subgroups were tested by t-test for normally distributed variables and by Mann-Whitney U test for independent samples for non-normally distributed variables. Statistically significant differences were tested with Chi-square test.

**Results:** We enrolled 51 total patients, 12 (23%) had PE (table 1). Of the 44 patients for whom the D-dimer assay was available, 79.5% (35) had elevated D-dimer values (upper limit of normal 0.25 mg/L). D-dimer values were not significantly different between patients with or without PE. Serum IgG (S-IgG) value showed a statistically significant negative association with PE, even after correction for body temperature (BT) and systolic blood pressure (SBP). Values of S-IgG > 11.85 g/L in our series, presented 100% specificity for the absence of PE.

**Conclusions:** D-dimer value in patients with SARS-CoV-2 pneumonia may not be informative for diagnosis of PE, at least when used as a single observation, whereas low levels of S-IgG could be a possible marker of PE. Furthermore the role of elevated serum IgG as negative predictor for PE needs further study.

**Reference**

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**Table 1.** Clinical findings of population.

Parameters	All patients	Patients without PE (number or media±standard deviation or median and range)	Patients with PE (number or media±standard deviation or median and range)	p
<b>Sex (M/F)</b>	51 (36/15)	39 (28/11)	12 (8/4)	Ns
<b>Age (years)</b>	67±18.9	65.6±20 (38)	71.0±13.6 (11)	Ns
<b>BMI (range)</b>	26.0±3.54	26.1±3.9 (38)	25.7±2.6 (11)	Ns
<b>Systolic blood pressure (mmHg)</b>	137±23	142±21 (36)	120±26 (10)	0.009
<b>Diastolic blood pressure (mmHg)</b>	73.8±12	75±12 (36)	67±10 (10)	Ns
<b>Heart rate (beats/minute)</b>	93±20	91±20 (36)	101±20 (10)	Ns
<b>Respiratory rate (breaths/minute)</b>	28.4±7.8	25.6±7.5 (36)	33.6±6.0 (10)	0.06
<b>Body temperature (°C)</b>	37.1±0.99	37.3±1.0 (36)	36.6±0.7 (10)	0.05
<b>D-dimer (mg/l)</b>	0.54 [0.30-1.57]	0.850 [0.365-2.715] (34)	0.32 [0.255-0.645] (12)	0.096
<b>Ferritin (mcg/l)</b>	814 [258-1147]	612 [243-1153]	835 [340-1125]	Ns
<b>C-reactive protein (mg/l)</b>	55 [12.5-117.5]	55[13.5-117.5]	55 [8.25-130.7]	Ns
<b>Procalcitonin (mcg/l)</b>	0.13 [0.06-0.35]	0.13 [0.05-0.46]	0.11 [0.08-0.2]	Ns
<b>Serum IgG (g/L)</b>	10.12±2.54	10.7±2.3 (29)	8.05±2.2 (9)	0.003
<b>Serum IgA (g/L)</b>	2.58±1.32	2.5±1.42 (29)	2.68±0.97 (9)	Ns
<b>Serum IgM (g/L)</b>	1.20±0.847	1.34±0.91 (29)	0.77±0.37 (9)	0.079
<b>pO<sub>2</sub> (mmHg)</b>	66±30	66.6±34.2 (31)	67.1±13.5 (11)	Ns
<b>pCO<sub>2</sub> (mmHg)</b>	35±7.8	35.4±8.6 (31)	33.8±4.7 (11)	Ns
<b>Lactate (mmol/l)</b>	1.49±7.34	1.45±0.76 (24)	1.62±0.68 (8)	Ns
<b>P/F (mmHg)</b>	224±108	200±109 (31)	302±70 (11)	Ns

**Abbreviations:** PE pulmonary embolism; P/F PaO<sub>2</sub>/FiO<sub>2</sub>; NS not significant.

### ID# 103

### Fight Lung Cancer in a Population of At-Risk Smokers

#### Rosastella Principe

Pneumological Day Hospital and Pulmonary Interstitial disease-Smoking Cessation Center, S. Camillo-Forlanini Hospital, Rome, Italy

**Introduction:** On November 10, 2014, the American medical insurance program MEDICARE approved Lung cancer screening, in light of the scientific evidence provided by the National Lung Screening Trial (NLST) 1 - which demonstrated a 20% reduction in lung cancer mortality with early diagnosis linked to screening projects with low-dose helical chest computed tomography LDCT- in subjects between 55 and 74 years old. In Italy, lung cancer screening has not yet been included in the Essential Assistance Levels (LEA). For this reason we have joined in our hospital to a national multicenter work in order to provide data.

**Objects:** The S.Camillo-Forlanini Hospital of Rome participated through funding from the European Oncological Institute of Milan in a national multicentre study lasting 2 years and aimed at early diagnosis of lung cancer through LDCT and the participation of the Smoking Cessation Center SCC, in order to diagnose the cancer early and to know the response to smoking cessation within the screening.

**Methods:** The study used LDCT in a population range of smokers and former smokers at risk > 55aa of age and Pack Year>30

or former smokers of less than 15ya. This screening saw as protagonists - in a multidisciplinary team with a personalized approach to the patient - the UUOOCC of thoracic surgery for the selection of smoking patients, of radiology for the execution of the LDCT and the pneumological SCC, this achieved through group/individual meetings with cognitive-behavioral and pharmacological therapy: NRT, bupropion, varenicline, cytosine.

**Results:** In our Hospital out of 860 LDCTs performed, 13 lung tumors were identified and it was possible to operate 10 people. Of the smokers only the residents of Rome went to the SCC for a total of 282 and decided to start the smoking cessation process 76 (27%), the percentage of cessation at one year was 56%, well above the percentages obtained by the same SCC (30%) outside a lung cancer screening program.

**Conclusions:** The positive interaction between LDCT execution and smoking cessation program produced an unexpected result on smoking cessation rates and other Review Article have confirmed our evidence later (2). Unfortunately in Italy lung cancer screening it has not yet been approved by our National Health Service, now for the realization it is necessary a collaboration with the health institutions dedicated to prevention and SCC must be an integral part in lung cancer screening because quitting smoking in this area reduces mortality (3).

### References

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2. Moldovanu D, et al. Tlcr 2021;10:2.
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ID# 104

## An Unusual Case of "Pleuritis"

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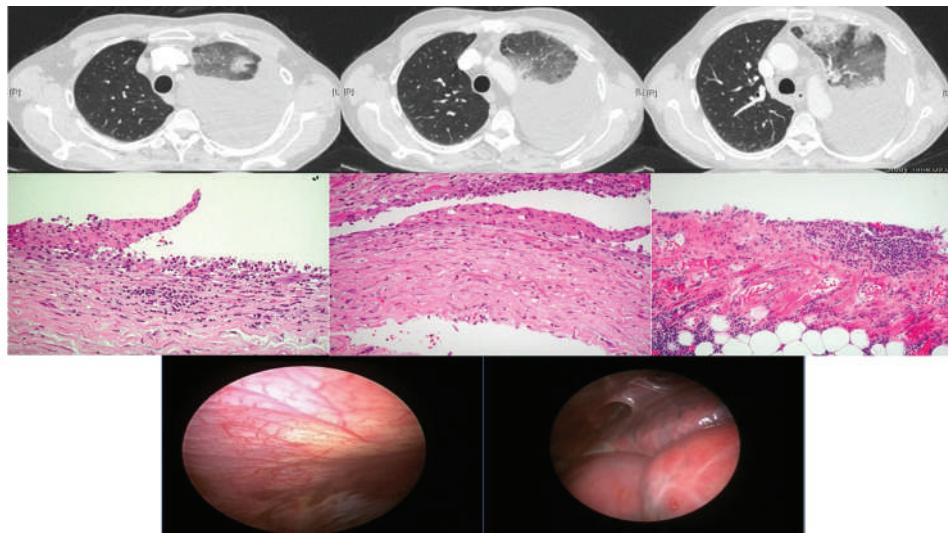
**Case report:** A 62 year-old caucasian male was evaluated by our consultant for six months history of exertional dyspnea, dry cough and fatigue. He was a previous smoker (20 pack/year,) quitted 10 years ago. His medical history was characterized by dyslipidemia and permanent Atrial Fibrillation (AF) in anticoagulant therapy (Rivaroxaban 20 mg) resistant to double radiofrequency ablation (2018- 2019) Laboratory exams showed: mild anaemia (Hb: 11.4 g/dl) and increased values of c reactive protein (6.9 mg/dl), erythrocyte sedimentation rate (96 mm/h), Dimer: 788 ng/ml, and B-type natriuretic peptide (105 pg/ml). Blood gas was normal. Pulmonary function test was compatible with a restrictive pattern. TC scan excluded pulmonary embolism and revealed a large left pleural effusion, associated with parenchymal consolidations of left lower lobe and ground-glass opacities. A thoracentesis was performed and pleural liquid was compatible with an exudate. Cultural exam resulted negative and cytologic evaluation showed mesothelial reactive cells. A medical thoracoscopy was performed and showed pleural hyperemia associated with prominent subpleural blood vessels. No pleural mass or nodular lesions were detected. Histologic exam was compatible with pulmonary capillary

hemangiomatosis and arterial medial hypertrophy and considering patient's medical history a diagnosis of acquired pulmonary vein stenosis (PVS) was proposed. Transthoracic Echocardiography showed mild bi-atrial dilatation, mild right ventricle dilatation with normal function. Normal systolic function (EF: 55%). Pulmonary Arterial Pressure (PAPs) was 45 mmHg Patient denied consent to perform further diagnostic procedures in order to confirm iatrogenic pulmonary vein stenosis and he refused cardiological follow-up and any potential treatment.

**Conclusions:** PVS is a rare condition characterized by a progressive lumen size reduction of one or more pulmonary veins and subsequent raising of lobar capillary pressure and It can have congenital or acquired origin. Radiofrequency ablation for AF has become the main cause of acquired PVS and it should be considered in all patients presenting with respiratory symptoms after cardiac surgery or radiofrequency ablation. In asymptomatic or mild form (<50% stenosis), no intervention is required. On the other side, symptomatic or ≥ 75% stenosis needs surgery or transcatheter therapy. Although imaging techniques are essential to rule out other causes of PVS and to assess its hemodynamic effect, it appears crucial the role of multidisciplinary interaction among clinicians from different specialties (pulmonologist, cardiologist, internal medicine specialist) and pathologists in order to achieve the challenging diagnosis such as PVS and to define a correct treatment, since its poor prognosis.

## References

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**Fig. 1.**

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ID# 105

## A Patchy Pneumothorax Associated with SARS-CoV-2 Pneumonia

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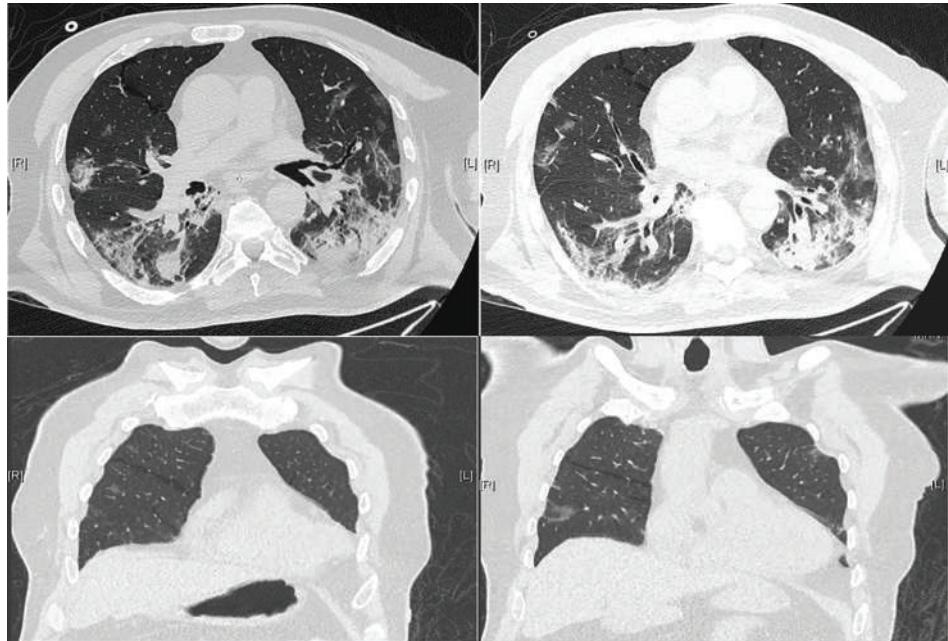
**Case report:** A 65 year-old caucasian male was admitted at Covid Unit of our Department for six days history of fever ( $38^{\circ}\text{C}$ ), dyspnoea, dry cough and fatigue. He was a previous smoker (20 pack/year) quitted 20 years ago. His medical history was characterized by dyslipidemia and hypertension. Laboratory exams showed: mild anaemia (Hb: 11.4 g/dl), leucocytopenia and increased values of c reactive protein (11.2 mg/dl), erythrocyte sedimentation rate (127 mm/h) and Dimer (788 ng/ml). Blood gas on room air was compatible with hypocapnic respiratory failure (pH: 7.48; PaO<sub>2</sub>: 49 mmHg; PaCO<sub>2</sub>: 32 mmHg). Chest xRay shows a bilateral ground glass opacities, suspicious for an interstitial pneumonia SARS-CoV-2 RT-PCR nasopharyngeal testing was positive. Patients was treated with high flow nasal cannula and standard medical therapy (heparin, Remdesivir and methylprednisolone) Chest TC scan confirmed the presence of bilateral ground glass opacities, but pneumothorax and pneumomediastinum were excluded. After 3 days, he developed sudden onset right-sided chest pain. A cardiovascular origin of symptom was excluded and a second chest TC

scan revealed a little pneumomediastinum (PM) associated with a patchy, intrascissural pneumothorax (PNX) on the right side. For particular position and small dimension of PNX, invasive procedure (like thoracentesis and chest drainage tube) was excluded and a conservative approach was preferred. A control chest TC scan, performed after one week, showed a complete resolution of PNX and pneumomediastinum.

**Conclusions:** Usually pneumothorax is caused by an external agent (like trauma), but it can develop spontaneously. Typical patient is a tall and thin man, with congenital (like alpha-1 anti-trypsin deficiency or Marfan syndrome) or acquired pulmonary disease (chronic obstructive pulmonary or malignancy) PNX and PM are relatively common complication during SARS-CoV-2 Pneumonia, particularly in mechanically ventilated patients, who experimented worse prognosis and a higher mortality compared to those who did not develop this complication. Moreover spontaneous PNX can be an unusual manifestation COVID-19, but it is more frequent than in general population and it is associated with worse outcomes. The mechanism, although not clear, could be due to the association between damage and consecutive rupture of subpleural alveoli (due to infection) and increased intrathoracic pressures (secondary to cough). In conclusion PNX and PM could be considered in patient with SARS-CoV-2 pneumonia, with rapid and apparently inexplicable onset of chest pain and shortness of breath.

## Reference

Mirò O, et al. Chest 2021;159:1241–55.



**Fig. 1.**

ID# 106

## **Compliance with Drug Therapy During SARS-CoV-2 Lockdown in Patients with Respiratory Disease**

Rosastella Principe

Pneumological Day Hospital and Pulmonary Interstitial disease-Smoking Cessation Center, S. Camillo-Forlanini Hospital, Rome, Italy

**Introduction:** Low compliance with drug therapy in patients with chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD) was a well-known issue even before the current coronavirus pandemic, for this reason we wanted to investigate this aspect during this period.

**Objects:** The aim of the study was to verify adherence to drug therapy in patients with respiratory disease during the COVID-19 pandemic caused by severe acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2), which led to lockdown in Italy from March 2020 to May 2020 with consequent suspension of monitoring visits.

**Methods:** From June 2020 to September 2020, every patient with access to pneumological check-up who had been unmonitored during lockdown was given an anonymous voluntary questionnaire, where self-reported information was requested; personal data, as well as multiple-choice questions about respiratory disease, continued treatment, respiratory therapy interruption or reduction during lockdown, the reasons for interruption, the medications affected, presence or absence of disease recurrence, the name of the referring physician, tobacco abuse and the result of a SARS-CoV-2 test, if done. The completed questionnaire data were digitized and collected in a database after two-step verification of the information.

**Results:** In total, 418 questionnaires were collected, 39 (9.3%) were not filled out; 33 (7.9%) had been completed by Stop Smoking Clinic patients with or without respiratory disease or tobacco-related symptoms; 58 (13.9%) had been answered by first access patients; and 4 (1%) had been filled out by patients that do not take any medication. The remaining 284 (67.9%) were completed by patients with respiratory disease who were undergoing drug treatment before lockdown, and these represent the subject of this study: 179 patients (63.0%) responded positively to the

pathologies		num ber of pa- tien- ts	age (years)	sex (%)		therapy continued during lockdown (%)					reasons for interruption (%)			exacerbations (%)			smoking (%)							
				men	women	yes	no	parti- cipa- tion	NA	geo- graphy	trou- bles	expi- riation	oth- er	ye- rs	no	NA	smo- ker	form	never/ smo- ker	NA				
1	ASTHMA	36	32, 19	24	65	0	0	65.8	26.3	5.3	2.6	21.1	0.0	5.3	0.0	5	84	10	10.5	21.1	60.5	7		
1	COPD	34	70, 19	52	41	5	0	79.4	17.6	2.9	0.0	5.9	2.9	8.8	0.0	2	94	2	2.9	4.	23.5	47.1	29.4	0
1	EMPHYSEMA	33	66, 12	51	45	3	0	60.6	36.4	3.0	0.0	21.2	0.0	6.1	0.0	1	8	1	42.4	39.4	18.2	0	0	
1	CHRONIC BRONCHITIS	26	6, 0	2	0	8	42.3	53.8	3.8	0.0	42.3	0.0	0.0	0.0	3	76	19	2	38.5	34.6	26.9	0	0	
1	PULMONARY FIBROSIS	26	70, 14	73	26	0	0	65.4	23.1	11.5	0.0	11.5	0.0	7.7	3.8	7	9	4	15.4	46.2	38.5	0	0	
1	BRONCHIECTASIS	14	8, 0	4	6	0	50.0	28.6	21.4	0.0	21.4	7.1	7.1	3	3	3	4	14.3	21.4	64.3	0	0		
1	other	37	8, 2	1	8	1	48.6	37.8	5.4	8.1	18.9	0.0	8.1	2.7	0	0	0	0	18.9	35.1	37.8	1	0	
2	CHRONIC BRONCHITIS AND ASTHMA	7	68, 10	28	71	0	0	85.7	14.3	0.0	0.0	14.3	0.0	0.0	0.0	14	85	0	0	0	0	0	14	0
2	COPD AND EMPHYSEMA	6	69, 3	66	33	0	0	93.3	16.7	0.0	0.0	0.0	0.0	16.7	0.0	0	3	7	0	0	14.3	14.3	57.1	0
2	EMPHYSEMA	5	70, 9	80	20	0	0	60.0	20.0	20.0	0.0	0.0	20.0	0.0	0.0	0	20	40	40	0	0	0	40.0	0
2	COPD AND ASTHMA	4	84, 8	25	75	0	0	50.0	25.0	25.0	0.0	25.0	25.0	0.0	0.0	0	25	75	0	0	0	0	100	0
2	CHRONIC BRONCHITIS AND COPD*	2	58	1	1	1	1									1	1						2	
2	EMPHYSEMA AND PULMONARY FIBROSIS*	2	75													1	1						2	
2	FIBROSIS*	2	86			2				2						1	1						2	
2	BRONCHIECTASIS AND PULMONARY FIBROSIS*	2	69													1	1						1	
2	CHRONIC BRONCHITIS AND PULMONARY FIBROSIS*	1	71			1			1			1			1	1						1		
2	COPD AND PULMONARY FIBROSIS*	1	58			1			1							1							1	
2	EMPHYSEMA AND BRONCHIECTASIS*	1	60			1			1							1							1	
2	CHRONIC BRONCHITIS AND BRONCHIECTASIS*	1	63			1			1							1							1	
2	ALL COMBINATIONS AT LEAST COPD, ASTHMA AND	14	68, 11	42	57	0	0	71.4	28.6	0.0	0.0	0.0	7.1	7.1	7.1	35	50	14	35.7	28.6	35.7	0	0	
2	EMPHYSEMA	6	66, 9	50	50	0	0	83.3	16.7	0.0	0.0	0.0	0.0	16.7	0.0	7	0	3	16	50	33	0	0	
2	COPD AND ASTHMA	5	64, 12	40	60	0	0	80.0	20.0	0.0	0.0	0.0	0.0	20.0	0.0	0	0	0	40	40	40	0	0	

\* group formed by 1 or 2 patients only; absolute values are reported instead of percentages

GP: general practitioner; TP: treatment plan; NA: not available

Respiratory patients grouped by type and number of coexisting respiratory pathologies: 19 patients out of 284 did not report on this question, and thus were not included in the table.

**Fig. 1.**

continuation of therapy, 18 (6.3%) reduced the dosage of their medication and 82 (28.9%) interrupted the therapy.

**Conclusions:** Although the study was conducted on a small number of cases our conclusions are in agreement with the OsMED report for the 2020 lockdown period (1,2). OsMED attributed this success to the health strategy used to support continuity of care for chronically ill patients, which involved extending the period of validity of treatment plans; encouraging access to medication by the use of electronic prescriptions; and continuously updating relevant information on institutional sites during lockdown. This pandemic has shown the need for new digital communication platforms to improve health education and to provide answers to patients seeking healthcare information with inclusion of the role for pharmacists in the treatment and monitoring of patients with chronic conditions.

## References

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2. The Medicines Utilisation Monitoring Centre. Report on Medicines use during COVID 19 epidemic Year 2020. Rome: 2020 www.aifa.gov.it

blood chemistry tests, ABG and cardiological evaluation. In addition to the standard therapy, we gave patients an aerosol with Taurisolo® (3 times a day) for the entire hospitalization.

**Results:** The sample had an age of  $55 \pm 10.13$  years. The Chung score (for evaluate the extent of disease at CT) was between 8/20 and 17/20. Most of the patients were male (70.9%). All enrolled patients had a  $pO_2/FiO_2 > 200$ . With the exception of one patient, who died of massive pulmonary embolism and suffered from severe cardiological comorbidities, no patients treated with Taurisolo® needed to be admitted to the Intensive Care Unit. They reported an improvement in dyspnea already from the first administrations. The average hospital stay of the patients was 7 days, with home discharge. At the 28-day follow-up, no patients required oxygen therapy, nor did they report cough or myalgia. No serious adverse events: a patient with a history of asthma reported cough, so we stopped the somministration with disappeared of synthom.

**Conclusions:** In this preliminary study, the administration of Taurisolo® seems to reduce the need for admitted to the Intensive Care Unit. Patients reported improvement in respiratory symptoms, with a reduction in hospital stay. Further studies may highlight the role in reducing inflammation index levels. In the future, perhaps, Taurisolo® can be used at home in early COVID-19 patients, even in other viral infections.

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### ID# 108

#### The Potential Therapeutic Role of Taurisolo® in the Outcome of Patients with COVID-19 Pneumonia

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**Introduction:** The SARS-CoV-2 pandemic records a significant rate of morbidity and mortality. The pathogenesis of pneumonia and acute respiratory distress syndrome is characterized by widespread endothelial, capillary and alveolar damage with release of inflammatory cytokines, pulmonary edema and oxidative stress. Taurisolo® is a polyphenolic extract obtained from the pomace of Aglianico cultivars with antioxidant and anti-inflammatory activity. Taurisolo® can reduce Reactive Oxigen Species (ROS) levels by direct scavenging of free radicals, modulation of endogenous anti-oxidant defenses, inhibition of metal-dependent production of free radicals and the activity of enzymes that produce them.

**Objects:** In our study, we evaluated the role of Taurisolo® to improve the outcome in patients with COVID-19 pneumonia. The admitted rate for the Intensive Care Unit represents a solid clinical endpoint that well characterizes the clinical progression of the disease.

**Methods:** We recruited 31 patients (22 males and 9 females) with COVID-19 pneumonia at U.O.C. Pneumotisiologia Federico II, Monaldi Hospital (Naples), from November 2020 to May 2021. All patients performed nasopharyngeal swab for SARS-CoV-2, high-resolution chest CT scan for evaluation of extend of disease,

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### ID# 109

#### Radio-Histological Correlation in Patients with Pulmonary Vein Stenosis: a Case Series

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**Introduction:** Worldwide, atrial fibrillation (AF) affects 1-2% of the population, with increasing prevalence. Left atrium (LA) transcatheter linear radiofrequency (RF) ablation is a therapeutic option in patients with AF. 1 Recent advances in knowledge allowed a significant reduction of complications. Nonetheless, transcatheter RF ablation has been associated with rare but life-threatening complications, such as pulmonary vein stenosis (PVS). 2 Here we present two cases of PVS after transcatheter RF with data obtained by pleural/lung parenchyma biopsies and discuss the radiologic-pathologic correlations.

**Methods:** Patient N 1. A 48-years-old non-smoker woman presented with a history of waxing and waning left lower lobe consolidations, recurrent fever, moderate dyspnea on exertion and left chest pain. She was treated with a RF ablation 14 months before for a long-standing AF. Pulmonary function tests (PFT) showed only a slight decrease of  $DL_{CO}$  (62% of predicted). Laboratory tests

revealed mild leukopenia, moderate anemia with normal CRP level. Patient N 2. A 50-years-old nonsmoker was admitted for hemoptysis. He was treated with a RF ablation 10 months before for an uncontrolled paroxysmal AF. PFT were unremarkable and laboratory tests documented only a mild anemia. Patients underwent high resolution CT (HRCT) scan and lung biopsy. In case N 2 a pleural biopsy was also carried out.

**Results:** In both cases HRCT scan showed, in affected areas, multiple ill-defined rounded opacities in the subpleural regions, smooth and peripheral thickening of the interlobular septa. Mediastinal window of the CT scan showed a stenotic aspect of pulmonary veins. Furthermore, in case N 2 a significant pleural thickening associated with loculated effusion was present. The histological examination, obtained by transbronchial and pleural biopsy with cryoprobe, showed chronic fibrosing pleuritis and multiple hemosiderin macrophages in the alveolar lumen. The visceral pleura appeared thickened and fibrotic with mesothelial hyperplasia. The interlobular septa, as well, looks thickened because of edema and fibrosis. The pulmonary veins presented partial or complete obliteration of the lumen by organized thrombi. The alveolar spaces mainly around interlobular septa were occupied by hemosiderin-laden macrophages and the alveolar septa were expanded by dilated capillary superimposed in rows (capillary hemangiomatosis-like aspects). Areas of parenchymal ischemic necrosis were also evident.

**Conclusions:** CT aspects of pulmonary vein stenosis (PVS) as a complication of transcatheter RF are comparable to that observed in veno-occlusive disease as the histological background suggests. The presence of ischemic, infarction necrosis is dissimilar; indeed, alveolar consolidation is the more significant difference between the two entities.

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ID# 110

### Role of HACOR Score in Predicting Noninvasive Ventilation Failure in Severe SARS-CoV-2 Pneumonia

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**Introduction:** During SARS-CoV-2 pandemic many cases of acute hypoxic respiratory failure (AHRF) associated with interstitial pneumonia have been observed. Noninvasive ventilation (NIV) can represent a valid pulmonary support in patients with severe pulmonary SARS-CoV-2-related disease. Actually it is

difficult to obtain an early prognostic stratification for these patients. The HACOR score can be a useful tool to predict NIV failure in order to avoid a delayed intubation.

**Objects:** The aim of this study is to assess the prognostic performance of HACOR score in predicting NIV failure in patients affected by SARS-CoV-2 infection with AHRF. Failure is defined as a need for intubation or death.

**Methods:** In this observational retrospective cohort study 40 patients admitted to Respiratory Disease Ward and Respiratory Intensive Care Unit (RICU) of Perugia Hospital with pulmonary SARS-CoV-2-related disease who were receiving NIV were enrolled. They were divided into two groups: Group 1, patients who died or required endotracheal intubation, and Group 2, patients with successful weaning from NIV. Demographic data, clinical symptoms and signs, clinical index and laboratory data were analyzed. HACOR score, consisting in bedside variables (heart rate, acidosis, consciousness, oxygenation and respiratory rate), were calculated at the start of NIV and in 24 hours. Patients requiring urgent intubation or treated with NIV after intubation were excluded.

**Results:** Patients were analyzed according to the success or failure of NIV: 22 (55%) had a successful treatment while 18 (45%) failed. In the success group there was a significant improvement in HACOR score in 24 hours ( $p<0.001$ ). Patients with NIV failure had a higher HACOR score at initiation ( $p=0.004$ ) and after 24 hours ( $p<0.001$ ). An high value of HACOR score at admission and after 24 hours despite NIV showed good predictive power for failure. At admission and at 24 hours of NIV assessment, the areas under the receiver operating characteristic curve were 0.77 ( $p=0.023$ ) and 0.89 ( $p<0.001$ ). We found that HACOR score at admission at a cutoff point  $>6$  had 47% sensitivity and 94% specificity; HACOR score after 24 hours at a cutoff point  $>4$  had 100% sensitivity and 72% specificity.

**Conclusions:** The HACOR score is a clinically useful bedside tool for the prediction of NIV failure in hypoxicemic patients with COVID-19. A HACOR score  $>6$  at start and  $>4$  after 24 hour of

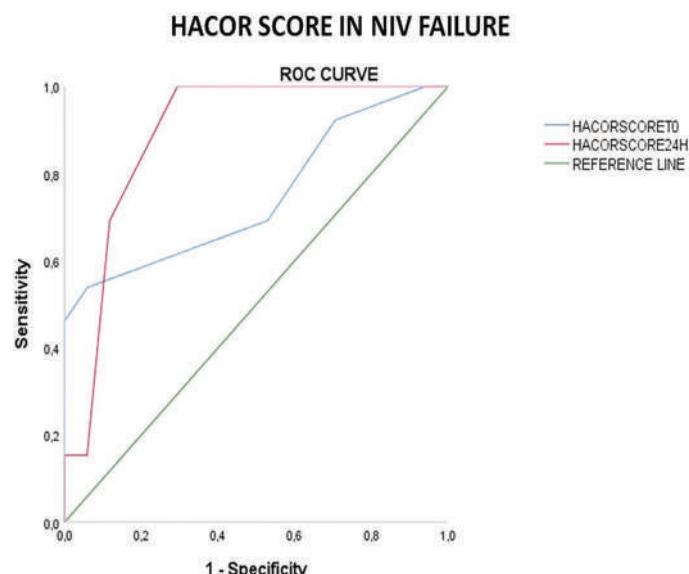


Fig. 1.

NIV highlights patients with high risk of failure. Early intubation in high-risk patients should be considered to reduce the hospital mortality rate.

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ID# 111

### Mediastinal Lymphadenopathy in a DCD-Patient: a Novel Indication for EBUS-TBNA?

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**Introduction:** Endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA) has emerged as a minimally invasive technique for evaluating the mediastinum and for staging patients with lung cancer. The procedure is safe and permits to obtain cytological samples suitable for immunohistochemistry and tumor genotyping, with high sensitivity, specificity, and predictive diagnostic values.

**Objects:** We present this case report, showing how performing EBUS-TBNA was crucial in determining the suitability of a potential organ donor.

**Case report:** A 64-year-old female patient, smoker (50 p/y), no previous medical history, was taken to the emergency room for aphasia and vomiting, rapidly evolving into coma (GSC 3). After intubation and sedation, a brain CT scan showed a 56x53 mm intraparenchymal hematoma located in the left hemisphere. As the neurological status appeared very compromised, with poor short-term prognosis, abandonment of therapy was the choice. Following consent to organ donation from the family, the process of donation after cardiac death (DCD) was started. As a consequence, all the necessary investigation aimed at verifying the suitability of the organs were performed. CT scan showed a right paratracheal (4R) lymphadenopathy (20x15 mm) suspicious for malignancy. This finding could lead to the exclusion of the patient from the process of organ donation. To overcome the stand-off, we performed EBUS-TBNA on the intubated patient.

**Results:** No suspicious lymphadenopathies were detected by the EBUS, other than the 4R lymph node detected on the CT scan. Using a 22 G needle, adequate cytological samples from the 4R lymph node were obtained (4 needle passages, the material was fixed in a formalin-like solution for cell block processing). The cytological examination showed fragments of lymph node with aspects of antracosis, with no signs of neoplasm. This result permitted to exclude neoplastic nature of the lymph node, and to resume the process of donation avoiding to lose the organs of the

potential donor. When the organs were removed, the 4R lymph node was analyzed by the pathologist, and the benign nature was confirmed. Liver, kidneys, corneas, cardiac valves and skin tissue were collected and made available for donation.

**Conclusions:** To our knowledge, this is the first case in which EBUS-TBNA was used to evaluate a suspicious mediastinal lymph node in a potential DCD organ donor. In this specific event, EBUS-TBNA played a decisive role into avoiding to exclude a DCD patient from the process of donation. In our opinion, this technique could be considered a useful tool to grant an efficient donor selection in particular cases.

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ID# 112

### Prevalence and Predictors of Progressive Phenotype in Fibrosing Interstitial Lung Diseases

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**Introduction:** IPF can be considered the prototype of progressive fibrosing interstitial lung diseases (ILDs). Although the other fibrosing ILDs have the potential for improvement and stabilisation with appropriate management, a subset of patients will develop progressive fibrosis (1), but prevalence and baseline predictors of this subgroup have yet to be fully established.

**Objects:** To evaluate the prevalence of the progressive phenotype in patients with fibrosing ILDs to and to assess clinical and functional variables associated with 2-year mortality and with development of the progressive phenotype.

**Methods:** This was a retrospective single-center observational study, in which patients with new or previous diagnosis of fibrosing ILD, referred to our clinic in the period between 07/12/2016 and 31/01/2019, were recruited. Clinical and functional data were collected (LTFs, CPI, GAP score). The progressive phenotype was defined as follows: relative decline in FVC% pred  $\geq 10\%$  over 2 years or relative decline in FVC% pred between 5% and 10% from baseline with relative decline in DL<sub>CO</sub>% pred  $> 15\%$  over 2 years (2).

**Results:** Overall, 68 patients were included in the present study, 23 with progressive phenotype (34%) and 45 (66%) with non-progressive phenotype. The following clinical features were significantly different between the two groups: age at diagnosis (69.3 vs 70.8 years;  $p=0.007$ ); FVC % pred (77.4% vs 90.4%,  $p=0.007$ ), FEV<sub>1</sub>%pred (79.2% vs 29.8%,  $p=0.0354$ ), DL<sub>CO</sub>% pred (45.3% vs 54.9%,  $p=0.0171$ ); mean CPI (46.2 vs 37.9,  $p=0.007$ ) and mean GAP score (3.9 vs 3.2,  $p=0.022$ ); relative one-year decline in FVC% (-6.4% vs +4.0%,  $p=0.00007$ ), FEV<sub>1</sub>% (-4.17% vs +5.52%,  $p=0.001$ )

and  $\text{DL}_{\text{CO}}\%$  (-14.96% vs +0.15%,  $p=0.0006$ ). No significant differences were found for smoking habits. Significant predictors of 2 year mortality were FVC%pred,  $\text{DL}_{\text{CO}}\%$ pred and CPI at baseline.

**Conclusions:** The prevalence of the progressive fibrosing phenotype appears to be in line with what is reported in the literature. Although the course of PF-ILDs remains unpredictable, our findings suggest that selected functional parameters and CPI at baseline might be valuable predictors of progression and worse outcomes.

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### ID# 114

#### Efficacy of Pitolisant in Reducing OSAS-Induced EDS: an Individual Patient Data Meta-Analysis

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**Introduction:** Pitolisant (PIT) is a Histamine H3-receptor antagonist/inverse agonist which enhances wakefulness. It has been approved by EMA for the treatment of Excessive Daytime Sleepiness (EDS) in adults with Obstructive Sleep Apnea Syndrome (OSAS), treated or not treated with primary OSAS therapies. HAROSA-1 and HAROSA-2 were the two international, multi-center, double blind, randomized (3:1), placebo controlled, 12 weeks pivotal trials that showed PIT's efficacy and safety at doses up to 20mg/die. The two studies were designed to be meta-analyzed.

**Objects:** This Individual Patient Data (IPD) meta-analysis synthesizes the outcomes of HAROSA-1 and HAROSA-2 in a comprehensive population of 512 OSAS patients with EDS, treated or not with Continuous Positive Airway Pressure (CPAP).

**Methods:** The IPD meta-analysis is based on the original trials' databases, differently from common meta-analyses on literature that are based on studies' outcomes. Epworth Sleepiness Scale (ESS) and Oxford Sleep Resistance (Osler) tests were co-primary endpoints tested at 0.025 significance and Fatigue (Pichot Scale) was secondary.

**Results:** A significant mean ESS reduction of -3.06 ([95%CI -4.1,-2.02],  $P< 0.001$ ) was reached with PIT versus placebo and 81% more patients had final ESS normalized to less than 10

(RR= 1.81 [95%CI 1.36, 2.39],  $p< 0.001$ ). The ratio Final/Baseline of Osler outcomes was 18% better (ratio=1.18[95%CI 1.02,1.35],  $P=0.022$ ) with PIT. The clinically meaningful EDS effect of Pitolisant, measured by the aggregate Z-score on ESS and Osler, was 0.71([0.46, 0.97],  $P< 0.001$ ). Finally, a significant mean Pichot Fatigue reduction of -1.23 ([-2.29,0.18],  $P=0.022$ ) was found. These effects were shown invariant across different subgroups of the population, according to age, gender and work conditions. Finally, these effects were not impacted as to whether or not CPAP was used. Side effects incidences were similar in both groups.

**Conclusions:** in OSAS real world practice both patients treated and not treated with CPAP could complain EDS. In the population pooled in this IPD meta-analysis, PIT showed a significant efficacy, versus placebo, in improving EDS, vigilance and fatigue in OSAS patients with pathological sleepiness, irrespective of CPAP use. Side effect incidence confirmed PIT's safety profile observed in other indications.

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### ID# 115

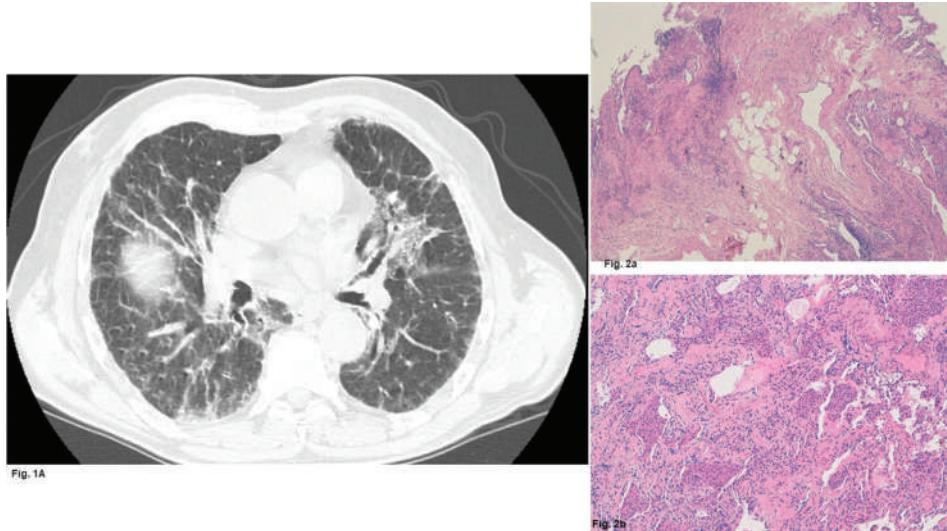
#### The Importance of an Accurate ILD Diagnosis, a Clinical Case

Leonardo Giuntoli<sup>1</sup>, Luca Ciani<sup>1</sup>, Valentina Luzzi<sup>1</sup>, Leonardo Gori<sup>1</sup>, Valeria Pasini<sup>2</sup>, Camilla Eva Comin<sup>2</sup>, Sara Tomassetti<sup>1</sup>

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**Introduction:** ILD are a heterogenous group of disorders that may be idiopathic or associated with known causes such as connective tissues diseases. Differential diagnosis of fibrotic ILDs is of key importance to achieve the best therapeutic approach and an indiscriminate antifibrotic treatment regardless of the underlying diagnosis should be discouraged.

**Case report:** We present the case of a 78 y.o. caucasian male nonsmoker with no occupational/environmental or family history relevant for ILD. Relevant medical history only includes systemic arterial hypertension treated with AT1-antagonist. Three years ago the patient presented to an external center for incidental HRCT findings of fibrosing ILD, atypical for UIP. Laboratory tests revealed ANA titer 1/160 homogeneous, negative ENA screening without available myositis profile. He was classified as IPF without biopsy and treated with Pirfenidone. Pirfenidone treatment was not tolerated due to recurrent skin toxicity managed with doses reductions and interruptions. After three years the drug had finally to be discontinued due to severe eczema. At follow-up both pulmonary function tests (% FVC from 96 to 70 and % pred.  $\text{DL}_{\text{CO}}$  from 78 to 70%) and HRCT revealed an inexorably progression of the interstitial lung changes as shown in Figure 1. The patient came to our center and after multidisciplinary evaluation underwent



**Fig. 1.**

BAL, transbronchial lung cryobiopsy and full rheumatologic evaluation. At serology ANA titre was found increased to 1:320, homogenous, with anti-NXP2 and MDA5 positivity. BAL cell profile was normal with negative microbiology and virology panel. Histology by TBLC confirmed the presence of mixed fibrotic and cellular NSIP with focal areas of organizing pneumonia, in line with the HRCT appearance of NSIP/OP (Figure 2A/B). The final MDT diagnosis was NSIP/OP related to anti-MDA5 syndrome with prevalent lung involvement. The patient started treatment with systemic corticosteroids and mycophenolate (2000 mg day).

**Conclusions:** This clinical case highlights the importance of an accurate diagnosis of ILDs. Fibrotic ILDs are a heterogeneous group of diseases that encompass a wide spectrum of disorders ranging from purely fibrotic and relentlessly progressive disorders such as IPF to more cellular, acute/subacute forms with an underlying immunological and inflammatory pathogenic background. First line treatment of these disorder is strikingly divergent and an indiscriminate use of antifibrotics in the absence of a precise diagnosis should be discouraged due to possible adverse events and unproven superiority compared to immunomodulation in non-IPF fibrotic ILDs.

pneumonia and acute respiratory distress syndrome. Chest Computed Tomography (CT) represents the gold standard for the diagnosis of SARS-CoV-2 related pneumonia. Besides pulmonary complications, COVID-19 is characterized by an increased risk of metabolic complications such as: diabetes and insulin resistance. A worse metabolic profile seems to associate with a poor prognosis.

**Objects:** The present study was aimed to explore the relationship between pneumonia extension evaluated through CT severity score and insulin resistance evaluated as triglycerides/glucose index (TyG). Furthermore, we examined the role of the TyG index as a predictor of hospital stay and non-invasive ventilation needing (High Flow Nasal Cannula (HFNC), Continuous Positive Airway Pressure (CPAP), or Bi-level Positive-Pressure ventilation (Bilevel-PAP)).

**Methods:** For our aims, we retrospectively examined the record of 46 hospitalized patients diagnosed with SARS-CoV-2 related pneumonia. Each patient underwent a high-resolution CT scan, blood gas analysis, clinical and laboratory examinations. The CT score was calculated for each of the 5 lobes on the basis of the extent of anatomic involvement (0: 0%; 1, <5%; 2:5–25%; 3:26–50%; 4:51–75%; 5, >75%; range 0–5; global score 0–25). TyG index was calculated as:  $\text{Ln} [\text{Fasting triglyceride (mg / dl)} \times \text{Fasting glucose (mg / dl)}]/2$ .

**Results:** In simple correlation analyses, CT score was found directly related with hospital stay ( $r=0.64$ ;  $p<0.001$ ), needing of non-invasive ventilation ( $r=0.37$ ;  $p=0.01$ ), C-Reactive Protein ( $r=0.36$ ;  $p=0.01$ ), and inversely related with blood oxygen saturation ( $r=-0.43$ ;  $p=0.003$ ). TyG index directly related with CT score ( $r=0.45$ ;  $p=0.002$ ), C-Reactive Protein ( $r=0.36$ ;  $p=0.01$ ), hospital stay ( $r=0.47$ ;  $p=0.001$ ), needing of non-invasive ventilation ( $r=0.48$ ;  $p=0.001$ ). The association between TyG and CT-score was confirmed also in multiple regression analysis after correction for confounding factors.

**Conclusions:** The present investigation offers various talking points. First, it confirms the correlation between CT severity score and clinical and biochemical parameters of SARS-CoV-2-related

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ID# 116

## Severe Acute Respiratory Syndrome CoronaVirus-2 Pneumonia and Insulin Resistance

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**Introduction:** Coronavirus disease (COVID-19) typically presents with flu-like symptoms but can progress to interstitial

pneumonia. Second, for the first time, it demonstrates the association between pneumonia extent and insulin resistance evaluated as TyG index. Finally, TyG index seems to predict the need for non-invasive ventilation in these patients. Future investigations are warranted to clarify the mechanisms underlying these findings and their clinical usefulness.

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ID# 117

### Diagnostic Accuracy of Endobronchial Ultrasound Needle Aspiration with and without Suction

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**Introduction:** The role of ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for the diagnosis of hilar/mediastinal lymphadenopathies is well-established. However, different aspiration techniques are available and it is not clear if there is a significant difference between suction vs no-suction aspiration. Of great interest is the role of different aspiration techniques in EBUS-TBNA in determining the diagnostic accuracy for histopathological evaluation, including molecular biology and PD-L1 amplification assessment in lung cancer diagnosis. In this context, no comparative studies have been performed; moreover,

considering only suction techniques, data exploring the difference between aspiration with EBUS dedicated syringe and manual aspiration are still lacking. It is very important for clinical practice to definitively assess the non-inferiority of no-suction techniques in EBUS-TBNA in terms of diagnostic yield and to provide information regarding the quality of histologic sample.

**Objects:** The primary endpoint was to test the non-inferiority of no-suction aspiration techniques over the other techniques in terms of diagnostic yield. The secondary endpoints included the assessment of adequacy for molecular study in lung cancer and to provide a qualitative evaluation of the sample by the pathologist.

**Methods:** Eligible patients were randomized 1:1:1 to either the no-suction aspiration technique or ex-vacuum aspiration with EBUS-TBNA dedicated syringe or manual applied aspiration technique group.

**Results:** A total of 77 patients were randomized to either no-suction (n=33) or EBUS-TBNA dedicated syringe (n=23) or manual aspiration syringe (using a pistol-grip syringe holder) (n=21). The diagnostic yield of manual aspiration was lower (85.7%), but not significantly inferior to the other techniques (no-suction: 100% and EBUS dedicated syringe: 95.7%, p >0.05). Similarly, the sample resulted suitable for molecular assessment in 90.9% of no-suction group, in 82.6% of EBUS-TBNA dedicated syringe group and 81.0% of manual aspiration group, showing a lower quality of samples of the latter two techniques, though not statistically significant (p > 0.05).

**Conclusions:** All the available aspiration techniques resulted to be excellent as diagnostic tool of hilar/mediastinal lymphadenopathies, all providing a high diagnostic yield, obtaining histological samples of high quality, even suitable for pathological molecular assessment in lung cancer (i.e. PD-L1 expression). However, these preliminary data suggest that manual syringe aspiration provides a lower diagnostic accuracy, result that needs to be confirmed at the end of the trial reaching an adequate sample size.

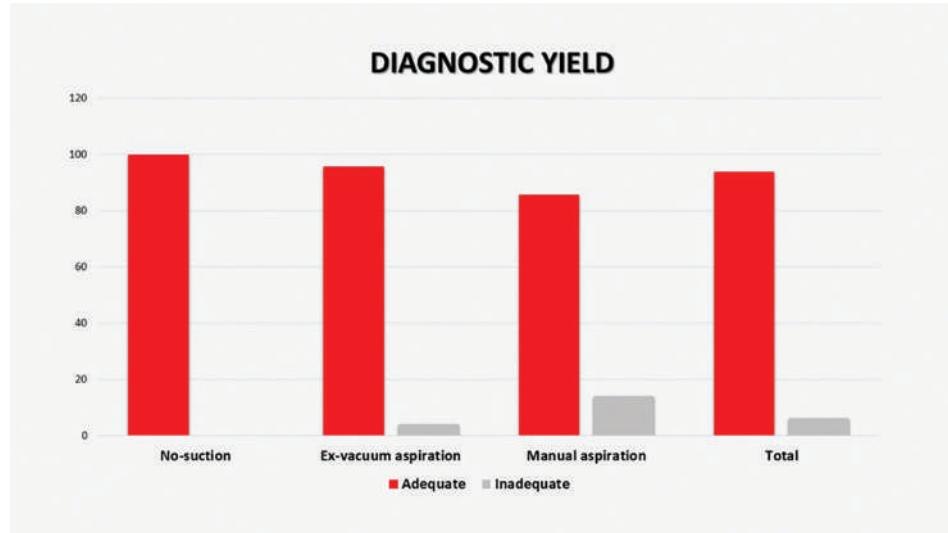


Fig. 1.

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ID# 118

## Persistent Symptoms in Post-Covid Disease

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**Introduction:** Coronavirus disease is an important multisystemic infection caused by SARS-CoV-2, a new coronavirus. The most dangerous aspects of this syndrome are its high spread rate and high mortality rate. The most common symptoms are fever, dry cough, fatigue, anosmia and dysgeusia and in the most several cases, especially in those with comorbidities, distress respiratory syndrome (ARDS) might happen. The coexistence of all these symptoms might lead the patient to death. Some of the symptoms

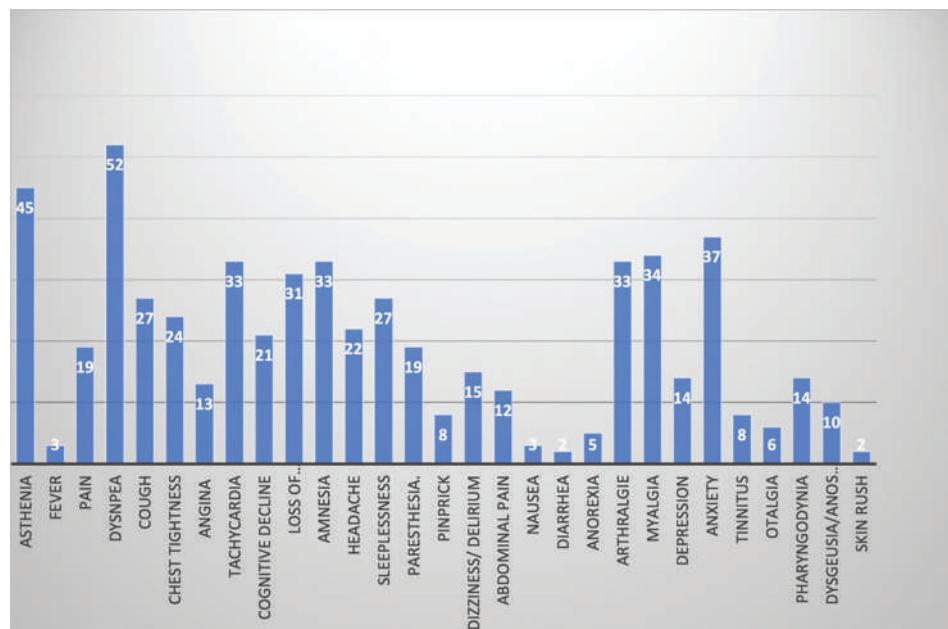
manifested during the disease might be kept even after the healing, such as fatigue, dyspnea, cough, angina, palpitations, delirium, dizziness, abdominal pain, etc.

**Objects:** This study is aimed to highlight the post covid highest frequency symptoms, in our experience 93 patients have been recruited and they have been submitted to a multiple answer questionnaire evaluating constitutional, respiratory, cardiovascular, neurological, gastrointestinal, muscle-skeletal, psychological, otolaryngologist and dermatological symptoms.

**Methods:** All of them have been taken care of by U.S.C.A of Catanzaro and were then followed at the Medical Center for Travel and Immigration of the Giovanni Paolo II Hospital in Lamezia Terme.

**Results:** 55.81% of the patients suffered of dyspnea, 48.39% showed asthenia, 36.56% showed myalgia and arthralgia, 35.48% suffered of tachycardia and amnesia. Loss of concentration affected 33% of patients, while 29% manifested cough and sleeplessness. 25% showed chest tightness, 23.66% had headache, 22.58 manifested cognitive decline, 20.43% was affected by paresthesia. Dizziness and delirium were present in 16.13% of the total, 13.98% showed angina and 12.90% moaned because of abdominal pain. The other symptoms are showed in the table.

**Conclusions:** The aim of this study is to highlight the sequelae of the disease in patients after recovery and especially giving inspiration to define possible therapeutic interventions to ensure a better quality of life in this category of people.



**Fig. 1.**

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ID# 119

## At-Home Short-Term Oxygen Therapy for COVID-19 Patients: a Pilot Project

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**Introduction:** Supplemental oxygen is one of the backbones of COVID-19 therapy. During COVID-19 surges, at-home short-term oxygen therapy (AHSTOT) protocols (up to 30 days) are a possible strategy to reduce pressure on hospitals, especially for cases that do not require mechanical ventilation, for oxygen weaning allowing early hospital discharge, and for palliative care in patients not eligible for intensive care. An AHSTOT protocol for COVID-19 patients was tested as a pilot project in AUSL-IRCCS Reggio Emilia, Italy, between November 2020 and April 2021.

**Objects:** To assess the feasibility of an AHSTOT protocol for COVID-19 patients.

**Methods:** A retrospective analysis of the COVID-19 population for whom the AHSTOT protocol was activated was performed. For each patient, an observation time frame of two months was considered.

**Results:** 63 COVID-19 patients (37 males and 23 females) were included in the study, with a mean age of 77 years. Overall mortality resulted in a 5% (excluding 4 patients who received the AHSTOT for palliative care). Patients mortality presented a statistically significant association (One-way ANOVA,  $p < 0.001$ ) with quantitative parameters of oxygen therapy ( $O_2$  l/m flow, daily consumption), with greater mortality for higher flows or daily consumption. The hospitalization rate was 24%, higher for those patients who received the AHSTOT at an early stage of the disease, compared to the rehospitalization rate for those discharged from the hospital with AHSTOT for oxygen weaning. Interestingly, the prolongation of the AHSTOT beyond 30 days was quite frequent (29%) especially in the discharged from hospital group. Prolongation of the AHSTOT presented a statistically significant association (One-way ANOVA) with the following variables: duration of the SARS-CoV-2 RT-PCR nasopharyngeal swab positivity ( $p < 0.01$ ); P/F ratio at the start of the AHSTOT ( $p = 0.05$ ); severity of lung involvement assessed through radiological imaging (RX/CT/US) ( $p < 0.05$ ); Red cell distribution width (RDW) ( $p < 0.05$ ). Mortality and hospitalization rates were higher compared to the general COVID-19 population of the province (1.7% and 7% respectively), however, this result is easily explainable since patients who do require oxygen therapy during COVID-19 have a more severe illness. Mean hospital stay duration for AHSTOT patients (13.9 days, SD= 7.9 days, 95%CI) was similar to those of the general COVID-19 population (13.4 days, SD= 9.9 days, 95%CI).

**Conclusions:** AHSTOT protocols for COVID-19 patients may be a helpful intervention to reduce pressure on hospitals during COVID-19 surges. Dedicated randomized controlled trials to thoroughly assess AHSTOT effectiveness and safety are advised.

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ID# 120

## Outcomes of Patients with SARS-CoV-2 Pneumonia Treated with CPAP

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**Introduction:** The pandemic COVID-19 disease may cause severe acute respiratory syndrome. In patients with mild/moderate respiratory failure, continuous positive airway pressure (CPAP) may represent a valuable approach.

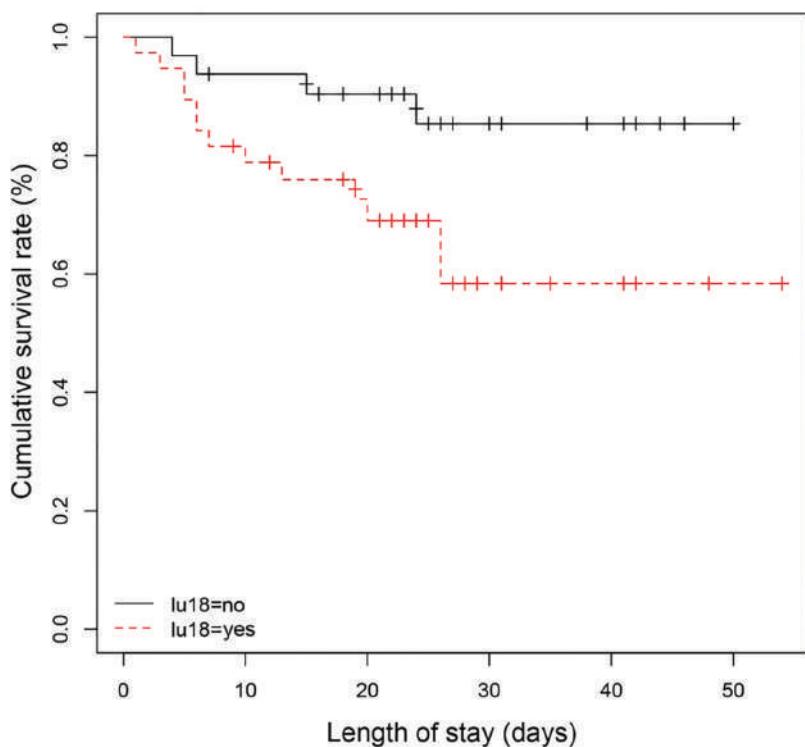
**Objects:** Evaluate the outcomes of patients with SARS-CoV-2 pneumonia treated with CPAP, in particular endotracheal intubation (ETI), improvement in gas-exchange, length of stay (LOS), mortality.

**Methods:** We conducted a monocentric, retrospective, observational study. 148 patients were enrolled (March 14 – May 15 2020). All patients were treated with CPAP in the Respiratory Care Unit (RCU). Criteria for treatment with CPAP were  $\text{PaO}_2/\text{FiO}_2 < 300$ , respiratory rate  $> 24 \pm$  respiratory distress. Lung ultrasound score (LUS) at the time of RCU admission, was also assessed.

**Results:** Median age was 72.5 [34-92] years; 99 patients were male. 37 patients underwent ETI. 40 patients died. Patients who underwent ETI had a higher risk of death (RR 2.08 - 95%CI 1.23 – 3.53;  $p=0.008$ ).  $\text{PaO}_2/\text{FiO}_2$  at RCU admission was not different between patients who underwent ETI and patients who overcame successfully CPAP (160 vs 170;  $p=0.35$ ), while a significant difference was observed at 1 and 48 hours ( $\text{PaO}_2/\text{FiO}_2$  155 vs 220  $p<0.0001$  and 154 vs 239  $p=0.001$  respectively). No improvement in  $\text{PaO}_2/\text{FiO}_2$  after 1 hour of CPAP was associated with an increased risk of ETI (RR 2.57 - 95%CI 1.47 – 4.47;  $p<0.0001$ ) and death (RR 3.26 - CI 95% 1.89 – 5.61;  $p<0.0001$ ). SAPS II was not different between the two groups (36 [31-41] vs 33 [29-39] respectively;  $p=0.14$ ) but a SAPS II  $>/= 34$  was related with an increased risk of death (RR 6.45 – 95% CI 2.67 – 15.55;  $p<0.00001$ ); no difference was observed in hospital LOS (26 [10-42] vs 19 [12-27] days respectively;  $p=0.09$ ). A LUS score  $> 18$  at RCU admission was associated with an increased risk of mortality ( $p=0.04$ ). Older age ( $> 72$  years), was associated with an increased risk of death (RR 4.37 – 95% CI 1.95-9.80;  $p<0.001$ ).

**Conclusions:** Early improvement in gas exchange may identify patients who can undergo successfully CPAP treatment. Variables associated with CPAP failure, that should encourage early intubation, are a severe LUS at admission and age over 72 years.

## LUS at admission and survival



**Fig. 1.**

ID# 122

### Mortality Predictors in COVID-19 Patients Admitted to a Respiratory Intermediate Care Unit

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**Introduction:** although numerous studies have investigated the prognostic determinants of acute respiratory failure (ARF) due to SARS-CoV-2 disease (COVID-19), mostly in intensive care units (ICUs), predicting mortality in such patients remains an elusive task. Furthermore, due to the overwhelming, rapid diffusion of the disease, ICUs became saturated early in the course of the COVID-19 pandemic, and a role for respiratory intermediate care units (RICUs)s, specialised settings for non invasive respiratory support (NRS) has emerged.

**Objects:** to evaluate predictors of mortality and to describe the trend of clinical parameters, alveolar-arterial oxygen gradient (A-aO<sub>2</sub>) and partial pressure of arterial oxygen to inspiratory oxygen fraction (P/F) data prior to NRS and after 24h in a single center retrospective observational study on patients with ARF due to COVID-19 admitted to our RICU between October 2020 and April 2021 and treated with NRS (cPAP with full-face mask). A-aO<sub>2</sub> was calculated from the alveolar gas equation

**Results:** we enrolled 100 consecutive patients: 68 were discharged (group1), 15 died after being transferred to an ICU (group2), 17 died while in the RICU (group3) after a multidisciplinary consensus was reached and the patients were deemed to be unsuitable for invasive ventilation. Risk of mortality for patients not in group3 was associated with (odds ratio, 95% confidence interval): age (1.27, 1.09-1.49 per year), cardiovascular comorbidities (5.91, 1.03-34.09), respiratory distress, defined as respiratory rate > 30 breaths/min and/or dyspnea at rest and/or use of accessory respiratory muscles and/or paradoxical breath (12.93, 1.54-108.83), P/F prior to NRS <100 mmHg (24.82; 0.73-844.51). None of these risk factors showed a significant association with mortality in group3 patients. After 24h of NRS, group2 and group3 compared to group1 showed persistently higher A-aO<sub>2</sub> (median [interquartile range]): 239.8 [229.8-329.6] mmHg; 295.8 [236.6-335.8] mmHg; 218.0 [181.5-244.8] mmHg, for group 2, 3 and 1 respectively, p<.001; lower P/F: 146 [114-210] mmHg; 135 [98- 171] mmHg; 188 [148-241] mmHg; for group 2, 3 and 1 respectively,

p<.003 and higher proportion of patients with respiratory distress: 13% vs 24% vs 3% for group 2, 3 and 1, respectively, p <.012.

**Conclusions:** age, cardiovascular comorbidities, respiratory distress and P/F<100 mmHg prior to NRS were predictors of mortality in patients who died after being transferred to an ICU. No predictor was identified for patients who were deemed to be unsuitable for invasive ventilation and died in RICU. Persistently low values of P/F, high values of A-aO<sub>2</sub> and persistent respiratory distress despite NRS were associated with worse outcome.

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**ID# 123**

### **Improvement Respiratory Diseases Patients Journey through Direct Drugs Distribution and Monitoring**

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**Introduction:** The National Chronicity Plan (PNC) defines the management details of major chronic diseases such as asthma and Chronic Obstructive Pulmonary Disease (COPD). Multidisciplinary approach was successful in the most effective and virtuous care organizations in order to optimize the Patient Journey, prevent complications and slow down the evolution of diseases. Direct Drugs Distribution (DD), at the time of inpatients and outpatients discharge (L.405/2001), is a solution of care continuity, monitoring and governance strategy for the National Health Service (NHS).

**Objects:** The aim of the experience was to enhance DD, for asthma/COPD patients, as a tool for optimizing the Patient Journey and sustainability for the NHS.

**Methods:** At the A.O. Ordine Mauriziano, a multidisciplinary team, made up of physicians and hospital pharmacists, defined: -panel of molecules to ensure appropriate therapeutic management to patients; -care paths to facilitate patients in therapeutic education, supplying, training, switching and monitoring. To evaluate the impact of the described work, the data relating to the first 2021 semester and 2019 were compared.

**Results:** DD, in the half year considered, offered assistance to 576 (+134% compared to 2019) patients in Inhalation Therapy (IT) (261(45%) M) and 66 (+40%) in therapy with monoclonal antibodies (mAbs)(23(35%)M), for a total of 853 dispensations (+116%). Mean and median age of patients was 64 and 68 years respectively. In 65% of cases, the pharmacist trained on the use of

a specific prescribed device. 787 (+132%) packs of IT(ATC R03AC/ AK/AL/BB) and 370 (+57%) packs of mAbs (ATC R03DX) were dispensed for a total value of €19,393.79 and €205,272.71 respectively. 75% of the patients afferent to DD came from Pulmonology (prescriptions: 50%LABA+ICS; 35%LAMA; 8%LAMA+LABA+ICS; 3%LAMA+LABA; 2%LABA; 2%SABA), Allergology/Immunology (prescriptions: 60%LABA+ICS; 22%LAMA; 1%SABA; 1%LAMA+LABA+ICS) and Emergency Medicine (prescriptions: 57%LABA+ICS; 36%LAMA; 4%LAMA+LABA+ICS; 2%LAMA+LABA; 2%SABA). The prescriptions for mAbs were: 63% omalizumab, 24% mepolizumab; 13% benralizumab. Compared to territorial economic agreements, the dispensation through hospital generated cost savings for the NHS of € 21,478.00 (€ 19,221 and € 2,257 for IT and mAbs respectively), equal to about € 45,000/year.

**Conclusions:** A multidisciplinary model in the management of Asthma/COPD guarantees, according to the literature, more effective care pathways. DD has proved to be a tool able to support patients in the set goals and ensuring the rationalization of pharmaceutical expenditure. It is crucial to expand the team, develop customized solutions for monitoring adherence and structure collaboration with Territorial Services.

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**ID# 124**

### **Comparison of 2 Cohorts of SARS-CoV-2 Patients Admitted During the First and Two Pandemic Waves**

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**Introduction:** Pneumology received patients with acute respiratory failure due to SARS-CoV-2 interstitial pneumonia. During the first wave there was a limited equipment availability.

**Objects:** To highlight any differences in population characteristics, therapeutic approach and health outcomes of the 2 cohorts of patients, admitted in the periods March-April 2020 and October-January 2020-2021, respectively. To assess overall characteristics and outcomes of all enrolled patients.

**Methods:** Data from 169 patients, 109 males and 60 females, mean age 61.7 years (19-89), divided into 2 cohorts of 87 (age 65;24-89) and 82 cases (age 67;19-89) respectively, were retrospectively analysed. Statistical analysis was performed using Student's t-test.

**Results:** The mean hospital stay of the total number of patients was 14.4 days (range 1-47), with a statistically significant difference in the number of days between survivors and deceased in both cohorts (17 vs 9, p<0.001 - 15 vs 9, p<0.01); there was also a significant difference between the mean age of survivors and deceased in cohort 1 (61.6 vs 73.6, p<0.0001). The total number of deaths was 38 (25.8%); 23 (26.4%) and 15 (18%) in the 2 cohorts respectively. The main comorbidities and smoking habits (126 atients) are shown in Table 1. The mean number of comorbidities was 1.7 for

**Table 1.**

COMORBIDITY AND SMOKING HABIT		
	number	%
High Blood Pressure	81	48
other CV diseases	45	27
dyslipidemia	23	14
diabetes mellitus	8	25
obesity	23	14
COPD	13	8
Bronchial Asthma	4	2
smokers	8	6
ex-smokers	30	24
non-smokers	88	70

CV = cardiovascular

deceased patients and 1.8 for survivors. All patients were treated with conventional oxygen therapy, 78 (46%) with cPAP (Continuous positive airway pressure)/NIV (non-invasive mechanical ventilation), 10 with high flows (6%) and 18 with a combination of both (11%). cPAP/NIV was used in 38% of patients in cohort 1 and 65% in cohort 2, as an effect of the ventilator shortage that occurred in wave 1. In cohort 1, 62 patients (71%) were treated with antibiotics, in cohort 2, 39 (48%).

**Conclusions:** There was a substantial age difference between deceased and survived patients in cohort 1, demonstrating the greater frailty of the elderly. The hospital stay was significantly longer in survivors in both cohorts, showing an early mortality (on average 9 days after admission). The proportion of deaths was reduced in the 2nd wave. The number of cases treated with cPAP/NIV was significantly higher in the second cohort, while the number of antibiotic treatments decreased, reflecting the availability of ventilators and a more appropriate therapeutic approach respectively. The 2 populations were similar in terms of comorbidities and smoking habits.

**ID# 126**

### Ruxolitinib as a Possible Trigger for Pulmonary Alveolar Proteinosis

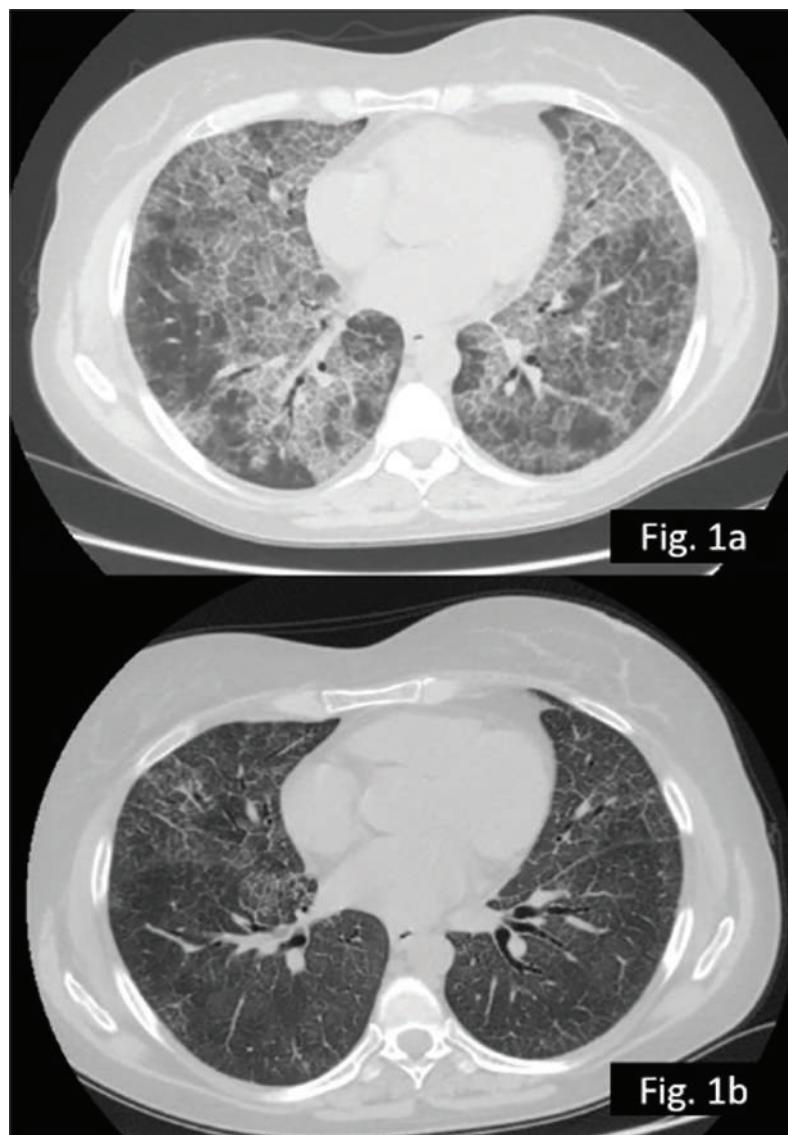
Angelo Canora<sup>1</sup>, Ludovica Capitelli<sup>1</sup>, Marianna Scola<sup>1</sup>, Antonio Russo<sup>1</sup>, Alfonso Pecoraro<sup>2</sup>, Severo Campione<sup>3</sup>, Emanuele Ciasullo<sup>1</sup>, Antonio Starace<sup>1</sup>

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**Introduction:** Pulmonary alveolar proteinosis (PAP) is characterized by the accumulation of surfactant in alveolar macrophages and alveoli, resulting in impaired gas exchange. Autoimmune PAP occurs when anti-GM-CSF antibodies lead to deficiency of bioavailable GM-CSF. Secondary PAP results from alveolar macrophage dysfunction due to inhalation exposures, hematopoietic disorders, infections, drugs. High-resolution chest CT scans usually highlights patchy ground-glass opacities. The first step to confirm PAP is usually a broncho-alveolar lavage, which might demonstrate characteristic opalescent or milky-appearing fluid. Histopathology shows diffuse dense acellular eosinophilic material in the airways with minimal interstitial inflammation. Transbronchial biopsy increases the diagnostic yield and should be considered if bronchoalveolar lavage fluid is not characteristic. In patients with clinically significant lung disease, whole-lung lavage remains the standard initial treatment method.

**Case report:** We present a clinical case of a 52-year-old female, non-smoker. She had a diagnosis of primary myelofibrosis (PMF)

since 2016. In 2018, she began treatment with ruxolitinib to ameliorate anemia and splenomegaly. Two years later, she developed respiratory failure and was admitted to our hospital. At the recovery, the patient presented a severe respiratory failure and underwent non-invasive ventilation. The High-Resolution chest CT showed a "crazy paving" pattern: In all pulmonary lobes, there were multiple ground-glass areas associated with thickening of intra and interlobular septa. She underwent to a broncho-alveolar lavage that was not diagnostic, but histological sample from trans-bronchial biopsy suggestive for PAP. We sent the blood sample to a specialized laboratory for the research of anti-GM-CSF antibodies, in U.S.A., which were positive. We did a pipeline to find out the possible causes of PAP, so we found two papers (1, 2) that emphasized the association of PAP with ruxolitinib. Therefore, the treatment was interrupted, with a significant improvement of respiratory condition. At CT scan after 2 months, the crazy paving disappeared.



**Fig. 1.**

**Conclusions:** Pulmonary alveolar proteinosis is a rare cause of respiratory failure. It should always be considered as a possible diagnosis in patients with dyspnea, cough and crazy paving at HRTC. The meaning causes are autoimmune diseases, hematopoietic disorders, infections, but it is necessary remember the possible role of drugs such as a trigger. The gold standard treatment for these patients is the whole lung lavage. In this clinical case, the interruption of the drug was enough to obtain the resolution of clinical and radiological alterations.

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**ID# 129**

## **Antithrombotics in Idiopathic Pulmonary Fibrosis and Antifibrotics: a Single Centre Real Life Study**

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**Introduction:** Due to the strong prevalence of cardiovascular comorbidities in idiopathic pulmonary fibrosis (IPF) patients, they often require anticoagulant therapy along with antifibrotics. Anticoagulant drugs increase the risk of bleeding in any patient and the concomitant use with antifibrotics is carefully evaluated by physicians.

**Objects:** To evaluate the bleeding risk in IPF patients in treatment with antifibrotics and concomitant use of antithrombotics.

**Methods:** We retrospectively evaluated the bleeding adverse events occurred in a cohort of 141 IPF patients treated with concomitant use of antifibrotics and antithrombotic. In this cohort as antifibrotic treatment, 63 patients received Pirfenidone, while 78 patients received Nintedanib.

**Results:** In relation to the antithrombotic therapy, 30 patients (48%) out of 63 treated with Pirfenidone received also antithrombotic, while 43 (55%) out of 78 patients in treatment with Nintedanib received them. The incidence of bleeding events in these patients was moderate (21%), and the entity of the adverse events was mild. Most common event was ecchymosis in the upper limbs (12.5%) followed by hematuria (3%), rectal bleeding (3%), gingival bleeding (1%) and subconjunctival bleeding (1%).

**Conclusions:** Our experience confirmed that antifibrotics are safe in patients with comorbidities requiring the use of

antithrombotic, and the choice of anticoagulant drug should be determined by the indication and the outcome of a risk-benefit analysis.

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**ID# 130**

## **Sarcoidosis and Severe Asthma: Dupilumab Treatment for Both Diseases? A Clinical Case**

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**Introduction:** Despite affecting virtually any organ, sarcoidosis is a chronic granulomatous disease with a typical pulmonary dominance, characterized by a T 1 inflammatory pattern. On the other hand, Asthma displays a Type 2 inflammatory pattern. In patients with concomitant Asthma and pulmonary sarcoidosis, patients seem to display an increased levels of type 2 cytokines (e.g., IL-4, IL-5, IL-13).

**Case report:** A 59-years old woman with asthma from the childhood, after a PET/CT scan for dyspnea, fever and thoracic pain showing an increased metabolic activity of pulmonary and

**Table 1.**

*Patient demographics and observational period*

Antifibrotic	N of patients	Female/Male	Age (Mean)	Follow up Time (Mean, years)
Nintedanib	78	30/48	81.5	2.7
Pirfenidone	63	21/42	75	3.2

*Antifibrotics/Antithrombotics distribution and adverse events details*

	Number of patients (%)	Number of Bleedings	Adverse event Type
<b>Nintedanib</b>	78		
Antithrombotics	43 (55)	8	
Anticoagulants	4 (9)	3	2 ecchymosis in the upper limbs; 1 subconjunctival bleeding
Acetylsalicylic	19 (44)	1	Rectal bleeding
Antiplatelets	16 (37)	4	3 ecchymosis in the upper limbs; 1 hematuria
NOAC	4 (9)	0	
<b>Pirfenidone</b>	63		
Antithrombotics	30 (48)	7	
Anticoagulants	0	0	
Acetylsalicylic	22 (73)	3	2 ecchymosis in the upper limbs; 1 hematuria
Antiplatelets	6 (20)	3	2 ecchymosis in the upper limbs; 1 rectal bleeding
NOAC	2 (7)	1	Gingival bleeding

mediastinal nodes (i.e., upper lobes – SUV 13.6; mediastinal – SUV 5.42, Barety space and pulmonary perily area- SUV SUV 5.18, PET/TC), performed a lung nodule biopsy, receiving a diagnosis of pulmonary-mediastinal sarcoidosis. Biochemical findings showed increased levels of eosinophils with normal values of ACE (88 U/l), serum and urine calcium levels (8.8 mg/dl and 11 mg/dL respectively). Therefore, prednisone (25 mg/die) and methotrexate (7.5 mg/week) have been prescribed, with a progressive reduction of metabolic activity at PET/CT scans of follow-up. As a result, after the first year, both drugs have been tapered; notably, whereas sarcoidosis continued its improvement, the patient displayed a worsening of her asthmatic symptoms, with an increased need for b-2 agonist inhalers and ICS, and oral corticosteroids. However, a progressive decrease of FEV<sub>1</sub> (from 84% to 69%) and an increase in Eosinophil cells (639 cells/uL), total IgE (502 U/mL), and FeNO (26ppb) was detected. Recent evidence suggests that the use of human monoclonal antibody against interleukin (IL)-4 receptor alpha that inhibits IL-4/IL-13 signalling, are useful in asthma control. Therefore, Dupilumab has been started with a significant improvement of asthma symptoms; notably, sarcoidosis signs have been improved under this treatment as documented by radiologic, functional and clinical exams.

**Conclusions:** The present clinical case suggests that the use of Dupilumab, a T2 inflammation modulator, is able to improve not only Asthma (a T2 disease) but also Pulmonary sarcoidosis, a typical Th-1 disease.

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### ID# 132

#### Prevalence of Cardiac Involvement in a Cohort of Patients with Sarcoidosis: a Single Center Study

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**Introduction:** Sarcoidosis is a systemic granulomatous disease of unknown aetiology and the cardiac involvement [cardiac sarcoidosis (CS)] represents an important prognostic factor. CS may be asymptomatic or present with severe tachyarrhythmias, heart failure or be the cause of sudden cardiac death. Recently, late gadolinium enhancement cardiac magnetic resonance (CMR) and 18F-fluorodeoxyglucose positron emission tomography have been demonstrated to be useful tools for the non-invasive diagnosis of CS.

**Objects:** To screen for CS in a population of patients with pulmonary or systemic sarcoidosis with late gadolinium enhancement cardiac magnetic resonance (CMR).

**Methods:** 122 unselected patients (mean age 59.15± 9.8, range 32-78; female 55%) admitted to the Sarcoidosis Unit of Respiratory Department of Naples (Southern Italy) from 2012 to 2020, were diagnosed (histologically confirmed) with mediastinal-pulmonary or systemic Sarcoidosis. Seventy patients prospectively underwent CMRI in order to detect cardiac involvement.

**Results:** 21/70 patients (30%) with pulmonary sarcoidosis had cardiac involvement. CMRI revealed non ischemic myocardial damage involving interventricular junction, left ventricular wall, septum and right ventricular free wall. At 5 year follow-up no patient died.

**Conclusions:** CMRI is a useful tool to detect cardiac involvement among patients affected by pulmonary or systemic sarcoidosis in order to achieve an earlier diagnosis at less advanced disease stages. Thus it represents an essential step of the diagnostic work-up in these patients.

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### ID# 134

#### A Case of Recurrent Hemoptoe and Systemic Symptoms

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**Introduction:** Hemoptoe can be the presenting symptom of different pathological conditions, especially when associated with fever, malaise and weight loss. The most common associated diseases are malignancies and infections, but inflammatory and immune-mediated pathologies must be kept in mind, too. Especially when there is sign of other organ dysfunction and systemic symptoms.

**Case report:** We describe the case of an ex-smoker 69 y.o. Caucasian woman, who was admitted to the emergency department with fever, back pain, dyspnea and severe hemoptoe. Her past medical history was remarkable for chronic atrial fibrillation, hypertension, obesity, and previous pleuro-pericarditis with cardiac tamponade. A few months earlier she was admitted to our hospital due to pneumonia complicated by haemoptoe. She had no previous history of pneumopathies or renal disease. Her serum creatinine level at dismissal was slightly elevated (1.81 mg/dL), but this was thought to be caused by the CT contrast media. A few days after dismissal she went to the emergency department with hemoptoe. She was treated with antibiotics and corticosteroids and then discharged.

**Results:** Her thorax CT scan showed diffuse ground glass opacities, consolidations and crazy paving in most of the right lower lobe and left superior lobe, signs of haemorrhagic alveolitis. Her serum creatinine level was highly elevated and her urine analysis showed macro hematuria, sub nephrotic proteinuria and cells

casts. The patient then developed skin purpuric lesions, so an immunologic consultation was made. Antineutrophil cytoplasmic autoantibody (ANCA) came positive, with high anti-myeloperoxidase (MPO) antibodies titre.

**Conclusions:** A diagnosis of ANCA-associated vasculitis was made with haemorrhagic alveolitis, end stage renal disease requiring dialysis and skin involvement. ANCA associated vasculitis are rare diseases and their diagnosis may be challenging. Presenting symptoms may be aspecific, so patients are often misdiagnosed with infections or malignancies. Lungs and kidneys are the most commonly involved organs and the diagnostic delay may lead to severe organ dysfunction, that may be prevented with a promptly and adequate treatment. Our patient's history highlights the importance of differential diagnosis and points out the fact that clinical suspect and multi disciplinary evaluation is fundamental in our everyday practice.

procedures were performed using fluoroscopic guidance. In case of inadequate samples at ROSE in control group, a shift to interventional group was provided by study design.

**Results:** Thirty five patients have been enrolled (20 in control group, 15 in intervention group). Nine of 20 patients in control group underwent subsequently TBNA with ultrathin bronchoscope for inadequate material at ROSE. Overall, diagnostic yields were 66% (10/15) in the ultrathin bronchoscopy group, 45% (9/20) in the conventional bronchoscopy group, and 65% in subgroup of patients who subsequently shifted to ultrathin bronchoscopy group.

**Conclusions:** This is the first randomized study aiming at directly comparing ultrathin bronchoscopy and conventional bronchoscopy under fluoroscopy guidance using TBNA as sampling instrument. Our preliminary findings suggest higher diagnostic yields for both ultrathin bronchoscopy and sequential approach over the conventional procedure, but we have to wait for study completion to draw definitive conclusions.

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#### ID# 135

### Conventional Versus Ultrathin Bronchoscope for the Diagnosis of Peripheral Pulmonary Nodules

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**Introduction:** The role of the transbronchial approach for diagnosis of peripheral pulmonary lesions has been well established. However, its diagnostic yield varies considerably and it seems to be related to size and localization of the lesion, to the sampling instrument used and to the operator's experience. The presence of bronchus sign, an underlying malignant process, lesion size>3 cm, the use of transbronchial needles (TBNA) and rapid on site examination (ROSE) seem to be predictors of a higher yield. More recently, advances in technology have led to the development of ultrathin bronchoscopes (diameter = 3 mm), that, compared to conventional bronchoscopes, offer the advantage of penetrating further into the periphery of the airways and of approaching the lesion more closely. However, although a superiority of ultrathin bronchoscopy over the conventional procedure could be reasonably supposed, evidence-based data from properly designed randomized studies are still lacking.

**Objects:** The aim of this study is to evaluate the diagnostic yield of ultrathin bronchoscope as compared to the conventional bronchoscope for the diagnosis of peripheral pulmonary nodules.

**Methods:** This is an ongoing single-center, prospective, randomized controlled trial conducted at the Pulmonary Disease Unit of the Azienda Ospedaliero-Universitaria "Ospedali Riuniti" (Ancona, Italy). From July 2019, patients referred to our Interventional Pulmonology unit with peripheral lung lesions ≤ 3 cm were randomized in two groups: the intervention group underwent TBNA with ultrathin bronchoscope while control group underwent TBNA with conventional bronchoscope. All

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#### ID# 136

### Use of Oral Corticosteroids and Comorbidities in Severe Asthma

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**Introduction:** Comorbidities in severe asthma (SA) are common, they complicate management and effect patient outcome. Comorbidities may frequently interact, contribute to poor disease control and mimic symptoms of asthma. They may also increase the cost of treatment for people with severe asthma and lead to overtreatment. It is therefore recommended that comorbidities be addressed in severe asthma. Moreover, prevalence rate of SA comorbidities are often increased by chronic Oral-Steroids (OCS) treatments.

**Objects:** We evaluated the prevalence of comorbidities in patients enrolled in the Italian Registry of Severe Asthma (IRSA).

**Methods:** 1218 patients were analysed and comorbidities were evaluated in four main treatments groups: (A) Long-Acting β2-Agonists+Inhaled-Cortico-Steroids (LABA+ICS), (B) LABA+ICS+other drugs, (C) LABA+ICS+Other drugs+Biologics, (D) OCS for over three months +Other drugs.

**Results:** 1196 patients were analysed and at least one comorbidity affected 88% of subjects. Most common comorbidities were: sinusitis (52%), gastroesophageal reflux (GER) (44%), nasal polypsis (44%), hypertension (31%), obesity (20%), osteoporosis

**Table 1.****Table.** Frequency distribution of comorbidities overall and according to different treatment groups in 1218 patients with severe asthma <sup>a</sup>

	All patients	Group A (n=54)	Group B (n=285)	Group C (n=616)	Group D (n=241)	p-value All groups	p-value A vs B	p-value A vs C	p-value A vs D	p-value B vs C	p-value B vs D	p-value C vs D
	n (%)	n (%)	n (%)	n (%)	n (%)							
Sinusitis	602 (52.0)	26 (59.1)	114 (43.0)	316 (53.6)	134 (56.3)	<b>0.008</b>	<b>0.047</b>	0.49	0.73	0.004	<b>0.003</b>	0.49
Nasal polypsis	501 (43.9)	22 (46.8)	98 (38.6)	261 (44.2)	105 (46.0)	0.33	0.29	0.73	0.92	0.13	0.10	0.63
Hypertension	378 (31.5)	18 (33.3)	85 (30.2)	182 (30.0)	86 (36.1)	0.35	0.65	0.61	0.70	0.95	0.16	0.09
Osteoporosis	217 (20.0)	7 (15.2)	43 (16.7)	96 (17.4)	69 (32.5)	< <b>0.001</b>	<b>0.80</b>	<b>0.71</b>	<b>0.02</b>	0.82	< <b>0.001</b>	< <b>0.001</b>
Cataract	100 (8.7)	3 (5.9)	15 (5.7)	45 (7.7)	37 (16.0)	< <b>0.001</b>	0.95	0.79	0.06	0.28	< <b>0.001</b>	< <b>0.001</b>
Diabetes	88 (7.3)	4 (7.4)	24 (8.5)	40 (6.6)	20 (8.4)	0.71	0.79	0.78	0.82	0.31	0.95	0.37
Obesity	234 (19.6)	8 (15.4)	53 (18.7)	119 (19.9)	51 (21.2)	0.77	0.57	0.43	0.35	0.69	0.49	0.67
Aspirin sensitivity	196 (17.3)	3 (6.7)	38 (14.3)	107 (18.6)	46 (20.2)	0.07	0.16	<b>0.04</b>	<b>0.03</b>	0.12	0.08	0.62
Gastroesophageal reflux	489 (44.0)	18 (40.0)	111 (43.7)	249 (43.5)	102 (46.1)	0.86	0.64	0.65	0.45	0.96	0.59	0.51
Psychiatric conditions	67 (6.6)	3 (7.0)	16 (7.2)	29 (5.5)	18 (8.8)	0.45	0.96	0.73	0.70	0.38	0.55	0.11
Aspergillus sensitivity	46 (5.2)	1 (3.2)	7 (3.5)	25 (5.5)	12 (6.3)	0.59	0.99	0.99	0.70	0.29	0.21	0.68
<b>Any comorbidity</b>	<b>1068 (87.7)</b>	<b>43 (79.6)</b>	<b>239 (83.9)</b>	<b>549 (89.1)</b>	<b>218 (90.5)</b>	<b>0.02</b>	<b>0.45</b>	<b>0.04</b>	<b>0.02</b>	<b>0.03</b>	<b>0.03</b>	<b>0.57</b>

<sup>a</sup> The percentages keep into account the presence of "I do not know" answers or missing information.

(20%), cataract (9%), diabetes (7%). Group D had more comorbidities with a prevalence of osteoporosis and cataract compared to other groups (D vs B and D vs C, p<0.001). Diabetes was common in Group B (8.5%) and D (8.4%). Obesity, GER and hypertension were equally distributed among Groups.

**Conclusions:** SA patients showed high comorbidities prevalence and reduced symptoms control. Some comorbidities can have a common etiopathogenesis (Th2 inflammation), while other comorbidities can be caused by the chronic use of OCS. For those reasons, Biologics treatment optimization and OCS sparing interventions should be considered to reduce related comorbidities.

due to frequent exacerbations and symptom burden. Oral corticosteroids (OCS) are commonly used for the management of severe asthma, either episodically for moderate-to-severe exacerbations, or chronically as maintenance therapy in patients who do not respond satisfactorily to inhaled therapies. As a result, patients with persistent severe asthma often suffer from systemic side effects of corticosteroids such as diabetes, hypertension, glaucoma, osteoporosis, and mood disorders.

**Objects:** We assessed asthma control and the characteristics of patients treated with OCS in Allergy and Pulmonology Departments adhering to the Italian Registry of Severe Asthma (IRSA).

**Methods:** IRSA is an Italian, multicenter, transversal/retrospective, non-interventional, observational study on patients ≥14 years affected by SA according to GINA Guidelines. Data on asthma control and patients regularly treated with OCS were analysed.

**Results:** Overall, 1216 patients (477 male, 739 female) were included in the analysis. According to the Asthma Control Test scoring, 409 patients were controlled with a mean FEV<sub>1</sub> 78±21%. As add-on to inhalation therapy, 31% patients took OCS: Dexamethasone 0.7%, Deflazacort 1.6%, Betamethasone 2.7%, Methylprednisolone 8.5%, Prednisone 17.6%. Among patients, 15% treated with OCS were controlled and 40% were uncontrolled asthmatics. Patients with uncontrolled asthma had high eosinophilia (577 cells/ul ± 800) compared with controlled (432 cells/ul ± 632). Moreover, patients with eosinophilia (n=675) took OCS in 34.5% of cases, and only 60% were treated with biologics (omalizumab n=365, mepolizumab n=322).

**Conclusions:** Despite high-dose ICS therapy plus additional controllers or OCS, only 34% of patients affected by SA had controlled asthma. Moreover, 31% of subjects daily took OCS. The percentage of patients adhering to the registry who use OCS daily is still very consistent. Of note, in this population the level of eosinophilia is elevated with a suboptimal use of biologics.

#### ID# 137

#### Assessment of the Level of Control and Use of Corticosteroids in Patients with Severe Asthma

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**Introduction:** Around 2.4% to 4% of patients with asthma suffer from a severe phenotype (SA). Compared to the general asthma population, these patients suffer from a higher rate of morbidity

**Table 1.**

**Table.** Frequency distribution of treatment use overall and according to controlled/uncontrolled asthma in 1218 patients with severe asthma <sup>a</sup>

	All patients	Controlled asthma (n=409)	Non controlled asthma (n=807)	p-value
<b>Use of Systemic steroids</b>				
No	835 (68.6)	347 (84.8)	486 (60.2)	
Yes	383 (31.4)	62 (15.2)	321 (39.8)	<0.001
Betametasone	33 (2.7)	2 (0.5)	31 (3.8)	<0.001
Deflazacort	19 (1.6)	6 (1.5)	13 (1.6)	0.85
Desametasone	8 (0.7)	1 (0.2)	7 (0.9)	0.28
Metilprednisolone	104 (8.5)	15 (3.7)	89 (11.0)	<0.001
Prednisone	214 (17.6)	36 (8.8)	178 (22.1)	<0.001
Other	4 (0.3)	0 (0.0)	4 (0.5)	0.22
<i>Duration of use of systemic steroids (users only)</i>				
Mean ± SD (months)	12.0 ± 22.0	16.7 ± 18.8	11.1 ± 22.5	0.003
<b>Use of monoclonal antibodies</b>				
No	453 (37.2)	94 (23.0)	359 (44.5)	
Yes	765 (62.8)	315 (77.0)	448 (55.5)	<0.001
Omalizumab	365 (30.0)	172 (42.0)	193 (23.9)	<0.001
Mepolizumab	322 (26.4)	119 (29.1)	202 (25.0)	0.13
Benralizumab <sup>b</sup>	85 (16.0)	26 (16.9)	58 (15.4)	0.68
<i>Duration of use of monoclonal antibodies (users only)</i>				
Mean ± SD (months)	20.1 ± 26.6	23.2 ± 24.6	17.8 ± 27.8	<0.001
<b>FEV1 (bronchodilator withhold, %)</b>				
Mean ± SD	71.8 ± 20.7	78.0 ± 20.9	68.5 ± 19.8	<0.001
<b>Eosinophils (Num)</b>				
<90	183 (15.4)	79 (20.3)	104 (13.1)	
90-150	117 (9.8)	52 (13.3)	65 (8.2)	
151-300	214 (18.0)	81 (20.8)	133 (16.7)	
>300	675 (56.8)	178 (45.6)	495 (62.1)	<0.001
Mean ± SD	529.9 ± 751.9	431.7 ± 632.3	577.6 ± 800.7	<0.001

<sup>a</sup> The sums may not add up to the total because of missing values.

<sup>b</sup> Information was not collected since the beginning of the Registry and is thus available for a subgroup of 532 patients.

## ID# 138

### Use of triple therapy in severe asthma: evidence from the Italian Registry Severe Asthma (IRSA)

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**Introduction:** Tiotropium is the first anticholinergic drug that has been approved for children and adults with poorly controlled asthma and is currently considered as an option for steps 4 and 5

of the Global Initiative for Asthma. In large randomized clinical trials enrolling patients with moderate to severe asthma, add-on therapy to corticosteroids (ICS)/Long-Acting  $\beta$ 2-Agonists (LABA) with tiotropium has demonstrated to be efficacious in improving lung function, decreasing risk of exacerbation and slowing the worsening of disease.

**Objects:** To assess the use of triple inhaler therapy in severe asthmatic patients included by Allergy and Pulmonology Departments into the Italian Registry of Severe Asthma (IRSA).

**Methods:** We analysed 1218 patients enrolled in the IRSA. All patients provided written informed consent.

**Results:** 1215 patients (477 male, 738 female) were included in the analysis. 41% patients were treated with ICS/LABA/TIO and 59% with ICS/LABA. Patients taking Triple therapy had a worse lung function (FEV<sub>1</sub> 67%±21 vs 75%±20; p<0.001), high number of exacerbation/year (3.9±4 vs 2.8±3; p>0.001) and were regularly treated with systemic steroids (37% vs 28%). However, they had reduced IgE levels (520±1475 vs 561±1194). In addition, 57% of ICS/LABA/TIO patients used biologics compared to 66% of LABA/ICS patients.

**Table 1.**

**Table.** Frequency distribution of selected clinical, laboratory and treatment data according to treatment with ICS/LABA with or without TIO in 1218 patients with severe asthma<sup>a</sup>

	ICS/LABA no TIO (n=720)	ICS/LABA+TIO (n=495)	p-value
	n (%)	n (%)	
<b>Sex</b>			
Females, n (%)	437 (60.7)	301 (60.8)	0.97
<b>Age</b>			
Mean ± SD	53.7 ± 14.2	57.0 ± 12.9	<0.001
BMI			
≥30	122 (16.9)	126 (25.4)	<0.001
Mean ± SD	26.1 ± 5.1	27.3 ± 4.9	<0.001
<b>Controlled asthma</b>			
No	436 (60.6)	368 (74.5)	
Yes	283 (39.4)	126 (25.5)	<0.001
<b>Atopic asthma</b>			
No	197 (27.4)	157 (31.8)	
Yes	522 (72.6)	337 (68.2)	0.10
<b>Asthma attacks</b>			
No	139 (19.3)	68 (13.7)	
Yes	581 (80.7)	427 (86.3)	0.01
Mean ± SD	2.8 ± 3.2	3.9 ± 4.4	<0.001
<b>Hospitalization</b>			
No	618 (85.8)	392 (79.2)	
Yes	102 (14.2)	103 (20.8)	0.002
<b>Total IgE</b>			
<100	79 (25.9)	82 (32.4)	
100-300	98 (32.1)	75 (29.6)	
>300	128 (42.0)	96 (37.9)	0.24
Mean ± SD	561.0 ± 1194.3	520.5 ± 1475.3	0.13
<b>FEV1 (bronchodilator withhold, %)</b>			
Mean ± SD	75.0 ± 19.9	66.9 ± 21.0	<0.001
<b>Use of systemic steroids</b>			
No	518 (71.9)	314 (63.4)	
Yes	202 (28.1)	181 (36.6)	0.002
<b>Use of monoclonal antibodies</b>			
No	241 (33.5)	212 (42.8)	
Yes	479 (66.5)	283 (57.2)	<0.001

<sup>a</sup> The sums may not add up to the total because of missing values.

**Conclusions:** To reduce exacerbations, LABA/LAMA/ICS are recommended in patients with uncontrolled SA. According to the GINA guidelines, the optimization of inhaler therapy is mandatory before starting biological treatment approach. IRSA network revealed a low percentage of patients treated with triple combination therapy also in those using biologics. Additionally, IRSA Centres used to prescribe triple therapy especially to patients with

more SA and a non-allergic phenotype. In view of the numerous ancillary effects acting on inflammation, airway remodelling, mucus production and cough reflex, along with the good safety profile and the broad spectrum of efficacy demonstrated in different disease phenotypes, tiotropium can represent a beneficial alternative in the therapeutic management of poorly controlled asthma.