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CO 001. TUBERCULOSIS SCREENING OF UKRAINIAN REFUGEES IN PORTUGAL

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Introduction: On February 24, 2022, Russia launched a military offensive in Ukraine that has already caused an undetermined number of deaths and more than 11 million refugees. At least 48 thousand refugees applied for temporary protection in Portugal by August 2022. Ukraine is one of the tuberculosis (TB) high-priority countries in the World Health Organization (WHO) European Region and one of the nine countries globally with a high burden of multidrug-resistant TB. In Portugal, there are no specific recommendations regarding TB screening among refugees, although according to Portugal's Directorate-General of Health, all citizens coming from the Ukraine should be asked about symptoms, exposure, comorbidities or risk factors for disease progression.
Objectives and methods: We conducted a cross-sectional study using an electronic survey. The aim was to understand what adjustments the different national Outpatient TB Centers (OTBC) made to comply with TB screening in Ukrainian refugees. The survey was sent five times via email to all OTBC coordinators to increase the response rate. Responses were collected during August 2022.
Results: Twenty-nine OTBC coordinators responded to the questionnaire, from a total 61 (response rate of 47.5%). Twenty-three OTBC (79.3%) mentioned that TB screening was performed in Ukrainian refugees, approximately fourteen days after arrival in Portugal. The screening process included a symptom questionnaire and chest radiography (52.2%). Additionally, 47.8% (n = 11) reported including latent TB infection (LTBI) screening with tuberculin skin test and/or Interferon Gamma Release Assay. In 65.2% (n = 15) of the OTBC carrying out TB screening of Ukrainian refugees, more than 20 were performed. OTBC coordinators flagged only one patient with a previous diagnosis of TB. There were 13 diagnoses of LTBI, mainly in the Northern RHA (76.9%). In this region, most of the centers (55.6%) only included a symptom questionnaire and chest radiography. Treatment for LTBI was carried out in 7 patients (53.8%). No new TB diagnosis were made. Nonetheless, the following problems were raised: refugees' mobility to another city, refusal to perform chest radiography, linguistic barrier, lack of human resources and response rate across all RHA.
Conclusions: TB screening is a current challenge and ensures that people with a previous diagnosis continue to be medically treated. However, it is not surprising that European Centre for Disease Prevention and control (ECDC) and WHO Europe recommended screening and testing only for certain refugee groups, such as people living with human immunodeficiency virus (HIV) or those who are contacts of TB patients. It is essential to balance benefits and harms, such as stigmatization, discrimination, resource use and mental health issues.

Keywords: *Mass screening. Portugal. Refugees. Tuberculosis. Ukraine.*

CO 002. 21ST CENTURY, YEAR 2022: THERE ARE STILL DEATHS FROM TUBERCULOSIS IN PORTUGAL

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Introduction: Tuberculosis (TB) remains one of the leading causes of death worldwide. Portugal is the country in Western Europe with the highest incidence rate. Despite the reduction in the number of reported cases in 2020/2021, there was an increase in the number of TB deaths. At Vila Franca de Xira Hospital, three cases of death from TB were registered in 2022, which are described below.
Case reports: Case-1: Male, 67 years old, born in Guinea-Bissau, evacuated to Portugal on April/2022 for study and treatment of consumptive status and lesion of the oropharynx. Tongue biopsy showed locally advanced oropharyngeal squamous cell carcinoma (cT4aN2M0). Cervico-thoracic-CT (30/04/2022) with several areas of consolidation outlining cavitations in the upper lobes and apical segment of the right lower lobe, with associated tree in bud pattern. Underwent several cycles of antibiotic therapy, without clinical improvement, and ended up being hospitalized before starting anti-tumor treatment, in a state of cachexia, fed by PEG. He was evaluated by pulmonology during hospitalization, who re-

quested a mycobacteriological study of sputum and started quadruple antibacillary therapy. BAAR and PCR-MTC (M. tuberculosis complex) were positive. Died on the 30th day of hospitalization (3rd antibacillary). Subsequent cultural isolation of MTC sensitive to 1st line antibacillars. Case-2: Male, 72 years old, leukodermic, autonomous. History of hypertension and heart failure due to ischemic heart disease, former smoker (55 pack-years). He was referred to the emergency department (ED) with a 5-month history of non-productive cough, dyspnea, asthenia and anorexia. Observation revealed marked cachexia. Chest-CT showed a micronodular pattern with random distribution and mediastinal and abdominal adenopathies. He was hospitalized for clarification, under antibiotic therapy. He was evaluated by a pulmonologist who, due to suspicion of disseminated TB, performed bronchofibroscopy and instituted antibacillary therapy. Died on the 5th day of hospitalization (1st antibacillary). Posthumous results of negative BAAR, positive PCR-MTC and culture, with isolation of MTC sensitive to 1st line antibacillars. Case-3: Male, 55 years old, leukodermic, autonomous. Personal history of hepatitis C infection, alcoholism, former drug addict on methadone program. He came to the ED with dyspnea, asthenia and unquantified weight loss over months. Chest-CT showed extensive consolidations with air bronchogram, associated with thick-walled cavitations in the upper lobes and apical segments of the lower lobes, mediastinal adenopathy, with virtually no subcutaneous fat. He was hospitalized for cachexia and probable active pulmonary TB. Sputum samples were collected and antibacillary therapy was started. Died on the 2nd day of hospitalization (1st antibacillary). Positive BAAR-test result on the same day after death.
Discussion: In Portugal, despite the sustained reduction in the tuberculosis notification rate, there has been an increase in the delay of diagnosis. This delay is partly attributable to the patient, due to fear and difficulty in accessing health care generated by the COVID pandemic and low TB literacy, especially in vulnerable populations, but also to health professionals, with a persistent increase in the delay until diagnosis, resulting from a low clinical suspicion for TB. Late diagnosis is associated with more extensive disease, with worse prognosis, as exemplified in the cases described.

Keywords: *Tuberculosis. Cachexia. Death.*

CO 003. CHILDHOOD TUBERCULOSIS IN PORTUGAL – CURRENT PORTRAIT OF THE CENTER REGION

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Introduction: Tuberculosis continues to be an infectious disease responsible for high morbidity and mortality worldwide, including in the pediatric population. The Bacillus Calmette-Guérin (BCG) vaccine is the only approved vaccine against *Mycobacterium tuberculosis* (Mtb) and it protects against severe forms of TB in children, with an efficacy of around 80%. In 2016, BCG vaccination ceased to be part of the National Vaccination Plan, becoming recommended for children belonging to risk groups aged 5 years or less.
Objectives: To study the evolution of the number of cases of Tuberculosis, and its main characteristics, in children up to 15 years of age, diagnosed from 2010 to 2021 in the Health Region of Central Portugal.
Methods: The authors analyzed epidemiological and clinical data of children aged up to 15 years with active or latent tuberculosis from 2010 to 2021. Data were extracted from SVIG-TB. Information on BCG vaccination status was also included.
Results: A total of 208 children were identified, 30 diagnosed with active tuberculosis and 178 with latent infection. Of the cases of active tuberculosis, 18 occurred from 2010 to 2015, 5 of them unvaccinated. From 2016 to 2021, 12 cases were observed, of which 7 were unvaccinated. Of the total number of cases, 56.7% (17) were male and the mean age was 7.27. Regarding the origin CDP, 10 were from Coimbra, 10 from Aveiro, 5 from Viseu, 3 from Castelo Branco and 2 from Leiria. It was observed that 24 cases had a negative HIV serology record. The most frequent location was pulmonary (18), followed by pleural (4), ganglionic (3), peritoneal (1), meningeal (1), bone (1), disseminated (1) and another location (1). The most frequent initial treatment scheme was isoniazid, rifampicin, ethambutol and pyrazinamide, in 17 cases. TOD was recorded in 17 cases. Complete treatment was verified in most cases (28), with 2 still being treated. Regarding latent infections, 52.8% (94/178) occurred up to the year 2015, of which only 3 children were not vaccinated. The remaining cases (47.2%) occurred between 2016 and 2021, and 15 of these children were not vaccinated. Of the 178 children, 54.5% (97) were male and the mean age was 8.43 ± 4.7 years. In 63.5% (113/178) of latent infections, the initial treatment was isoniazid, 11.2% (20/178) was isoniazid and rifampicin, and in (6/178) rifampicin alone. Only 1.1% (2/178) had a DOT prescription record. Complete treatment was verified in 88.2% (157/178) of cases, 4.5% (8/178) interruption/abandonment, 1.1% (2/178) transfer/emigration and the remaining 6.2% (11/178) are still being treated.
Conclusions: Despite the reduced numbers observed, the authors highlight the occurrence of severe forms of tuberculosis, with potential sequelae, in two unvaccinated children. The authors also emphasize that it is plausible that during the years 2020 and 2021 there was underdiagnosis and underreporting of tuberculosis related to the COVID-19 pandemic, as well as the potential protective effect of preventive measures such as the use of a mask and the reduction of social contacts.

Keywords: *Childhood tuberculosis. Vaccine. BCG.*

CO 005. STRATEGIES AND INTERVENTIONS TO PROMOTE TREATMENT ADHERENCE IN PEOPLE WITH ACTIVE TUBERCULOSIS: PRELIMINARY FINDINGS OF A SYSTEMATIC REVIEW

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Introduction: Despite significant worldwide efforts to eliminate tuberculosis (TB), it continues to be a major contributor to mortality, standing as the 13th leading cause of death and 2nd in terms of infectious diseases. People with TB face significant challenges during the treatment period, such as a long regimen with potential serious and adverse reactions; to which added hindrances, social and economic constraints can arise. In this sense, adherence should be understood as a result of a complex and interconnected system, where dimensions such as treatment administration options and social support should be taken into consideration and adequately assessed. Thus, with the present review we aim to assess the efficacy of different strategies, interventions and/or programs aimed at improving treatment adherence in people with active TB.
Methods: We conducted a systematic search of four electronic databases (MEDLINE/PubMed, WebOfScience, SCOPUS, and CENTRAL) according to PRISMA guidelines, during June 2023. Quality of the included studies was appraised with the Cochrane Risk of Bias tool, for randomised controlled trials; and for non-randomized studies with the Newcastle-Ottawa Scale. Primary outcomes were treat-

ment success (treatment completion and cure) and losses to follow-up, which were meta-analysed and confidence in results was assessed using GRADE.
Results: As of July 31st, 2023 a total of 24 studies with 20,226 participants (9,768 Control; 10,458 Intervention) were included. Preliminary findings suggest that for treatment success, directly observed treatment (DOT) combined with other mechanisms, namely social and psychological support, comprehensive health education, medication and/or appointment reminders; and community based DOT were found effective. Similarly for treatment completion, DOT combined with phone-based system reminders, social, community and psychological support were also found to be effective. For losses to follow-up, only community based DOT and treatment with follow-up in the health care centre, combined with educational strategy and monthly reminders were found to be effective. Interestingly, DOT appears to show variable effectiveness, highlighting that implementation, population and setting may play important roles.
Conclusions: Adherence remains a complex and challenging concept to define universally, leading to difficulties in identifying interventions aimed at promoting it and/or summarising research findings. Additionally, the lack of a standardised methodology to measure treatment adherence contributes to inconsistent outcomes, hindering the comparison of various interventions. So far, a notable gap in the majority of studies is the limited exploration of the experiences of people with TB regarding the interventions being evaluated. The absence of a comprehensive assessment of people with TB's perspectives, beliefs, and attitudes about these interventions is evident, hindering a more holistic understanding of their impact and effectiveness. Addressing these shortcomings will be crucial for advancing our knowledge and developing more patient-centric strategies to enhance adherence to TB treatment.

Keywords: *Adherence. TB. Tuberculosis. Treatment success.*

CO 006. TUBERCULOSIS EVERYWHERE? – BIOTECNHOLOGY DRUGS AND LATENT TUBERCULOSIS SCREENING

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Introduction: In recent years, biotechnological drugs have become treatment options for several diseases, across a number of Specialties. Because they are systemic immunossupressors, patients should be submitted to an infectious screening, particularly Latent Tuberculosis (LTB); physicians should evaluate epidemiology and exposure risk, interferon gamma release assay (IGRA) and tuberculin sensitivity test (TST), as well as thoracic imaging. In Portugal, they should be referred to the tuberculosis centers, Centros de Diagnóstico Pneumológico (CDP).
Objectives: Analysis of patients referred to CDP for LTB screening in the context of current/future biotechnology drug treatment. The main goal is to describe the indications, antitubercular drugs used and complications of LTB treatment.
Methods: Retrospective study using clinical records (SClinic®) of all patients submitted to LTB treatment in the context of biotechnology drug treatment in CDP Estuário do Tejo, in 2022 and first semester of 2023. The following parameters were evaluated: sex, age, smoking history, diagnosis, Specialty and Hospital referral, current and proposed biotechnology treatment, exposure or previous TB diagnosis, previous LTB treatment, risk exposure (occupation, nationality, prolonged stays in high incidence TB countries), clinical manifestation, HIV status, IGRA/TST result, imaging abnormalities, LTB treatment, complications and treatment changes.
Results: Of the 187 patients who underwent LTB screening (41.71% on the first semester of 2023 and 58.29% in 2022), 51.33% were women, median age 40.24 ± 16.54 years, the majority never-smokers (60.96%). Rheumatology (n = 82, 43.85%), Dermatology (n = 55, 29.41%) and Gastroenterology (n = 31, 16.58%) were the main referrals, 76.57% from public hospitals; the most common diagnosis were Psoriasis (32.09%), Rheumatoid Arthritis (17.65%) and Crohn's Disease (9.63%), mainly proposed for anti-TNF therapy (n = 77, 41.18%). Almost all patients were asymptomatic (99.47%). There were no suspicious active TB imaging abnormalities, however 21.93% individuals had evidence of TB sequelae. Immune testing was positive in 30.48% (20.32% positive IGRA; 27.27% positive TST, median diameter 14.91 ± 6.64 mm); all patients were HIV negative. Epidemiology inquiry revealed 4.82% with occupational risk exposure, 24.06% with prolonged stay in high incidence TB countries, 2 inmates, 3 patients with previous treatment for active TB and 12 (6.48%) for LTB. Based on these screening results, 85 patients started LTB treatment (45.45%), 89.41% com isoniazid (n = 76). Hepatotoxity was reported in 8 patients (9.41%), leading to treatment switch to rifampicin (87.5%, n = 7).
Conclusions: LTB screening is essential in patients proposed or currently under biotechnology drug treatment. In the past year, there has been a significant rise in CDP referrals, which highlights the increased usage of these drugs by physicians, as well as an important increment of patients followed in Portugal's CDP.

Keywords: *Biotechnology drugs. Tuberculosis. Latent tuberculosis. Screening.*

CO 007. RE-TREATMENT, RESISTANCE AND OUTCOMES IN TUBERCULOSIS: A HISTORICAL PERSPECTIVE

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Introduction: In 1992, multiple factors resulted in a worldwide increase in new TB and MDR-TB cases.
Methods: Analysis and historical comparison from a Portuguese cohort of re-treated inpatients in 1992.
Results: Twenty-nine patients with a 45-year mean age were admitted for re-treatment. Previous regimens included 1st-line drugs (81.5%) or kanamycin/FQ regimens (18.5%). Time from last treatment was variable (1-18 years). The most frequent resistances were H (72%), S (55%) and Z (41%). R resistance was rare (3%). Post-admission, 44.8% started HRZE/HRZS. Other regimens included Km (41.4%) and FQ (13.8%). 55% of patients achieved culture conversion. Comparison to current cohorts showed a significant difference between past and present treatments (p = 0.003).
Conclusions: Our study illustrates the MDR-TB treatment challenges in 1992. At the time, guidelines suggested the use of 3 effective drugs. Similar historical studies using a mean of 3.7 effective drugs achieved a culture conversion rate of 51.2%. Our cohort's high conversion rate, despite sub-optimal therapy, shows the impact of adherence in TB patients. New drugs like bedaquiline have changed the MDR-TB landscape, with regimens achieving > 80% culture conversion. An interesting finding was the low number of RR-TB cases in our cohort. Concurrent pharmacological studies showed considerable variation in the fitness of R-resistant strains compared to drug-susceptible or H-resistant strains. This aligns with our data, which shows low R resistance in patients with previous multiple treatments. New treatments are more effective in treating MDR-TB. Rifampicin-resistant strains were probably less fit at the time, resulting in fewer RR-TB cases.

Keywords: *MDR-TB (multidrug-resistant tuberculosis).*

CO 008. CHARACTERIZATION OF ADVERSE EFFECTS REPORTED BY PATIENTS UNDER ANTITUBERCULOSIS THERAPY

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Introduction: Tuberculosis remains a major public health problem and its treatment is mandatory. However, the treatment is long and complex consisting of a set of several drugs with potential adverse effects. The impact that the disease has on the patient's life is undeniable with adverse effects of therapy being a frequent negative contribution. **Objectives:** The aim of this work is to characterise most commonly reported adverse effects by patients on first-line treatment for active tuberculosis. Materials and **Methods:** For this study, voluntary self-completion questionnaires were prepared and distributed to patients under treatment for tuberculosis in 3 Pulmonary Diagnostic Centres in the Lisbon and Tagus Valley region during the month of May 2023. The questionnaires assessed demographic data and adverse effects of antituberculosis therapy reported by patients.
Results: Of the total of 67 questionnaires completed, 42 were by patients with active tuberculosis. Of these 42 patients, 57% (n = 24) were male. The majority (55%; n = 23) were Portuguese nationals, with the remaining being migrants coming from various countries, mainly PALOPs (Portuguese-speaking African countries). The adverse effects reported by patients were: nausea and vomiting in 29% (n = 12); abdominal pain in 19% (n = 8); diarrhoea in 12% (n = 5); paraesthesia in the limbs in 55% (n = 23); arthralgias in 45% (n = 19); hair loss in 24% (n = 10); 40% (n = 17) reported feelings of sadness. Of the patients assessed, only 12% (n = 5) denied any adverse effects. It should also be noted that 43% (n = 18) of patients reported 3 or more adverse effects associated with the therapy. Discussion and conclusions: The majority of evaluated patients reported adverse effects of antituberculosis therapy, often mentioning more than one adverse effect, suggesting a significant impact of antituberculosis therapy on their quality of life. Contrary to what has been described in the literature, the main adverse effect reported by the patients assessed was the sensation of paraesthesia in the limbs, followed by complaints of arthralgia. The high percentage of patients who reported feelings of sadness is also noteworthy, which makes it evident the importance of also questioning the patient's emotional state regarding the disease and its treatment, so that timely and effective help can be offered. A thorough assessment of adverse effects is of utmost importance in order to reduce the impact of therapy on patients' quality of life, which may lead to discontinuation.

Keywords: *Antituberculosis therapy. Adverse effects. Tuberculosis.*

CO 009. HYPERSENSITIVITY REACTIONS AND SUCCESSFUL DESENSITIZATION TO ANTITUBERCULOUS DRUGS

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Introduction: Tuberculosis remains an important public health issue in Portugal. Prompt treatment with the recommended regimen of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) is essential to improve prognosis and prevent the emergence of resistances. Hypersensitivity reactions to antituberculous drugs occurs in about 4% of patients with a variable clinical presentation, with delayed mild skin reactions being the most common. The drugs most implicated are rifampicin and pyrazinamide. Desensitization protocols have been associated with high success rates. We present two cases of patients with hypersensitivity reactions to antituberculous drugs who underwent successful desensitization.
Case reports: Case report 1: 52-year-old woman with a medical history of depressive syndrome, dyslipidemia and allergic rhinoconjunctivitis. She denied any history of smoking, alcohol consumption or known drug or food allergies. She was diagnosed with multidrug-sensitive pulmonary tuberculosis. Treatment with HRZE was initiated, but she presented with an immediate urticarial reaction 10 minutes after the first dose. The case was urgently referred to Allergy specialists and the patient was admitted to reintroduce the drugs according to the defined protocol. The oral provocation test was positive for pyrazinamide, with the patient showing a generalized pruritic erythematous rash 90 minutes after completion of the test. She had no accompanying symptoms and the rash resolved after administration of clemastine and hydrocortisone. The drug was reintroduced using a 3-day desensitization protocol, without further adverse reactions. Skin tests (prick and intradermal) and oral provocation tests were negative for the remaining antituberculous agents, which were reintroduced without complications. The patient is currently medicated with the full-dose HRZE regiment, with good tolerance. Case report 2: A 39-year-old woman with no known medical history, regular medication use, allergies, or harmful habits, was diagnosed with cavitary and bacillary multidrug-sensitive pulmonary tuberculosis. She initiated treatment with HRZE and after two weeks of treatment, she presented with an extensive skin reaction characterized by a disseminated pruritic erythematous papular rash, accompanied by edema of the face and lips, without stridor or choking sensation. All antituberculous drugs were suspended, and she was given antihistamines and oral corticosteroids with significant improvement. The case was discussed with Allergy specialists and it was decided to admit the patient in a negative pressure room for reintroduction of the drugs using an oral provocation test with 72hour intervals. The test was positive for pyrazinamide, with the patient showing a mild skin reaction. Pyrazinamide was reintroduced using a desensitization protocol without further complications. No other adverse reactions were observed, and the patient was discharged under full-dose HRZE treatment with tolerance.
Discussion: Discontinuation of HRZE treatment is a significant risk factor for the development of drug-resistant tuberculosis and second-line antituberculous drugs are associated with a higher rate of adverse effects, making drug desensitization essential in patients with hypersensitivity reactions to the first-line regimen. These cases highlight the variability of hypersensitivity reaction presentations and emphasize the importance of a prompt collaboration with Allergy specialists, which is crucial for the successful identification of the responsible drug and the continuation of the recommended treatment.

Keywords: *Pulmonary tuberculosis. Pyrazinamide. Drug hypersensitivity. Desensitization.*

CO 010. IGRA TEST – DO THE ENDS JUSTIFY THE MEANS?

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Introduction: The Interferon Gamma Release Assay (IGRA) has proven to be an adjunct method of diagnosing Tuberculosis latent infection (TBL) mainly in countries where BCG vaccination is widespread. It assesses the adaptive immune response to mycobacterial antigens. It assumes an immunocompetent response by the individual and does not distinguish between active, latent or past TB. Studies on the advantage of this test as an aid in the diagnosis of active tuberculosis have been less than encouraging and the guidelines do not recommend it in the diagnostic march. Nevertheless, in spe-

cific situations, this test is used when the suspicion is pertinent and the directed tests are negative.
Methods: Retrospective study of IGRA tests performed in a level II hospital during the year 2022, and their usefulness. Requests were considered appropriate when requested according to current guidelines. Descriptive statistical analysis using Microsoft Excel®.
Results: In this period 267 IGRA tests were performed, mostly in male individuals (n = 151 - 56.56%). The majority of requests were made to Portuguese patients (n = 230 - 86.14%), the remaining being from the following countries: Brazil (n = 22 - 8.2%), Mozambique (n = 4 - 1.4%), India (n = 4 - 1.4%), Ukraine (n = 3 - 1.1%), Guinea and Angola (n = 2 - 0.7%). The youngest patient was 12 months old and the oldest 90 years old. The reasons for requesting this test were: suspicion of active tuberculosis - 129 requests; candidates for/under immunosuppressive therapy - 90; HIV infection - 43; occupational health - 3; contact tracing - 2. The specialty/service with the highest number of tests requested was internal medicine (n = 97 - 36.6%), followed by the following specialties/services: Infectiology (n = 34 - 12.7%), Pediatrics (n = 29 - 10.8%), Gastroenterology (n = 23 - 8.6%), Pulmonology (n = 17 - 6.3%), Emergency Department (n = 16 - 5.9%), Dermatology (n = 15 - 5.6%), Ophthalmology (n = 10 - 3. 7%), Nephrology and Neurology (n = 6 - 2.2%), Pediatric Emergency Service (n = 6 - 2.2%), Occupational Health (n = 6 2.2%), Cardiology and Multipurpose Intermediate Care Unit (n = 2 - 0.7%), General Surgery (n = 1 - 0.3%). Regarding the assessment of the usefulness of IGRA requests in the 4 specialties/services with the highest number of requests: only 29 (29.9%) of the tests requested by Internal Medicine were considered adequate, compared to all requests from Infectious Diseases (performed as part of the HIV consultation), 10 (34.5%) requests from Pediatrics (contact screening and children proposed for immunosuppression) and 22 (95.7%) requests from Gastroenterology (patients with inflammatory bowel disease proposed for biotechnologies). Overall, the requests considered inappropriate were made to diagnose active tuberculosis, mostly in suspected lung disease.
Conclusions: The majority of requests made were considered appropriate. However, the number of inappropriately requested tests is still very significant. This reality requires targeted training in the various services of the hospital. It also requires regular updating on the indications for the IGRA test, since the scientific evidence on its usefulness in TB diagnosis is not very consistent.

Keywords: *IGRA. Requests. Usefulness.*

CO 011. LATENT TUBERCULOSIS – WHAT IS THE TRUE PERCEPTION OF PATIENTS?

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Introduction: Latent infection with *Mycobacterium tuberculosis* does not cause symptoms, nor does it carry a risk of contagion to the rest of the population. However, 5 to 10% of infected patients may develop active tuberculosis, which reinforces the importance and benefits of preventive treatment.
Objectives: The aim of this study was to understand the knowledge of patients with latent tuberculosis regarding this diagnosis and the risk of contagion they pose to the rest of the population, as well as the psychological impact of the diagnosis.
Methods: Optional self-completion questionnaires were distributed to patients who underwent therapy for tuberculosis at the Dr. Ribeiro Sanches, Venda Nova and Estuário do Tejo Pneumological Diagnostic Centers, during the month of May 2023. Demographic data and knowledge about the disease for which they were undergoing treatment were evaluated. Descriptive analysis of patients who were under therapy for latent tuberculosis.
Results: Of the 67 completed questionnaires, 25 corresponded to patients with latent tuberculosis. Of these, the majority, 64% (n = 16) were female and had a mean age of 48 (minimum 22, maximum 71 years). The majority were of Portuguese nationality - 76% (n = 19), with the remainder originating from countries such as Brazil (n = 4), Pakistan (n = 1) and Cape Verde (n = 1). Regarding the questions asked in the questionnaire, to the first question "Do you know why you are being followed in this consultation?" all patients answered "yes". Of the 25 patients, to the question "What is the name of the disease?", 56% (n = 14) answered "latent tuberculosis", the remaining 32% (n = 8) stated "tuberculosis"; 12% (n = 3), named pathologies such as "Ankylosing spondylitis", "Crohn's disease" and "Psoriasis". Regarding the question about the contagiousness of latent tuberculosis, it was found that 84% (n = 21) answered "No" and 16% (n = 4) of the 25 patients, answered "Yes". Regarding the psychological state of this group, to the question "Do you feel sad?" 4 of the patients answered "yes". Of these, 2 related their sadness to their conviction of the potential contagiousness of the disease.
Conclusions: There were significant gaps in patients' knowledge about their diagnosis, reason for follow-up in the CDP and risk of latent TB contagiousness. Notably, about 1/4 of patients could not specify the disease for which they are being medicated and 16% consider themselves a risk of infection for others. In these patients, misinformation may contribute to anxiety and risk of depression. These results highlight the need for education of our patients and the general population about the differences between tuberculosis disease and tuberculosis infection and the relevance of their treatment.

Keywords: *Latent tuberculosis. Literacy. Misinformation.*

CO 012. PLEUROSCOPY: ANALYSIS OF THE CASUISTRY OF A PULMONOLOGY SERVICE

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Introduction: Endoscopic techniques play an essential role in the diagnostic evaluation of patients with respiratory pathology. Medical thoracoscopy/pleuroscopy is a valuable technique in the study of exudative pleural effusion of undetermined cause after performing less invasive techniques, and may also have a therapeutic purpose. Compared to VATS, it is less invasive, has a lower cost and fewer complications, and has comparable diagnostic yield.
Objectives: Analyze the diagnostic yield, safety and the characteristics of the population subjected to pleuroscopy.
Methods: Retrospective observational study. All pleuroscopies performed in a pulmonology service between August 2010 and June 2023 were selected. Statistical analysis was performed using the SPSS software.
Results: During the aforementioned period, 82 pleuroscopies were performed. Most patients (57.3%) were male, with a mean age of 68.8 ± 12.4 years. Regarding smoking habits, most patients (53.3%) were non-smokers. Pleuroscopy was performed with diagnostic intent in most cases (95.1%). The most frequent indication was the study of pleural effusion of undetermined etiology (67.1%), followed by suspected malignant pleural effusion in patients with a history of cancer (11%) and collection of material for molecular study (8.5%) Most patients who underwent pleuroscopy had pleural effusion with characteristics of exudate (97.5%), with previous negative cytology for malignant cells (84%). Blind pleural biopsy had previously been performed in 53.7% of patients. The median volume of pleural fluid drained during the procedure was 1,200 cm^3. Changes were observed in the pleura in 74% of the cases. The diagnostic yield was 90.2%. In 53.3% the diagnosis was malignancy: the most frequent was lung adenocarcinoma (24.7%), followed by pleural mesothelioma (11.7%). In one patient (1.2%) there was pleural empyema after the procedure. The mortality rate was zero.

Conclusions: Pleuroscopy is a safe technique, with high diagnostic accuracy (90.2% in our sample). It is useful in obtaining a definitive diagnosis in pleural effusions whose previous investigations were inconclusive, as we verified in this sample, avoiding the need to perform more invasive procedures, associated with higher costs and complications.

Keywords: *Medical thoracoscopy. Pleuroscopy.*

CO 013. MALIGNANT PLEURAL MESOTHELIOMA – EXPERIENCE OF A HOSPITAL CENTER

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Introduction: Malignant pleural mesothelioma (MPM) is a rare neoplasm with poor prognosis and a median overall survival (OS) of 4-18 months. It represents less than 2% of all neoplasms.
Objectives: Descriptive analysis of the experience of a central hospital in the management of MPM.
Methods: Retrospective analysis of the clinical files of MPM cases diagnosed and/or followed at our hospital center between January 2000 and July 2023.
Results: We identified 39 cases of MPM, 66.7% (n = 26) in males. The mean age at diagnosis was 73.1 ± 9.7 years. Most patients (69.2%) had no history of smoking and of the 30 patients with information on asbestos exposure, 76.7% had a positive past history of exposure. The median time from symptom onset to diagnosis was 2 months (maximum 25 months), and the most frequent forms of presentation included dyspnea (71.1%) and constitutional symptoms (65.8%), followed by thoracic pain (60.5%) and cough (47.4%). The most frequent radiological finding was pleural effusion, present in 92.1% of cases, 63.2% had pleural thickening and 42.1% pulmonary nodules. Diagnosis was obtained mostly by pleuroscopy and transthoracic biopsy (each one accounting for 29.7%), followed by blind pleural biopsy (24.3%). Out of the 34 patients with information on the histological type of MPM, 29 (85.3%) had epithelioid MPM, four (11.8%) had sarcomatoid and one had (2.9%) biphasic. Twenty-four patients (61.5%) were at stage IV (TNM) and eight (20.5%) at stage III when diagnosed. Fifteen patients (39.5%) underwent prophylactic radiotherapy of pleural tracts. First-line treatment included chemotherapy in 21 patients (53.8%), multimodal therapy with extrapleural pneumectomy in one case (2.6%) and immunotherapy with Nivolumab + Ipilimumab in another case (2.6%). Sixteen patients (41.0%) received best supportive care. Five patients received second-line and one third-line immunotherapy. Of the seven patients who received this treatment, four experienced toxicity symptoms: gastrointestinal (n = 2), cutaneous (n = 1) or both (n = 1), with no need for permanent treatment discontinuation. Median OS was 6.0 months. There was a statistically significant difference (p = 0.026) in median OS in patients diagnosed at early stages (I-II) (29.0 months) and advanced stages (III-IV) (4.0 months). The absolute survival rate in a 2-year span was 16.1%, dropping to 9.7% in a 5-year period.
Conclusions: Our sample consisted mostly of non-smoking men, with non-specific symptoms and advanced stage at diagnosis. The association of MPM and asbestos exposure is well known, although not always reported by patients, and the disease may develop several decades after cessation of exposure. Prognosis is poor and tightly related to stage at diagnosis (median OS 29.0 for stages I-II vs. 4.0 months for stages III-IV), therefore early diagnosis is essential. Recently, after decades of investigation, the introduction of immunotherapy in the treatment of MPM has provided a therapeutic alternative that can significantly improve survival rates.

Keywords: *Malignant pleural mesothelioma. Pleura. Asbestos. Neoplasm staging.*

CO 014. TREATMENT OF PNEUMOTHORAX WITH PLEURAL VENT® DEVICE – SINGLE CENTER EXPERIENCE

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Introduction: Outpatient treatment of simple pneumothorax with devices is included in the recent BTS guidelines to allow rapid relief of symptoms and enable treatment without the need for hospitalization. The Pleural Vent® is a small-sized, one-way valve drainage device with a built-in reservoir, which is placed with a minimally invasive technique. It is used to treat simple, spontaneous and iatrogenic pneumothorax and does not require subsequent hospitalization of the patient. It is mainly intended for symptomatic cases without high-risk features and should consider the patient's preference over other therapeutic approaches.
Methods: The present work aims to present the initial experience of a center with Pleural Vent® in the treatment of spontaneous and iatrogenic pneumothorax, without high-risk features, through the retrospective analysis of a series of cases from the beginning of placement in November 2022 to July 2023. Demographic characteristics, smoking history, pneumothorax classification, pulmonary pathology diagnoses, occurrence of hospitalization, time under Pleural Vent® placement and outcome (resolution vs therapeutic failure) were assessed.
Results: A total of 7 patients undergoing Pleural Vent® placement were identified. The majority were male (71.4%, n = 5) with a mean age of 55 years (minimum of 28 and maximum of 78 years), and 4 were smokers. There were 3 cases of iatrogenic pneumothorax after transthoracic aspiration biopsy, 3 cases of primary spontaneous pneumothorax and 1 case of secondary pneumothorax (patient refused to stay in hospital and a chest drainage was used as a bridge for elective thoracoscopy). Outpatient management was performed in 5 cases (3 primary spontaneous pneumothorax and 2 iatrogenic pneumothorax) with success in 4 of the cases and possibility of device removal on average on the 3rd day (minimum 1 maximum 5 days). In the other case, of primary spontaneous pneumothorax, treatment failure was assumed due to lack of complete lung reexpansion on the 4th day of Pleural Vent®, so hospitalization and placement of conventional chest drainage was chosen. In the context of hospitalization, in a case of iatrogenic pneumothorax after transthoracic aspiration biopsy during hospitalization, Pleural Vent® was placed and successfully removed on the 4th day. In none of the cases were there any major complications with the device, particularly in the case of secondary pneumothorax.
Conclusions: The literature and scientific societies increasingly highlight the possibility of outpatient management of pneumothorax as a way of reducing costs and length of stay and improving patients' quality of life. This case series, although small, portrays the experience of using Pleural Vent® so as its feasibility and safety.

Keywords: *Pleural vent®. Pneumothorax.*

CO 015. SERIAL ENDOSCOPIC EVALUATION OF THE EVOLUTION OF ENDOBRONCHIAL TUBERCULOSIS

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Introduction: Endobronchial tuberculosis (EBTB) is a form of pulmonary tuberculosis that affects the tracheobronchial tree and can

be present in up to 30% of patients with active pulmonary tuberculosis. EBTB is classified into 7 subtypes based on bronchoscopic findings: caseous, edematous-hyperemic, fibrostenotic, tumoral, granular, ulcerative, and nonspecific bronchitis. Objective: To describe the evolution of endobronchial tuberculosis from diagnosis to the conclusion of anti-tuberculosis treatment through serial bronchoscopy and identify predictors of evolution based on our data.
Methods: Between January and June 2023, we included patients with confirmed EBTB by biopsy who underwent bronchoscopy at diagnosis, 2 months, and 6 months after starting anti-tuberculosis treatment.
Results: Fifty patients were included, with 34 being female (68.0%), aged between 21 and 82 years (mean age 42.84 ± 15.49). Eleven cases of caseous EBTB changed to fibrostenotic type (40.0%), while the other 15 cases healed without sequelae. Four out of 7 cases of edematous-hyperemic EBTB changed to fibrostenotic type (57.1%), and the remaining cases resolved after 6 months of treatment. Four out of 6 cases of granular EBTB, 2 cases of nonspecific bronchitis, and 1 case of ulcerative EBTB resolved without complications. However, the other 2 cases of granular EBTB changed to fibrostenotic type (33.3%). Two cases of fibrostenotic EBTB showed no improvement despite treatment. All 6 cases of tumoral EBTB progressed to fibrostenotic type (100%). In 23 patients, bronchoscopic changes were located in the right bronchial tree (46.0%), in 20 (40.0%) in the left, and in 7 (14.0%) were bilateral. The upper lobar bronchus was the most frequently affected, involved in 34 cases (68.0%), either alone or in combination with other bronchi. The type of lesion visualized on bronchoscopy at 2 months of treatment was the only statistically significant predictor of lesion outcome, whether fibrostenotic or healed ($p < 0.001$, $r = 0.932$). All patients had positive Mycobacterium tuberculosis culture in bronchial lavage.
Conclusions: The therapeutic outcome of each EBTB subtype can be predicted through follow-up bronchoscopy starting at 2 months of treatment. Tumoral EBTB often progresses to bronchial stenosis, so there may be a benefit in shortening the time until endoscopic reassessment, especially to evaluate the need for additional treatment techniques (endoscopic dilatation, argon plasma application, cryotherapy).

***Keywords**: Endobronchial tuberculosis. Classification. Endoscopic techniques.*

CO 017. PREDICTING SURVIVAL IN MALIGNANT PLEURAL EFFUSIONS: THE ROLE OF PROMISE SCORE

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Introduction: Malignant pleural effusion (MPE) represents a common manifestation of advanced disease and a with significant morbidity and mortality impact, affecting up to 15% of cancer patients. The overall median survival from diagnosis is 3-12 months, underscoring the importance of tailoring level of care provided by identifying patients who would benefit from more invasive pleural interventions. The PROMISE score allows for the estimation of 3-month mortality rates in MPE patients, proving to be superior to other validated scoring systems. This study aims to evaluate the performance of the PROMISE score in predicting survival among MPE patients treated in a secondary hospital setting.
Methods: A retrospective study was conducted on patients diagnosed with MPE between January 1, 2017, and December 31, 2021. The parameters required to calculate the PROMISE score (haemoglobin, leukocytes, C-reactive protein, primary tumor, ECOG performance status, and previous history of chemotherapy/radiation therapy) and patients' demographics were recorded. The PROMISE score was calculated, classifying patients into respective mortality risk groups: Group A (< 25%); Group B (2549%); Group C (50-74%); and Group D (75%). Survival was determined via Kaplan-Meier curves and compared using the log rank test. The Cox proportional hazards model was used for multiple analysis.
Results: Ninety-one patients were included, categorized by PROMISE score: Group A (n = 31), Group B (n = 29), Group C (n = 27), and Group D (= 4). The median age at MPE diagnosis was 71.2 (41.1-91.2) years, with 51% patients of female gender and 54% displaying ECOG < 2. Lung cancer was the most frequent primary tumor (55%), followed by breast cancer (11%) and gastric cancer (10%), with 64% of patients presenting MPE at initial diagnosis. The median overall survival was 2.5 (95%CI 1.8-5.1) months, showing a significant difference when comparing distinct PROMISE score groups ($p < 0.001$): 9.4 (95%CI 2.6-21) months in Group A; 2.7 (95%CI 1.8-5.1) months in Group B; 0.92 (95%CI 0.4-3.5) months in Group C; 0.46 (95%CI 0.07-0) months in Group D. Only 20% of patients remained alive at the 12-month mark after MPE diagnosis. In multiple analysis, the PROMISE score was as an independent predictor of survival in all risk groups [Group A vs. B: HR 1.92 (95%CI 1.03-3.56; $p = 0.039$); Group A vs. C: HR 2.96 (95%CI 1.63-5.37; $p < 0.001$); Group A vs. D: HR 6.67 (95%CI 2.08-21.39; $p = 0.001$)]. The presence of MPE at diagnosis did not impact survival [HR 0.95 (95%CI 0.57-1.59; $p = 0.86$)]. The 3-month mortality rates for Groups A, B, C, and D were 36%, 55%, 70%, and 75%, respectively.
Conclusions: The PROMISE score proved to be an effective tool in predicting survival among MPE patients, consistently correlating with observed 3-month mortality rates in our population. Its application as a clinical decision-support tool holds potential for a more personalized approach to MPE treatment, identifying patients who would benefit solely from supportive measures and those who potentially benefit from more invasive interventions, ultimately enhancing their quality of life.

***Keywords**: Malignant pleural effusion. Promise score. Mortality.*

CO 018. EFFICACY AND SAFETY OF TRANSESOPHAGEAL ULTRASOUND-GUIDED ASPIRATION WITH AN ECHOBRONCHOSCOPE PERFORMED BY PULMONOLOGISTS

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Introduction: Transesophageal endobronchial ultrasound-guided fine-needle aspiration (EUS-B-FNA) is a well-established procedure that allows pulmonologists to independently perform complete mediastinal lymph node staging in the context of lung cancer. In addition, the transesophageal approach also allows the diagnosis of thoracic diseases (malignant or benign) that may not be anatomically accessible via the endobronchial route. With the increased use of this procedure by pulmonologists, concerns about its efficacy and safety are of paramount importance.
Objectives: To determine the diagnostic yield and safety of EUS-B-FNA performed by pulmonologists.
Methods: A retrospective analysis was performed from January 2020 to December 2022 of all patients who underwent EUS-BFNA at a tertiary oncology referral hospital. Demographic data, indication for the procedure, final diagnosis and complications were assessed.
Results: 334 patients were included in the analysis. Mean age was 64.4 ± 12.1 years; 235 (70.4%) were male. Most procedures were for suspected malignant disease (220, 65.9%), either for diagnostic purposes (190, 56.9%) or for staging (30, 9.0%). Additionally, 111 (33.2%) procedures were performed for suspected benign disease (mostly granulomatous pathology). Lymphoproliferative diseases were the main suspicion in 2 (0.6%). Combination with EBUS-TBNA occurred in 37 (11.1%) cases. Samples were adequate in 311 (93.1%) procedures. The diagnosis was obtained directly in 208 (62.3%) patients, most frequently lung adenocarcinoma (77, 23.1%) and sar-

coidosis (45, 13.5%). Negative or indeterminate results were observed in 126 (37.7%) patients. Of these, 21 (6.3%) underwent mediastinoscopy (13, 3.9%), video-assisted thoracic surgery (5, 1.5%) or percutaneous biopsy (3, 0.9%), which allowed diagnosis in 13 (3.9%) additional cases. The remaining negative cases were followed up and 77 (23.1%) were considered true negatives after completing 12 months of clinical and imaging stability. The overall diagnostic yield of EUS-B-FNA was 95.7%. EUS-B-FNA-related complications were observed in 6 (1.8%) patients (mediastinitis 2, 0.6%; lung abscess 1, 0.3%; pericarditis 1, 0.3%; esophageal wall hematoma 1, 0.3%; fever 1, 0.3%). A total of 17 (5.1%) patients died within 30 days of the procedure (median time to death 16.9 days). The attributed causes of death were disease progression in 14 (4.2%). No deaths were considered procedure related.
Conclusions: To the best of our knowledge, this is the largest cohort evaluating the operational characteristics of EUS-B-FNA. Our results portray this procedure as highly effective and safe, although complications occurred at a higher incidence than reported in the EBUS-TBNA literature.

Keywords: *EUS-B-FNA. Echoendoscopy. Yield. Safety.*

CO 019. THE ADVANTAGES OF THE COMPLEMENTARY USE OF ENDOBRONCHIAL ULTRASOUND (EBUS) TECHNIQUES: THE EXPERIENCE OF AN ONCOLOGY CENTRE

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Introduction: The complementary use of radial (R-EBUS) and linear (L-EBUS) EBUS probes can improve the cost-effectiveness of procedures and allow simultaneous diagnosis and mediastinal staging of lung cancer.
Objectives: To characterise the procedures performed in an oncology centre in which radial R-EBUS and L-EBUS probes were used in a complementary manner.
Methods: We analysed the clinical records of patients undergoing R-EBUS and L-EBUS at IPO-Lisboa between January 2017 and June 2022. We assessed the indications and demographic, imaging and endoscopic variables, as well as the cytohistological results of R-EBUS-guided transbronchial biopsies (EBUS-TBB), L-EBUS-guided needle aspiration (EBUS-TBNA) and the final diagnosis of the patients.
Results: A total of 993 procedures were performed using the L-EBUS probe and 575 procedures using the R-EBUS probe during this period. The two probes were used in a complementary manner in 44 exams. Patients were mostly male (n = 33) and had a median age of 69 years (IQR 60-77.5 years). The purpose of the procedure was simultaneous diagnosis and staging in 52.3% of cases (n = 23), diagnosis in 38.6% (n = 17) and collection of biological specimen in the remainder (n = 4). The lesions had a median size of 28 mm (IQR 19.5 - 29 mm, n = 41) and were mostly central (located in the median 1/3, n = 18). Around seventy per cent of the procedures (n = 31) were initiated using the L-EBUS probe, 5 of which showed no suspicious lymph nodes. The remainder were negative (n = 23), suspicious (n = 1) and positive (n = 2) for neoplastic cells on rapid on-site examination (ROSE), the latter with R-EBUS being performed due to insufficient material on EBUS-TBNA or suspicion of synchronous neoplasms. Among the examinations initiated with R-EBUS (n = 13), the distal lesion was identified in 12 cases. ROSE of EBUS-TBB was positive or suspicious in 5 cases. The procedure yielded a malignant specimen in 47.7% of patients (n = 21). Among the remainder, 4 had a final benign diagnosis and 15 an oncological diagnosis obtained through surgery (n = 5), transthoracic biopsy (n = 3), repeat R-EBUS (n = 3) or clinical corroboration (n = 4). Three patients were lost to follow-up and 1 is awaiting surgery. A total of 16 patients (36.4%) benefited from complementary probing by obtaining diagnosis on EBUS-TBB after negative EBUSTBNA (n = 6), on EBUS-TBNA after negative/inconclusive EBUS-TBB (n = 5), mediastinal staging after positive EBUS-TBB (n = 4) and diagnosis and staging of synchronous lesions (n = 1).
Conclusions: The complementary use of EBUS probes allows to obtain determinant information in a relevant percentage of patients with suspected lung cancer.

Keywords: *Bronchology. Endobronchial ultrasound. Lung cancer.*

CO 020. AGREEMENT BETWEEN CLINICAL AND PATHOLOGIC STAGING OF NSCLC: THE N COMPONENT

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Introduction: A correct nodal staging of non-small cell lung cancer (NSCLC) is critical in making treatment decisions, namely in the decision of the possibility of surgical treatment. Clinical N stage (cN) should be based on chest CT, PET-CT and in some cases on invasive methods as EBUS/EUS TBNA and/or mediastinoscopy. However, pathologic N stage (pN) of the surgical specimen may differ from cN, with implications for the patient.
Objectives: Investigate the agreement between the cN and pN in NSCLC.
Methods: Retrospective study, including all patients diagnosed with NSCLC, followed in our Thoracic Tumours Unit, who underwent surgical treatment, between 2012 and 2021. Demographic data, histology, clinical staging techniques, cN stage, pN stage, extent of resection and time between staging and surgery were collected from patient's clinical files. Agreement between clinical and pathologic stage was calculated by Cohen's k.
Results: We included 157 patients (table 1). Clinical and pathologic staging was different in 17 (11.1%) patients: 14 (9.2%) were upstaged and 3 (1.9%) downstaged, = 0.431.
Conclusions: There was moderate agreement between the N clinical and pathological staging. EBUS is an important tool to stage mediastinum but it should be complemented with other techniques, such as EUS or mediastinoscopy, mainly for nodes not accessed by EBUS. Our results also point out that some nodes may have cancer even if they are PET-CT negative and no formal indication for EBUS, questioning if invasive staging should be done in these cases.

Keywords: *Lung cancer. Staging.*

CO 025. CHEMOIMMUNOTHERAPY IN RESECTABLE NON-SMALL CELL LUNG CANCER – EXPERIENCE AT IPOLFG

IPOLFG.

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Introduction: Immunotherapy (IOT) is one of the main weapons in the fight against metastatic non-small cell lung cancer (NSCLC) by altering the tumor microenvironment and blocking methods of tumor immune evasion. More recently, its use at earlier stages has also been proposed, in the context of neoadjuvant in surgical candidates, with very favorable results in the CheckMate 816, which led to the approval of IOT with nivolumab in the neoadjuvant setting by the European Medicines Agency.
Objectives: To analyze patients followed at IPOLFG since 2022, diagnosed with NSCLC and undergoing chemotherapy with immunotherapy in the context of neoadjuvant therapy.

Methods: Observational study including patients diagnosed with NSCLC and resectable disease, followed between January 2022 and July 2023, undergoing chemotherapy and immunotherapy in the context of neoadjuvant therapy. Patients were staged according to the ESMO guidelines and discussed in MDC. Chemotherapy was cisplatin 75 mg/m^2 and pemetrexed 500 mg/m^2, in the case of adenocarcinoma histology, and carboplatin AUC 5 and paclitaxel 200 mg/m^2, in epidermoid histology) together with nivolumab 360 mg every 21 days. In the absence of disease progression criteria and if there was surgical resectability criteria, patients were submitted to surgical intervention up to 6 weeks after the last cycle. A demographic, clinical, analytical analysis (with quantification of PD-L1 and mutational study by NGS), anatomopathological analysis (including the evaluation of the pathological response, through the % of residual viable tumor of the surgical specimen of the primary tumor and lymph nodes) and imaging comparison (using RECIST v1.1 criteria) was carried out.
Results: Three patients with NSCLC were included, all locally advanced with a stage IIIA (cT4N0M0), with a mean age of 55 years, all with PS 1. Histologically, two cases corresponded to squamous cell carcinoma and one to adenocarcinoma. Two of the cases had PD-L1 > 50% and one had PD-L1 < 1%. In the reassessment after the 3 cycles of systemic therapy, there was a partial response in two cases and disease progression in 1 case, due to metastases in the central nervous system. In the 2 cases in which surgical intervention was performed, there was a complete pathological response in one case and a major pathological response in the other. Both are currently under surveillance – with time from initiation of treatment to the last assessment of 4 months and 14 months, respectively. In the case of disease progression, the patient died 11 months after starting first-line therapy. Of the adverse effects observed with chemo-immunotherapy, G2 fatigue, G2 nausea and 1 case of scalp folliculitis G1, with resolution after antibiotic therapy, were noted.
Conclusions: Immunotherapy together with chemotherapy, in the context of neoadjuvant therapy, is a strategy associated with better survival rates and complete pathological responses. The use of this therapeutic option in these first patients at IPOLFG has obtained promising results.

***Keywords**: Non-small cell carcinoma. Checkmate 816. Nivolumab. Neoadjuvance. Pathological response.*

CO 026. FINDING WHAT YOU'RE NOT LOOKING FOR: LYNCH SYNDROME IDENTIFIED IN LUNG ADENOCARCINOMA

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Introduction: Mutations in the DNA repair system or Mismatch Repair (MMR) include variants of MLH1, MSH2, MSH6 and PMS2 and are associated with Lynch Syndrome (LS), a genetic disease that predisposes to the appearance of multiple neoplasms. The diagnosis of LS is therefore essential for the treatment and risk reduction of cancer in carriers of these mutations. The association between LS and non-small cell lung cancer (NSCLC) is poorly studied and rarely described. We present a case of diagnosis of LS after identification of a pulmonary adenocarcinoma.
Case report: Female 70 years old, PS 0, non-smoker, with a history of arterial hypertension. In June 2021, in the preoperative evaluation for surgical correction of urinary incontinence, the chest X-ray shows a mass in the left upper lobe. Chest CT reveals a spiculated mass and bilaterally scattered nodules. The transthoracic needle biopsy established the diagnosis of lung adenocarcinoma with EGFR mutation in exon 21. Staging exams identified 3 cranioencephalic lesions suggesting secondary deposits. Stage IVB (T4N3M1c) was established. Osimertinib was started, with complete pulmonary response and reduction of central nervous system (CNS) lesions. In January 2023, the patient presented CNS progression and was submitted to radiosurgery. Due to disease progression under first-line Tyrosine Kinase Inhibitor (TKI), she entered a clinical study to identify resistance mutations by liquid biopsy and it identified a TP53 p.R273L mutation (allele frequency 0.22%) in a complete genetic study, as well as a gene variant of PMS2 (allele frequency 44%), classified as pathogenic. The patient was referred to a Genetic consultation, where the diagnosis of Lynch Syndrome was established, and subsequently referred to Gastroenterology and Gynecology consultations. Evaluation of family members at risk was advised.
Discussion: LS is a genetic disease that increases the predisposition of cancer, especially colorectal (CRC) and endometrial cancer, but also stomach, small intestine, ovary and urothelium. Literature on the association between SL and NSCLC is scarce and requires further investigation. So far, SL doesn't seem to have a greater probability of developing NSCLC, however, the concomitant presence of PMS2 (altered in 2.18% of NSCLC) with other mutations, in this case mutation in the tumour suppressor gene 53 (TP53), can potentially trigger the oncogenesis process. There is biological heterogeneity between the different MMR genes and recent studies point to a lower risk of cancer in PMS2 mutation carriers compared to MLH1, MSH2 and MSH6. The lifetime risk of CRC is approximately 9-20% and endometrial cancer 12-26%. Current recommendations include: total colonoscopy from the age of 35, with annual/biannual periodicity; annual endovaginal ultrasound and CA125 measurement; *Helicobacter pylori* screening and eradication. Performing extended NGS (next-generation sequencing) allows detection of mutations that help establish a diagnosis of hereditary syndromes in patients with cancer, which has implications on the screening of other cancers in the patient and their family.

***Keywords**: Lynch syndrome. Adenocarcinoma. ECGF.*

CO 027. PREDICTIVE FACTORS OF PEMBROLIZUMAB RESPONSE IN PATIENTS WITH NON-SMALL CELL LUNG CANCER: A MULTICENTRIC RETROSPECTIVE STUDY

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Introduction: Lung cancer remains the leading cause of cancer death worldwide. However, treatment with immune checkpoint inhibitors (ICI) significantly improved the prognosis of these patients. This therapy focuses on the expression of PDL1 in tumor cells, which is a predictive value of therapeutic response. However, despite being the accepted biomarker for selecting patients for treatment with ICI, not all have a positive response to treatment. Thus, the identification of new predictive biomarkers is essential in clinical practice.
Objectives: Characterize the non-small cell lung cancer (NSCLC) patients that are on first-line therapy with pembrolizumab and to identify predictive factors of treatment response.
Methods: Retrospective observational study of all patients with NSCLC on first-line therapy with pembrolizumab, followed at Centro Hospitalar de Leiria and Centro Hospitalar Universitário de Coimbra between 01/01/2017 and 21/12/2021. Patients' demographic characteristics, analytical values such as LDH, PD-L1 value, type and stage of neoplasia and response to pembrolizumab were analyzed, performing a univariate analysis of these variables and a Kaplan-Meier survival analysis to assess progression-free survival (PFS) and overall survival (OS) of patients. Statistical analysis was performed using IBM SPSS Statistics 27.
Results: The study included 104 patients, 80.8% male, with a mean age of 65 years. Patients with LDH < 400U/L and with a number of

metastatic sites < 3 were found to respond better to pembrolizumab (p-value of 0.006 and 0.025, respectively), with all responders having a LDH value < 400 U/L. There was no correlation with any other of the analyzed variables, including the PD-L1 value. When PFS and OS were analyzed, it was found that: in the total sample, patients with PD-L1 between 60-89% have a higher OS; patients with LDH < 400U/L have a higher PFS; responders who had toxicity had a higher OS; in non-responders, a lower age has a higher OS and a number of metastases < 3 correlates to a higher PFS (no difference in OS).
Conclusions: Considering the prevalence and mortality of lung cancer, it is urgent to identify better predictive biomarkers of response (clinical, analytical, molecular imaging alone or in combination) that allow for truly personalized medicine. In our study, patients with lower LDH and fewer metastases seem to respond better to immunotherapy therapy and have a higher PFS.

Keywords: *NSCLC. Pembrolizumab. PDL-1.*

CO 028. PLEURAL MESOTHELIOMA: 5-YEAR RETROSPECTIVE ANALYSIS IN A CENTRAL HOSPITAL

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Introduction: Malignant mesothelioma originates in the mesothelial cells that line the serous surfaces, with the pleura being the most affected site, corresponding to 70-80% of cases. Pleural mesothelioma is the most common primary malignant tumor of the pleura. Its main etiology is exposure to asbestos. Clinically, it mostly presents with pleural effusion (90% of cases). It is a locally aggressive tumor, invading the chest wall and lung parenchyma, with distant metastasis in advanced stages. Their median survival is 9-12 months.
Objectives and methods: The objective of this work is to characterize patients diagnosed with pleural mesothelioma and its evolution. This is a retrospective analysis of patients diagnosed in the last five years (2018-2022) and followed up in an Oncological Pulmonology consultation at Hospital de Egas Moniz. Data were obtained from clinical files.
Results: Over the last five years, fourteen patients were diagnosed with pleural mesothelioma, mostly male (85.7%, n = 12), with a mean age of 77 years (66-86 years). Regarding smoking habits, most patients were non-smokers (64.3%, n = 9), followed by former smokers (21.4%, n = 3) and active smokers (14.3%, n = 2). It was found that 42.9% (n = 6) of the patients had been exposed to asbestos throughout their lives. The main comorbidities were arterial hypertension (71.4%, n = 10), diabetes (50%, n = 7) and dyslipidemia (50%, n = 7). In terms of location, most tumors were located in the left pleura (64.3%, n = 9). Regarding the histological subtype, 42.9% (n = 6) were epidermoid and 14.3% (n = 2) were sarcomatoid, the remainder (42.9%, n = 6) did not show differentiation. Regarding initial staging, 42.9% (n = 6) were in stage I, 28.6% (n = 4) in stage III and 28.6% (n = 4) in stage IV. Only 14.3% (n = 2) of the patients presented metastasis, one of them to the adrenal gland and the other to the bone, liver and contralateral lung. With regard to treatment, of patients in stage I, 66.7% (n = 4) underwent only supportive therapy, as they did not have conditions for treatment, the remaining 33.3% (n = 2) underwent chemotherapy (CT); patients in stage III, 50% (n = 2) underwent CT, 25% (n = 1) CT and radiotherapy, being proposed for immunotherapy (IO) and 25% (n = 1) supportive therapy; patients in stage IV, 75% (n = 3) underwent CT and 25% (n = 1) supportive therapy. In terms of prognosis, of patients in stage I, only 16.7% (n = 1) are under surveillance after CT, the remaining 83.3% (n = 5) died with a median survival of 9.1 months ; of patients in stage III, only 16.7% (n = 1) are under surveillance awaiting the OI, the remaining 75% (n = 3) died with a median survival of 4.8 months; of the patients in stage IV, all progressed and died, with a median survival of 7.8 months.
Conclusions: Through this analysis, we can conclude that pleural mesothelioma has a poor prognosis, regardless of its initial stage, corroborating the existing literature. This pathology benefits from a multidisciplinary approach, both in terms of diagnosis and therapy, and in the palliation of symptoms. The incidence of this entity, especially at advanced ages, leads to an increase in morbidity and mortality due to the performance status of patients and their comorbidities.

Keywords: *Lung cancer. Pleural mesothelioma.*

CO 029. PATIENTS WITH UNRESECTABLE STAGE III NON-SMALL CELL LUNG CARCINOMA CANDIDATES FOR CONSOLIDATION WITH DURVALUMAB: REAL-WORLD EXPERIENCE FROM A TERTIARY HOSPITAL

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Introduction: Durvalumab has changed the treatment of non-small cell lung carcinoma (NSCLC) patients with locally advanced unresectable disease. In Portugal, it is approved as consolidation therapy after QT/RT in patients with unresectable stage III NSCLC with positive PD-L1, with improvement in PFS and OS compared to the previous standard of care.
Methods: Retrospective observational study including adults diagnosed with unresectable stage III NSCLC with positive PD-L1 expression from June 2019 to December 2022. Data were collected by consulting clinical files and analyzed using SPSS.
Results: During the period under review, 41 patients with unresectable stage III NSCLC with positive PD-L1 expression were identified. Thirteen (31.7%) were not candidates for Durvalumab due to progression after or during QT/RT (n = 6), decline in performance status (n = 3), radiation pneumonitis (n = 2) and awaiting evaluation after QT/RT (n = 2). This subgroup of patients was not analyzed. The remaining 28 patients (68.3%) were treated with durvalumab. They had a median age of 63.8 (43-85) years and the majority were male (75%). Fifty-seven percent were ex-smokers, 39% smokers and 4% never smokers. There was no histologic predominance (46% non-squamous, 43% squamous and 10% other histologies). Fifty percent were stage IIIB at diagnosis, 25% IIIA and 25% IIIC. The majority underwent concomitant QT/RT (n = 20, 71.5%). After the end of QT/RT, 67.8% achieved partial response and 32.2% stable disease. The main adverse effects of QT/RT were pneumonitis (n = 5 grade 12) and esophagitis (n = 9 grade 1-2 and n = 1 grade 3). The median time between the end of QT/RT and the start of Durvalumab was 35 (11-69) days. During the first 3 months of Durvalumab therapy 1 patient developed thyroiditis and another pneumonitis. After 3 months, 5 had thyroiditis, 5 pneumonitis, 1 arthralgias and myalgias and 1 hypophysitis. Nine patients discontinued therapy: 5 due to progression, 3 due to adverse effects and 1 due to death during treatment. Median follow-up was 20.33 (136.6) months. Median PFS at 24 months was 19.573 months (95%CI 13.571-25.485) and median OS at 24 months was 29.148 months (95%CI 25.848 to 32.448).
Conclusions: The study population presented similar characteristics to the PACIFIC-R: a predominance of patients over 75 years old, ex-smokers and stage IIIB and IIIC at diagnosis, as well as a higher number of patients who underwent concomitant QT/RT. Despite the small sample size and short follow-up time, median PFS at 24 months was similar to PACIFIC-R (21.7 months) and higher than PACIFIC (17.8 months), with most adverse effects being grade 1 or 2. These data revalidate the superiority of durvalumab consolidation com-

pared with QT/RT alone in these patients, while maintaining an acceptable safety profile.

Keywords: *Durvalumab. Non-small cell lung carcinoma. Stage III. Consolidation.*

CO 030. MOLECULAR PROFILING OF PATIENTS WITH PULMONARY ADENOCARCINOMA UNDERGOING SURGICAL RESECTION

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Introduction: In early-stages (I-IIIA) of lung adenocarcinoma, surgery remains the treatment of choice. However, up to 50% of patients with complete tumor resection eventually recur within the first 5 years after surgery. In 2021, ESMO recommended Osimertinib as adjuvant therapy for patients with stage IB-IIIA lung adenocarcinoma within the first 3 years after complete resection. Nevertheless, the molecular profile of early-stage adenocarcinoma patients is not well-known, as reflex next generation sequencing (NGS) is not a common practice. Our goal was to perform a clinical, pathological and molecular characterization of patients with lung adenocarcinoma who underwent complete surgical resection.
Methods: We identified patients with lung adenocarcinoma who underwent surgery between June 2018 and December 2020. Clinical, pathological and molecular data were collected. Fisher's exact test and Chi-square test were used to compare categorical variables.
Results: A total of patients were evaluated, 53 of whom were male (61.6%). 30 were nonsmokers (34.9%). Median age at diagnosis was 66 years (60-73) and median follow up time was 3.7 years (2.7-4.2). 58 patients were at stage IA (67.4%). Molecular profiling with NGS was performed in 62 patients (72.1%), revealing EGFR mutations in 14 (16.3%) [6 exon 19 (7.0%); 1 exon 20 (1,2%); 7 exon 21 (8.1%)] and KRAS mutations in 15 patients (17.5%). Among patients with identified EGFR mutations, 3 experienced recurrence, with a median disease-free survival of 3.4 years. 78.6% of patients with EGFR mutation were non-smokers ($p < 0.001$), 78.6% were female (p 0.004) and 46.7% had tubular histologic subtype (p 0.021).
Conclusions: Understanding the molecular profile of patients with lung adenocarcinoma allows us to define prognostic factors and identify candidates for adjuvant targeted therapies. While the prevalence of EGFR mutations in advanced-stage lung adenocarcinoma has been extensively studied, the same does not apply to early-stage adenocarcinoma. Considering that targeted therapies based on tyrosine kinase inhibitors may be an option as adjuvant therapy for patients undergoing complete surgical resection, a better molecular characterization of these patients becomes essential.

Keywords: *Lung cancer. Adenocarcinoma.*

CO 031. EFFECTS OF SELF-MANAGEMENT INTERVENTIONS IN PEOPLE WITH INTERSTITIAL LUNG DISEASE – SYSTEMATIC REVIEW

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Introduction: Self-management interventions (SMIs) aim to empower people to effectively manage their health and have shown to be effective in people with chronic respiratory diseases, such as chronic obstructive pulmonary disease and asthma. Knowledge about its effectiveness in people with interstitial lung disease (ILD) is, however, limited.
Objectives: To summarize the effects of SMIs on functionality (i.e., functional capacity and performance), psychological and social outcomes, symptoms, exacerbations, and survival in people with ILD.
Methods: After registering the protocol (PROSPERO ID: CRD42022329199), a search was carried out in May 2022 for randomized controlled studies in six databases with monthly updates until May 2023. Studies implementing SMIs, defined according to Effing *et al.* [Eur Respir J. 2016;48(1):46-54], in adults with any type of ILD, were included. Two independent reviewers assessed the risk of bias (Cochrane RoB2). Between-group differences were used to summarize the results.
Results: Four studies that examined 217 participants (81% men, 71 years old, 91% idiopathic pulmonary fibrosis) were included. There was great heterogeneity in the duration, content, and structure of SMIs and little detail in the reporting of control interventions. No between-groups differences were observed for any of the outcomes analyzed. No study assessed the effects of SMIs on functional capacity, exacerbations, and survival. The risk of bias in the results ranged from high to some concerns.
Conclusions: Current studies show that SMIs have no effect on people with ILD when compared with usual care. This conclusion is limited by the high methodological heterogeneity of the studies. A consensus definition of SMIs is needed to implement more comparable interventions and strengthen results.

Keywords: *Chronic respiratory disease. Empowerment. Healthcare. Health-related quality of life. Pulmonary fibrosis.*

CO 032. DESQUAMATIVE INTERSTITIAL PNEUMONIA – A RETROSPECTIVE COHORT STUDY IN A PORTUGUESE CENTRE

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Introduction: Desquamative interstitial pneumonia (DIP) is a rare form of idiopathic interstitial pneumonia, characterized by extensive alveolar infiltration of pigmented macrophages, which primarily affects smokers. Information about this entity is scarce and the study of these patients is essential for a better understanding of their clinical evolution.
Objectives: To characterize clinical data, exposures, radiology, pathology features, treatment strategies and outcomes of a Portuguese cohort of patients with histopathologically-confirmed DIP.
Methods: Retrospective study including patients with DIP followed up in the Pulmonology Department of CHUSJ.
Results: 51 patients were included, with a mean age at diagnosis of 56.9 9.7 years, most of them, 58.8% (n = 30), male. We found a high incidence of ever smoking in patients with DIP, 98.0% (n = 50), and the majority, 78.4% (n = 40), were active smokers. Average pack-years of smoking were 40. Most patients presented with exertional dyspnea and cough. Upon physical examination, crackles were heard in 58.8% (n = 30). Chest CT showed bilateral ground-glass opacities in all the 51 cases. Pulmonary function tests at diagnosis presented a decreased diffusion capacity in 86.3% (n = 44) of cases (mean 58.2 15.3% of the predicted value) and an obstructive pattern in 29.4% (n = 15). Bronchoalveolar lavage demonstrated a high number of pigmented macrophages and 68.6% (n = 35) had eosinophilia (mean 1.7 5.4%). Transbronchial cryobiopsies established the diagnosis of DIP in 72.5% (n = 37). The others were confirmed with a surgical lung biopsy. Regarding treatment, 21.6% (n = 11) stopped smoking and 43.1% (n = 22) started corticosteroid therapy, most

frequently prednisolone. The average duration of this treatment was 12.2 7.4 months. The other patients were under immunosuppressive therapy or surveillance. Of the 44 patients from whom it was possible to obtain follow up data, 18.2% (n = 8) had an unfavorable evolution.
Conclusions: This cohort of patients confirms its unavoidable association with smoking. Although most patients have a favorable evolution, there is a subgroup with disease progression who are important to identify, given the need for therapeutic intervention and monitoring.

Keywords: *Desquamative interstitial pneumonia. Smoking. Transbronchial cryobiopsy. Corticosteroid therapy.*

CO 033. CHESTER STEP TEST: ITS RESPONSIVENESS AND CLINICALLY IMPORTANT IMPROVEMENTS FOLLOWING PULMONARY REHABILITATION IN INTERSTITIAL LUNG DISEASE

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Introduction: Impaired functional capacity in interstitial lung disease (ILD) accelerates the disease progression and mortality risk. Pulmonary rehabilitation (PR) has shown benefits in improving this meaningful outcome in ILD. These benefits have been mostly measured using the 6-minute walk test (6MWT) which requires the availability of a 30m corridor. Other measures to assess functional capacity in space constraint settings are needed and the Chester step test (CST) has been proposed as a possible alternative. It has shown to be valid and reliable in people with ILD, however, its responsiveness and clinical interpretability are still unknown. Therefore, this study aimed to establish its responsiveness and minimal clinically important difference (MCID) in people with ILD after PR.
Methods: A secondary analysis of data from 2 studies (NCT03701945 and NCT04224233) was conducted. People with ILD completed a 12 week community-based PR programme with 2 weekly sessions of exercise training and 1 session every other week of education and psychosocial support. The following measures were collected pre and post PR: the CST; the 1-minute sit-to-stand test (1minSTS) and the Functional Assessment of Chronic Illness Therapy-Fatigue Subscale (FACIT-FS). The 1-minSTS% predicted was also computed. The responsiveness was explored between the change in the CST and the changes in the 1-minSTS, 1minSTS% predicted and FACIT-FS. Significant correlations of 0.3 were considered adequate. Anchor- and distribution-based methods were used to compute the MCID. The anchors explored were the changes in the CST with changes in the 1-minSTS (raw and % predicted values) and in the FACIT-FS. The MCID of the CST was calculated using three anchor-based methods: mean changes, receiver operating characteristic (ROC) curve and linear regressions. The standard error of measurement (SEM), 1.96SEM, 0.5*standard deviation, minimal detectable change with 95% confidence (MDC95) and Cohen's effect size were used as distribution-based methods. The pooled MCID was computed using the arithmetic weighted mean (2/3 anchor- and 1/3 distribution-based methods).
Results: Fifty-five patients (67 ± 11 years; 64% female; FVC = 79.8 ± 17.7% predicted and DLCO = 51.2 ± 18.7% predicted) were included. A significant improvement in the CST after PR (mean difference = 23.3 ± 33.3 steps) was observed. Significant correlations were found between changes in the CST and in the 1-minSTS ($r = 0.305$; $p = 0.025$), the 1-minSTS%predicted ($r = 0.317$; $p = 0.020$) and the FACIT-FS ($r = 0.431$; $p < 0.001$). The pooled MCID was 23 steps.
Conclusions: This study shows that CST is a responsive measure and an improvement greater than 23 steps in the CST seems to be clinically meaningful in people with ILD after a 12-weeks community-based PR programme. The estimated MCID of the CST will aid health professionals to understand the effects of PR on functional capacity and guide to tailor PR to one of the most challenging daily activities (stair climbing) for people with ILD.

Keywords: *ILD. Chester step test. Responsiveness. Minimal clinically important difference. Pulmonary rehabilitation.*

CO 037. IDENTIFICATION OF EXPOSURE IN HYPERSENSITIVITY PNEUMONITIS: A COMPARISON BETWEEN PATIENT-REPORTED EXPOSURE AND HOME EVALUATION

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Introduction: The identification and elimination of the disease-causing antigen is essential in the diagnosis and management of Hypersensitivity Pneumonitis (HP). Identifying the antigen is associated with better outcomes. However, it is not always possible to do so. This study aims to compare the information obtained from patients regarding their exposure with the identification of antigens in patient's houses by a researcher.
Methods: Patients diagnosed with HP within the last 3 years were included in the study. A comprehensive home environmental assessment was conducted by a researcher trained in public health. The assessment involved a methodological checklist for the indoor and outdoor environment, building characteristics, and furniture. Air samples were also collected using a microbiological air impactor with agar plates and malt extract. After incubation, colonies were quantified and microscopically identified.
Results: A total of 35 patients with HP were included, 19 (54.3%) of whom were male, with a median age of 71 (min 32 – max 83) years. The majority of cases (n = 27, 77.1%) have fibrotic HP. Patients reported exposure to birds in 74.3% (n = 26), to fungi in 45.7% (n = 16), and to other antigens in 40% (n = 14) of cases. The researcher identified home exposure to birds in 48.6% (n = 17) of cases, fungi in 45.7% (n = 16), and other antigens in 5.7% (n = 2) of cases. Regarding avian exposure, there was agreement between patient report and researcher findings in 79.5% (n = 27) of cases. In 23.5% (n = 8) of cases, exposure to birds was reported by the patient but not found by the researcher. In no case did the researcher find exposure that was not reported by the patient. As for exposure to fungi, the concordance between patients and the researcher was 45.7% (n = 16). In 37.1% (n = 13) of cases, home exposure was found by the researcher despite not being reported by the patient. In 6 cases, the patient reported exposure to fungi that was not found by the researcher during visual inspection.
Conclusions: There was a higher agreement between observations regarding avian exposure than fungal exposure. In many cases, patients underestimated their exposure to fungi. In several cases, patients reported exposure that was not confirmed by the researcher, which could be due to compliance with antigen avoidance recommendations. Environmental assessment by a researcher can enhance the identification of antigens causing HP, enabling their elimination, which is an essential measure in the treatment of the disease.

Keywords: *Hypersensitivity pneumonitis. Inhaled antigen. Avian exposure. Fungi.*

CO 038. DIAGNOSIS OF HYPERSENSITIVITY PNEUMONITIS – TIME FOR A PARADIGM SHIFT?

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Introduction: The current diagnostic workup of suspected Hypersensitivity Pneumonitis (HP) is based on the application of the ATS/JRS/ALAT Clinical Practice Guideline, standardized for multidisciplinary discussion (MDD) based on clinical, radiological, and histological findings. Some authors suggest that by restricting the significance of pre-invasive diagnostic procedures, the ATS guideline can underestimate the likelihood of HP, particularly in a population with higher prevalence. The CHEST Guideline and Expert Panel Report on Diagnosis and Evaluation of HP, not currently applied routinely on MDD, is another consensus paper on this matter that seems to broaden the pre-biopsy predictive value of non-invasive/less invasive procedures.
Objectives: To apply both the ATS and CHEST guidelines to a population of patients with confirmed fibrotic HP (fHP) and determine whether different consensus would result in a significantly different MDD decision.
Methods: Retrospective study including patients submitted to transbronchial lung cryobiopsy (TBLC) with a final MDD diagnosis of fHP between 2014 and 2022 in a tertiary center. Both guidelines were applied to all patients, classifying them according to the level of confidence in a fHP diagnosis. McNemar's chi-square test was used to compare the proportions of confidence level changes during the MDD process.
Results: 112 patients were included, 51.8% were male, with a mean age at the time of TBLC of 65.5 ± 8.5 years. Most patients (51.8%) were either active or former smokers. Almost all were symptomatic (91.1%), most frequently complaining of dyspnea (77.7%), chronic cough (64.3%) and anorexia (17.9%). Although most patients had no functional impairment on spirometry and plethysmography, most (93.6%) presented reduced diffusion capacity, moderate-to-severe in more than half (63.4%). A clinically relevant history of environmental exposure was present in 92% (n = 103) of patients, most frequently avian exposure (69.6%) and humidity/mold (33.9%). Forty patients (35.7%) presented lymphocytosis (20%) on bronchoalveolar lavage (BAL). According to the ATS guideline, pre-TBLC confidence level in fHP diagnosis was as follows: not excluded in 52 patients (46.4%), low-confidence in 54 patients (48.2%), moderate-confidence in 5 patients (4.5%) and high-confidence in 1 patient (0.9%). When following the CHEST guideline, pre-TBLC confidence level in fHP was the following: HP unlikely in 4 patients (3.6%), provisional low-confidence in 59 patients (52.7%), provisional high-confidence in 35 patients (31.3%) and definite HP in 14 patients (12.5%). There was a statistically significant change in proportion towards higher-confidence levels when using the CHEST guideline ($p < 0.0001$). Changes were significant at three different levels: the proportion of patients in the ATS "not excluded" subgroup significantly upscaled to CHEST's "provisional low-confidence" subgroup (76.2% increase; $p < 0.001$) and the proportion in the ATS "low confidence" subgroup significantly upscaled to CHEST's "provisional high-confidence" (67.4% increase; $p < 0.001$) and "definite HP" (50% increase; $p < 0.001$) subgroups. No patients were downscaled in confidence level when applying CHEST guidelines.
Conclusions: This study suggests a significant increase in definite fHP diagnosis when applying the CHEST guideline versus the currently used ATS guideline. In our sample, 49 TBLC would have been waived due to a combination of less strict radiological criteria and a more prominent role of BAL.

Keywords: *Hypersensitivity pneumonitis. Transbronchial lung cryobiopsy. Chest. ATS. Diagnosis.*

CO 039. RETROSPECTIVE ANALYSIS OF PATIENTS WITH OBESITY-HYPOVENTILATION SYNDROME UNDER HOME VENTILATION

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Introduction: Obesity hypoventilation syndrome (OHS) is a prevalent condition, often underdiagnosed, with high morbidity and mortality if left untreated. Its diagnosis implies the presence of obesity (BMI 30 kg/m^2) and daytime arterial hypercapnia (paCO2 45 mmHg), in the absence of other causes that explain hypoventilation. It is therefore a diagnosis of exclusion. Growing evidence supports the use of HCO3- 27 mEq/L for its screening. Treatment consists in the application of a positive pressure in the airway, in the form of CPAP (continuous positive airway pressure) or non-invasive ventilation (NIV).
Objectives: The aim of this study was to analyze the population diagnosed with OHS, followed in the home non-invasive ventilation (NIV) consultation, as well as to verify if there is a correlation between the diagnostic criteria (BMI and paCO2) of this disease.
Methods: A retrospective analysis of the patients followed in the NIV consultation was made, between January 2014 and June 2023, in a tertiary hospital, with the diagnosis of OHS. The paired sample t-Test and the Spearman correlation statistical test were used.
Results: Of the 920 patients followed during this period, 137 had SOH. Most were female (75.2%), with a median age of 76 [67.0-83.5] years. Most patients (89.8%) were under NIV, and 30.7% of these had previously been under CPAP. A small percentage (10.2%) started NIV but later discontinued it (13 due to intolerance/refusal and 1 due to failing to meet criteria). The patients who began NIV, 64.2% had no hospitalizations due to respiratory pathology. There were 31 (22.6%) deaths, with a median time under NIV of 24 [9-43] months, 29% due to respiratory infection and 16.1% due to cardiovascular disease. We observed a statistically significant reduction ($p < 0.001$) in the value of paCO2 and HCO3- before the start of NIV and the last blood gas recording in consultation. It was found that there was no correlation between the patient's BMI and the paCO2 value ($r = -0.081$), as well as the HCO3 value obtained ($r = -0.031$). On the other hand, a positive and moderate correlation was documented between the value of HCO3- and paCO2, with a statistically significant difference ($r = 0.397$; $p < 0.001$).
Conclusions: OHS is a frequent indication for NIV, associated with multiple comorbidities. After treatment, a statistically significant decrease in paCO2 and HCO3- was obtained. Although BMI and paCO2 are necessary for diagnosis, no correlation was found between these two variables. On the other hand, with a statistically significant difference, a moderate correlation between HCO3- and paCO2 could be established, corroborating their role in documenting hypoventilation and, consequently, their usefulness in screening for OHS.

Keywords: *Obesity-hypoventilation syndrome. Home non-invasive ventilation. Diagnosis.*

CO 040. AMYOTROPHIC LATERAL SCLEROSIS SURVIVAL ANALYSIS BASED ON INITIAL ACHIEVEMENT

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Introduction: Amyotrophic Lateral Sclerosis (ALS) is a degenerative and progressive neurological disease involving upper and lower motor neurons. By compromising the respiratory muscles, it causes

episodes of alveolar hypoventilation and, consequently, hypercapnic respiratory failure, justifying the need to evaluate these patients in the home non-invasive ventilation (NIV) consultation. Mostly, the initial presentation is medullary/non-bulbar, but it can also present in the bulbar form.
Objectives: The aim of this study was to characterize and analyze survival between ALS with initial bulbar and non-bulbar presentation, from the beginning of follow-up at the NIV consultation.
Methods: A retrospective analysis was carried out of the patients followed in the NIV consultation, between January 2014 and June 2023, in a tertiary hospital, with the diagnosis of ALS. The patients whose initial presentation of the disease had bulbar symptoms were subdivided. The T test for independent samples was used.
Results: Of the 920 patients followed up during this period, 62 patients had ALS, with equal gender distribution (50%), and with a median age at the start of follow-up at the consultation of 68.0 [63.0; 74.3] years. During follow-up at the consultation, 48 patients started NIV (71.9%), 1 refused, and the rest were being followed up or died without ever having started NIV. In patients who started NIV, the median age at onset was 67.5 [63.0; 74.0] years, with the majority (83.3%) starting in the context of a NIV consultation, with a median pH of 7.42 [7.39;7.43] and pCO2 of 46.0 [41.3; 53.6] mmHg. The objective was, on average, with a statistically significant difference, that patients with non-bulbar ALS have higher values of FVC, MIP and MEP compared to those with bulbar ALS. Of those who started NIV, it was also found that the EPAP, at the last visit, of patients with non-bulbar ALS was superior to those with Bulbar ALS, as well as the time under NIV. About patient survival, at 3 years, after starting follow-up at the NIV consultation, there was a statistically significant difference ($p = 0.004$). Patients with bulbar ALS had a median survival of 10.5 [5.0; 17.0] months, while patients with non-bulbar ALS had a median of 20.0 [9.0; 25.0] months. During follow-up, 42 (67.7%) deaths were recorded.
Conclusions: Most ALS patients started NIV. Patients with the initial diagnosis of bulbar ALS had worse results in spirometry, less time under NIV, lower EPAP values, and higher mortality, with a median survival of 10.5 [5.0; 17.0] months, relative to patients with non-bulbar ALS, reflecting their worse prognosis.

Keywords: *Amyotrophic lateral sclerosis. Bulbar. Non-invasive home ventilation. Survival.*

CO 041. QUALITY OF LIFE IN PATIENTS UNDER NON-INVASIVE HOME VENTILATION IN THE LAST 6 MONTHS OF LIFE

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Introduction: Over the years, Non-Invasive Home Ventilation (NIHV) has progressively gained importance in the management of patients with advanced respiratory disease associated with chronic respiratory failure. Its use aims to achieve symptomatic control, reduce morbidity and mortality, and improve the quality of life (QoL). QoL can be assessed using validated questionnaires such as "The Severe Respiratory Insufficiency Questionnaire" (SRI). The results of each subscale can vary between 0 and 100, with 100 representing the best QoL.
Objectives: To evaluate the QoL in patients under NIHV in the last 6 months of life.
Methods: A retrospective analysis was conducted on patients under NIHV who had responded to the SRI. The individuals who had responded to the SRI within 6 months before their death (group 1) and patients who were alive 6 months after completing the questionnaire (group 2) were selected in a 1:2 ratio, based on the underlying lung disease. Sample comparisons were performed using Independent samples t-test, Mann-Whitney test, and Chi-square test. Results with $p < 0.05$ were considered statistically significant.
Results: Sixty-six patients were included. Most of the patients were male (65.7%) and 68% have been diagnosed with COPD. The mean age was 75.9 ± 7.8 years, and the median time under NIHV was 44.5 [18.0-91.5] months, with group 2 exhibiting a more extended duration of treatment. Regarding the latest follow-up, the median daily adherence revealed very similar values between the two groups, with a recorded value of 8.3 [6.3-9.7] hours. In the last gasimetric evaluation, the mean pCO2 was higher in the group of patients who died within 6 months after completing the SRI, although not statistically significant. The total SRI score was approximately 15 points higher in the group of patients who were alive 6 months after completing the SRI, however, this difference was not statistically significant. In the subscales "SRI_Respiratory symptoms" and "SRI_Social function", the surviving patients demonstrated statistically higher values. The "SRI_Physical function" was the subscale with the lowest score in both groups.
Conclusions: The group of surviving patients demonstrated higher scores in the subscales "SRI_Respiratory symptoms" and "SRI_Social function" (both statistically significant) as well as in the total scale. Although in the latter the difference in nearly 15 points was not statistically significant, it may imply a substantial clinical effect. Larger sample studies are needed.

Keywords: *"The severe respiratory insufficiency questionnaire". Quality of life. Non-invasive ventilation.*

CO 042. NON-INVASIVE HOME VENTILATION IN BRONCHIECTASIS

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Introduction: Bronchiectasis (BC) are commonly associated with various pulmonary pathologies, and the affected population is, generally, heterogeneous. In patients with chronic respiratory failure, the use of Non-Invasive Home Ventilation (NIHV) has become increasingly important in their treatment.
Objectives: Characterization of the patients with BQ under NIHV.
Methods: A retrospective analysis was conducted on patients followed in a NIHV clinic, from January 2014 to June 2023, with diagnosis of BC confirmed through High-Resolution Computed Tomography (HRCT). The data was compared using paired-sample t-test and Chi-square test. Results with $p < 0.05$ were considered statistically significant.
Results: Among the 921 individuals followed during this period, 106 (11.5%) were diagnosed with BC. Regarding the complications in the last follow-up, 37.1% had Pseudomonas isolation in sputum analysis and 49.5% experienced at least 1 exacerbation in the last 12 months. In total, 49.5% required hospitalization within a one-year period. There was a statistically significant decrease in the number of patients with hospitalizations in the year following the initiation of NIHV compared to the preceding year. Nine patients discontinued NIHV during follow-up due to non-compliance with therapy. There was no statistically significant decrease in the average pCO2 value, comparing the pre-NIHV period with the follow-up, despite good adherence to NIHV. However, the percentage of patients with hypercapnia ($pCO2 > 45$ mmHg) significantly decreased between the two evaluations (95.2 vs. 71.0%; $p < 0.001$).
Conclusions: In the sample, the coexistence of BC with another underlying pulmonary pathology was considerably more frequent when compared to the isolated diagnosis of BC. Consistent with prior studies, COPD was the most common associated pathology. After initiating NIHV, there was no decrease in the average pCO2 value, however the proportion of patients with hypercapnia had a

statistically significant reduction of more than 20%. The introduction of NIHV had a positive impact on reducing the number of respiratory-related hospitalizations in the first year of treatment.

***Keywords**: Bronchiectasis. Gasometric assessment. Non-invasive ventilation.*

CO 043. NON-INVASIVE HOME VENTILATION IN BRONCHIECTASIS: WHAT ARE THE SEVERITY CRITERIA PREDICTORS OF MORTALITY?

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Introduction: Bronchiectasis (BC) often coexists with various pulmonary pathologies, and the affected population is generally heterogeneous in terms of etiology, microbiology, and lung function. In patients with chronic respiratory failure, the use of NonInvasive Home Ventilation (NIHV) has shown controversial results.
Objectives: Assess the severity criteria in patients with BC at the NIHV initiation and its association with 5-year mortality.
Methods: A retrospective analysis was conducted on patients diagnosed with BC through high-resolution computed tomography (HRCT), under NIHV for at least 6 months and followed at a tertiary hospital between January 2014 and June 2023. From this group, patients with a follow-up period of 5 years or who died within 5 years after starting NIHV were selected. At the outset of NIHV therapy, six criteria from two validated severity scales (FACED score and BSI score) were applied: age > 70 years, FEV1% 50%, Pseudomonas colonization, involvement of > 2 lobes on radiology, hospitalization in the last 2 years, and BMI < 18.5 kg/m^2. Five-year mortality was assessed considering the different criteria, using the Chi-square test. Results with $p < 0.05$ were considered statistically significant.
Results: Applying the specified inclusion criteria, we established a cohort of 68 patients. Among these, 38 patients had a follow-up period of 5 years and 30 died within 5 years after initiating NIHV. Of the total sample, 50% were female, and the median age at the initiation of NIHV was 69.5 [61.1-75.5] years. Patients aged > 70 years at the outset of NIHV had a higher 5-year mortality rate compared to patients aged 70 years, with statistical significance. Furthermore, a greater 5-year mortality was observed in the group of patients with *Pseudomonas* isolation in sputum, also showing a statistically significant difference. The other severity criteria also led to increased 5-year mortality, although without statistical significance.
Conclusions: In the sample, age > 70 years and *Pseudomonas* colonization at the time of NIHV initiation were associated with higher 5-year mortality in patients with BC under NIHV for at least 6 months.

***Keywords**: Bronchiectasis. Severity criteria. Non-invasive home ventilation.*

CO 044. HOME HIGH-FLOW NASAL OXYGEN IN THE CONTEXT OF END-STAGE RESPIRATORY DISEASE – MORE THAN JUST A PALLIATIVE THERAPY?

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Introduction: High-Flow Nasal Oxygen Therapy (HFNOT) has gradually become a cornerstone in the context of severe acute hypoxemic respiratory failure. The well-recognized benefits in improving oxygen deficit while normalizing breathing rate by reducing inspiratory effort, as well as effects on airway humidification have led to an increase in its usage in exacerbations. Due to these physiological effects, it has been hypothesized that there might be a benefit in introducing this therapy for chronic respiratory failure patients presenting end-stage respiratory disease.
Objectives: We aimed to characterize the population of patients proposed to home HFNOT in the context of end-stage respiratory disease, as well as to assess its potential benefit beyond palliation of symptoms.
Methods: Retrospective study including all patients followed in the pulmonology department of a tertiary center who started home HFNOT until June 2023. t-Student and Mann-Whitney tests were applied for continuous variables and the chi-square test was used to compare categorical variables. ROC curves were used to determine the cut-off point of continuously distributed measurements.
Results: A total of 36 patients were included, of which 61.1% were male, with a mean age of 65.5 ± 11.6 years at the time of HFNOT initiation. The majority (61.1%) had interstitial lung disease while others presented mostly a clinical background of obstructive lung disease (30.6%). More than two thirds had either past or ongoing smoking history (69.4%). Hypercapnia was more frequent in obstructive patients ($p = 0.044$), while global respiratory failure was more frequently seen in patients with interstitial lung disease ($p = 0.039$). Although all had chronic respiratory failure, nineteen patients (52.8%) presented sustained acid-base disturbances (38.9% respiratory alkalosis and 13.9% respiratory acidosis). Median time from respiratory-related follow-up to home HFNOT start was 35 months (2;141). Overall median titrated fraction of inspired oxygen was 45% (30;70), significantly lower in obstructive patients versus interstitial lung disease patients [35% (30;65) versus 50% (30;70); $p = 0.05$]. Median titrated air flow was 45 L/min (15;60) with no significant differences between groups. Obstructive patients had a significantly higher number of pre-HFNOT emergency care admissions [4 (1;17) vs 2 (0;16); $p = 0.036$] and hospital stays [3 (2;12) vs 1 (0;5); $p = 0.012$] when compared to interstitial lung disease patients. All patients with obstructive lung disease had less post-home HFNOT hospital admissions versus pre-treatment start, in comparison with only 54.5% of interstitial lung disease patients ($p = 0.013$). While post-home HFNOT emergency care visits were also less than pre-treatment start for both groups, no statistically significant differences were found. Success in reducing PaCO2 6 mmHg on post-HFNOT blood gas analysis was predictive of better treatment outcome, defined as an overall reduction in hospital admissions (AUC 0.720; $p = 0.038$). Median time under home HFNOT was 4 months (0;34). Although mortality was high (77.8%), treatment was well-tolerated by most patients; 4 patients (11.1%) interrupted HFNOT, three due to lung transplantation and only one due to intolerance.
Conclusions: Home HFNOT proved to be an overall safe and well-tolerated treatment strategy for patients with end-stage respiratory disease. Obstructive lung disease patients benefited the most from the treatment, possibly due to hypercapnia correction.

***Keywords**: HFNOT. Oxygen. COPD. Respiratory failure.*

CO 045. SERVOVENTILATION IN CENTRAL SLEEP APNEA SYNDROME – EXPERIENCE OF A TERTIARY CENTER

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Introduction: Central Sleep Apnea Syndrome (CSA) accounts for 5-10% of sleep-disordered breathing, classified into different types according to the International Classification of Sleep Disorders (ICSD-3). Adaptive servo-ventilation (ASV) is a recent ventilation mode used as a second-line treatment in SAC.

Methods: Descriptive and retrospective analysis of patients undergoing ASV, followed at the Sleep and Non-Invasive Ventilation Unit (SNIVU) of a tertiary hospital, between October/22 - June/23. The sleep disorders were classified according to the ICSD-3 and the patients were grouped according to the type of CSA. Demographic characterization, central apnea index (CAI) at diagnosis, left ventricular ejection fraction, oxygen therapy and comorbidities were analysed. When appropriate, the apneahypopnea index (AHI) and the difference in time elapsed between the start of ASV and another ventilation mode were described.
Results: From a population of 594 patients with sleep-disordered breathing, 116 were identified undergoing ASV, with 82 (13.8%) included in the study, and the others were excluded due to lack of clinical information. The patients were mostly male (89%, n = 73) and were, on average, 75.1 ± 10.5 years old at the date of the last medical appointment and IAC 26 ± 13/hour. Patients were divided into 3 groups: A - treatment-emergent central sleep apnea due to positive pressure (PAP) (40.2%, n = 33); B - central apnea with Cheyne-Stokes breathing (29.3%, n = 33). 24); C - central sleep apnea due to a medical disorder without Cheyenne-Stokes breathing (30.5%, n = 25). Patients in group A had a mean age of 71 years and CAI 24/hour and a diagnosis of obstructive sleep apnea syndrome (OSA) with a mean AHI of 34 ± 16/h. They started ASV, on average, 7.8 months after PAP. Their main comorbidities were arterial hypertension (47%, n = 16) and obesity (32%, n = 11). Patients in group B were, on average, 78 years old and had an CAI of 30/hour. All had cardiovascular disease (as in 79% heart failure and 42% hypertension) and 21% had cerebrovascular disease (4 with a history of ischemic stroke). On average, they had been under PAP for one month before starting ASV. In group C, the patients were, on average, 76 years old and CAI 25/hour, all presenting cardiac disorders (such as 83% heart failure and 32% cardiac arrhythmia). Concomitantly, they presented pulmonary pathology (61%), neurological pathology (9%) and obesity (43%). It should be noted that 64% had a previous diagnosis of OSA (average AHI 26.5), having started ASV 96.5 months after PAP. Two patients in group C underwent long-term oxygen therapy. The left ventricular ejection fraction was compromised (30-45%) in 3% of the patients in group A, 52% in group B and 13% in group C, being preserved in the rest.
Conclusions: The prevalence of CSA in this study was higher than in the literature and the main type was the treatment emergent central sleep apnea. There was a high prevalence of cardiovascular pathology (mainly heart failure) and history of OSA. Patients with central apnea with Cheyne-Stokes breathing were older and had a greater number of central events.

Keywords: *Adaptive servo-ventilation. Central sleep apnea syndrome. Obstructive sleep apnea syndrome. Cheyne-stokes breathing.*

CO 046. BIOLOGICAL CLOCK DYSFUNCTION IN OBSTRUCTIVE SLEEP APNEA: TOWARDS NOVEL DIAGNOSTIC AND THERAPEUTIC INTERVENTIONS

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Introduction: Obstructive Sleep Apnea (OSA) has been recognized as a major health concern worldwide given its increasing prevalence, difficulties in diagnosis and treatment, and impact on society. Untreated, OSA has been associated with a host of comorbidities, including hypertension, cardiovascular and metabolic disorders. Recent studies suggest that OSA dysregulates the biological clock, which might contribute to the large spectrum of OSA comorbidities. Yet, the interplay between OSA, the clock, and OSA treatment is not fully understood. We proposed to evaluate the impact of OSA and OSA treatment on clock dysfunction, and its potential applications in OSA diagnosis and treatment.
Methods: We conducted a cohort study involving 34 patients with OSA (age: 55 ± 2 years; Respiratory disturbance index: 46 ± 4), before and after treatment short (4 months) and long-term (2 years) treatment with Continuous Positive Airway Pressure (CPAP), and 7 controls of the same sex (male) and age group (age: 50 ± 3 years; Respiratory disturbance index: 4 ± 1). The levels and temporal profile of clock physiological markers (plasma melatonin and cortisol; body temperature) and the expression of core-clock genes in peripheral blood mononuclear cells were monitored at four time points along 24 h. Machine-learning methods were applied for data analysis.
Results: Patients with OSA showed alterations in the levels and circadian profiles of melatonin and in the expression of several clock genes (e.g., melatonin levels at 8h: 134 ± 12 pg/mL; PER1 expression at 22h30: 0.3 ± 0.2), relative to control subjects (melatonin levels at 8h: 76 ± 15 pg/mL, $p < 0.01$; PER1 expression at 22h30: 1.0 ± 0.2, $p < 0.05$). Long-term CPAP treatment re-established the levels and profiles of melatonin and the expression of some of the evaluated clock genes (melatonin levels at 8h: 80 ± 17 pg/mL; PER1 expression at 22h30: 1.1 ± 0.5). Machine-learning clustering approaches, based on clock-associated markers, distinguished controls from untreated patients (F1 score = 0.95) and showed that long-term CPAP-treated patients better resemble controls than untreated/short-term treated (4 months) patients.
Conclusions: OSA disturbs the biological clock. Long-term CPAP has a positive effect, yet it does not fully re-establish the clock. Our results reinforce the need for new/complementary strategies for OSA treatment. Machine-learning approaches, based on clock-associated markers, show potential applications in OSA diagnosis, patient stratification and treatment response monitoring.

Keywords: *Obstructive sleep apnea. Biological clock. Biomarkers. Machine-learning. Diagnosis. Treatment.*

CO 047. ADVANCING OBSTRUCTIVE SLEEP APNEA DIAGNOSIS IN ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PERIPHERAL BIOMARKERS

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Introduction: Obstructive Sleep Apnea (OSA) has been recognized as a major health concern worldwide, given its increasing prevalence, difficulties in diagnosis and treatment, and impact on health, economy and society. Clinical guidelines highlight the need of biomarkers to guide OSA clinical decision-making, but so far, without success. In this systematic review and meta-analysis we proposed to gather candidates identified in the literature as potential biomarkers for adult OSA diagnosis.
Methods: The current study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (3) and was registered in the International Prospective Register of Systematic Reviews database (PROSPERO, ID CRD42020132556). Search strategies for eight different databases were developed. Studies exploring potential biomarkers of OSA, in peripheral samples of adults, with and without OSA (assessed by overnight Polysomnography in a sleep unit), with no comorbidities, published after 21st

March 2014 were considered as inclusion criteria. Eligible studies were evaluated through the 14-item Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS, (4)) and final studies were selected for meta-analysis.
Results: Among 1,512 screened studies, 120 met the inclusion criteria. Risk of bias was explored and only 16 studies with high methodological study designs were included. Those studies presented a high heterogeneity (I2 above 75%) in the variables assessed. Collectively, OSA group showed an increased percentage of males (11.91%; p = 0.007), older ages (4.22 years; p < 0.001) and higher BMI (3.41 kg/m^2; p < 0.001) in comparison with the control group. OSA patients also showed statistically significant differences in all detailed clinical variables (p < 0.001), with lower differences in daytime sleepiness (3.50; p = 0.010) and SpO2/SaO2 mean (-4.21; p = 0.002). Severity subgroups were further analyzed. Most studies pinpointed candidates with potential for OSA prognosis. Endocan and YKL-40 levels in serum, IL-6 and Vimentin levels in plasma, and ADAM29, SLC18A3, and FLRT2 gene expression in PBMCs revealed potential applications in OSA diagnosis that must be further explored. **Conclusions:** This study showed that OSA biomarkers research is still at an early stage. The identified potential biomarkers and upcoming alternatives must be explored in less biased and more transparent studies, with high methodological study designs, involving larger and non-community based cohorts (multi-centric), to validate biomarkers with application in the clinical management of such a complex multifactorial disorder as OSA.

Keywords: *Sleep apnea. Biomarkers. Diagnosis.*

CO 048. EVALUATION OF POLYSOMNOGRAPHIC CHARACTERISTICS IN CHRONIC LIVER DISEASE

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Introduction: Recent studies have suggested a potential association between chronic liver disease (CLD) and modifications in sleep characteristics, including reduced total sleep time (TST), decreased sleep efficiency, increased sleep onset latency and REM sleep, nocturnal awakenings, respiratory events and excessive daytime sleepiness. The aim of this study was to assess the polysomnographic characteristics of patients with CLD reporting sleep-related complaints and compare them with a control group without CLD.
Methods: Retrospective analysis of polysomnography conducted in a sleep laboratory during 2021 and 2022 at a secondary hospital. The sample was divided into two groups: group 1, patients with CLD, and group 2 (control), patients without CLD. Demographic characteristics, presence and characterization of CLD and etiology, as well as sleep characteristics including efficiency, latency, sleep stages, and respiratory disturbance index, were analyzed. Normally distributed continuous variables are presented as mean ± standard deviation. Data was analyzed using SPSS version 23.0 (IBM Statistics®).
Results: A total of 234 polysomnograms were performed, including 29 patients in group 1 (12.4%) and 205 in group 2 (87.6%). Within group 1, the most frequent etiology of CLD was non-alcoholic fatty liver disease (n = 24, 82.8%), followed by alcoholic fatty liver disease (n = 2, 6.9%, one of whom was transplanted), and genetic liver diseases (n = 2, 6.9%). There was one case of HCV+ viral hepatitis (n = 1, 3.4%) in group 1. In group 1, decreased sleep efficiency (mean of 78.2 ± 16.9%), and increased stage N1 sleep (15.9 ± 12.9%) were observed. Twenty-seven patients (93.1%) in group 1 exhibited study findings compatible with sleep apnea, with 11 classified as mild, seven as moderate, and nine as severe. Levene's test demonstrated no significant differences between the two groups in terms of age, sex, and body mass index (BMI).
Conclusions: The results reveal that in the evaluated sample, like findings in the literature show, patients with CLD exhibit reduced sleep efficiency and increased respiratory events compared to reference values. However, the results do not significantly differ from the control group. Study limitations include selection bias, as all patients were referred from sleep clinics, reporting suggestive sleep-related symptoms. Patients with CLD demonstrate alterations in sleep microstructure and presence of obstructive sleep apnea. Prospective studies are necessary in the CLD population to better understand the implications of this condition on sleep characteristics and associated pathologies.

Keywords: *Sleep disorders. Chronic liver disease.*

CO 049. COMBINED EFFECTS OF OCCUPATIONAL EXPOSURE AND TOBACCO IN COPD

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Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a chronic progressive disease and an important cause of morbidity and mortality in the world. Exposure to toxic particles and gases in both tobacco smoking and occupational exposure is a well recognized major risk factor for COPD but its contribution to the clinical pattern of the disease remains underappreciated.
Objectives: To assess the cumulative effect of occupational exposure in smokers/ex-smokers COPD patients.
Methods: A retrospective observational study was carried out involving smokers or ex-smokers with a diagnosis of COPD followed in a respiratory failure consultation at a Portuguese district Hospital. The presence of occupational exposure was evaluated (documented exposure to vapors, gases, dust or fumes) and subsequent comparative analysis of clinical and functional data was carried out between the following groups: A – COPD smokers or ex-smokers; B - COPD smokers or ex-smokers with concomitant occupational exposure. Patients with other concomitant respiratory pathologies, other etiologies of COPD, without respiratory functional evaluation or incomplete data were excluded. Analyzes were performed in SPSS-Statistics v.27.0 with p values < 0.05 considered statistically significant.
Results: A total of 79 patients were included, 49 in group A (GA) and 30 in group B (GB). The mean age was 68.7 ± 8.7 years (66.5 in GA vs 72.2 in GB; p = 0.04), with male dominance in both groups (57% in GA vs 93% in GB, p = 0.001). Most patients were exsmokers (59.1% in GA vs 56.7% in GB, p = 0.83), with no differences in smoking history between groups (median 60 pack-year in GA vs 50 pack-year in GB, p = 0.59). There were no differences in BMI values (median 25 kg/m^2 in AG vs 26 kg/m^2 in GB, p = 0.65) and in the frequency of cardiovascular comorbidities between the two groups. In the assessment of lung function, the mean FEV1 (% predicted value) was significantly lower in group B compared to group A (39.8 ± 17.2% vs 44.5 ± 20.4%, p = 0.05), with no difference in the remaining parameters evaluated (lung volumes, distance covered in 6mWT, BODE index or mMRC). 41.8% (42.9% in AG vs 40% in GB, p = 0.80) and 26.6% (26.5% in AG vs 26.7% in GB, p = 0.98) of patients were under long-term oxygen therapy and home non-invasive ventilation, respectively. There were no significant differences between the groups regarding the occurrence of exacerbations in the last year. (p = 0.17).
Conclusions: In addition to the higher prevalence and incidence of COPD found in people with both work-related and tobacco exposure, we could identify distinct clinical characteristics associated with this phenotype. In this series of COPD patients, the combined exposure subjects were older male patients who had more severe

airflow obstruction compared to the single exposure group, demonstrating that there is a potential negative synergistic effect associated with the combination of tobacco and occupational exposure in COPD patients. It is therefore essential in clinical practice to recognize the impact that this interaction may have on the clinical evolution and prognosis of these patients.

Keywords: *COPD. Tobacco smoking. Occupational exposure.*

CO 050. NIVO SCORE AS A PREDICTOR OF MORTALITY IN AECOPD PATIENTS: REAL-LIFE COHORT

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Introduction: Acute exacerbations of COPD (AECOPD) complicated by acute-on-chronic respiratory failure with acidemia are frequent. Non-invasive ventilation (NIV), when correctly used, reduces the need for mechanical ventilation and mortality. Predictive scales of mortality associated with AECOPD have been developed, such as the Non Invasive Ventilation Outcomes score (NIVO), designed to be applied to patients with complicated exacerbation of acidemia or need for assisted ventilation. This study aimed to evaluate the applicability of this instrument in our population.
Methods: Retrospective cohort study, from January/2017 to December/2021. Patients included were hospitalized for AECOPD with respiratory acidemia or need for NIV, all with spirometric confirmation of COPD. The NIVO score was applied to each patient, comparing the observed mortality with that was predicted by the scale. The primary outcome was in-hospital mortality and the secondary outcome was 90-day mortality. Sociodemographic data (age, gender, smoking status, BMI) and clinical data (comorbidities, GOLD stage, home NIV, LTOT - long-term oxygen therapy, number of exacerbations in the previous 12 months) were also analyzed. The discriminatory ability of the score was evaluated using the obtained ROC curve.
Results: 86 patients were included, 76.7% (n = 66) male, median age 67 years [AIQ 59-74]. The mean BMI was 24 kg/m^2 ± 5.6 and the median BODE index was 5 [AIQ 3-7]. 44.2% (n = 38) of the patients were active smokers and 52.3% (n = 45) were former smokers, with a median smoking history of 56.2 pack-years (AIQ 40-82.5). Most patients had severe (GOLD 3, 44.1% [n = 38]) and very severe obstruction (GOLD 4, 27.9% [n = 24]). Prior to admission, 31.4% (n = 27) were under home NIV, 37.2% (n = 32) under LTOT and 20% (n = 17) were under LTOT and NIV. The most frequent comorbidities were pulmonary hypertension (26%, n = 22), heart failure (21%, n = 18) and diabetes mellitus (17%, n = 15). The in-hospital mortality rate was 9.3% (n = 8). The main cause of in-hospital mortality was respiratory failure (62.5%, n = 6), and of these all had NIV as a therapeutic ceiling. Mortality was higher in patients with a greater number of moderate-severe exacerbations in the last year compared to patients who survived the hospitalization (median 2 vs 1, p = 0.023). When the NIVO score was applied, there were no differences between low-risk individuals (observed mortality 2.8% vs expected mortality score 5%, p = 0.439), intermediate risk individuals (observed mortality 22.2% vs expected mortality score 16.8%, p = 0.697) and high risk (observed mortality 100% vs expected mortality score 41.2%, p = 0.075). The application of the 90-day mortality score followed the same trend. The discriminatory power of the NIVO score for in-hospital mortality was 0.88 (88% sensitivity, 34% specificity), while 90-day mortality was 0.82 (80% sensitivity, 34% specificity).
Conclusions: As described in the literature, the NIVO score showed good discriminatory power as a predictor of in-hospital and 90-day mortality in the analyzed sample. It represents a useful tool in clinical practice, namely in the timely assessment of patients at higher risk of mortality and consequent better management of established therapies.

Keywords: *NIVO score. In-hospital mortality. COPD.*

CO 051. EVALUATION OF FEV1Q AS A PREDICTOR OF MORTALITY IN AMYOTROPHIC LATERAL SCLEROSIS – EXPERIENCE OF A DISTRICT HOSPITAL

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Introduction: The 2021 ATS/ERS guidelines introduced FEV1Q (forced expiratory volume in 1 second divided by the sex-specific first percentile values of the absolute FEV1 values found in adults with lung disease, that is 0.4 L for women and 0.5 L for men) to predict survival. The closer FEV1Q is to 1, the greater the risk of death. Currently, few studies address the real-life application of FEV1Q, namely in amyotrophic lateral sclerosis (ALS), in which FVC (forced vital capacity) is used in the assessment of survival.
Methods: Retrospective analysis of patients with ALS followed in a Pulmonology appointment at a district hospital between January/2017 and July/2023. Demographic characterization, presence of bulbar involvement at diagnosis, non-invasive ventilation (NIV), mechanical in-exsufflator and percutaneous endoscopic gastrostomy (PEG) were described. When appropriate, the time elapsed between diagnosis and death, initiation of NIV after diagnosis and until death was also described. The FEV1 and FVC values were taken from the pulmonary function tests carried out by the patients and were analyzed for their decline over time, and the FEV1Q was calculated. The predictive capacity of FEV1, FEV1Q and FVC was analyzed through survival analysis with the Cox Proportional Hazards method. Results with $p < 0.05$ were considered statistically significant.
Results: There were 47 patients identified with ALS, of which 45 were included, most of them were female (60%, n = 27), with a mean age at diagnosis of 69.2 ± 11 years. 36% (n = 16) of patients had bulbar involvement at diagnosis. It was found that 95% (n = 43) of the patients met the criteria for NIV, with 93% (n = 40) of these starting NIV (a median of 137 days after diagnosis). In addition, 91% (n = 41) started a mechanical in-exsufflator and 36% (n = 16) placed a PEG. The mortality rate was 57% (n = 26), with patients dying a median of 398 days (IQR 216.5-1218) after diagnosis and 99 days (IQR 58-366) after the last pulmonary function tests. It should be noted that of these patients, 56% (n = 12) had bulbar involvement and that 8% (n = 2) refused to undergo NIV (with the remaining undergoing NIV, on a median, 192 days before dying). Regarding pulmonary function tests, a decline in FEV1, FEV1Q and FVC was observed. FEV1 and FEV1Q were predictors of mortality with statistical significance ($p < 0.05$). The Akaike information criterion showed that FEV1Q was a better predictor of mortality than FEV1. The FEV1Q decreases by 0.7 per month, and death occurred, on average, when the FEV1Q was 2.68. FVC was not a predictor of mortality, either alone or as part of a multivariable model together with FEV1Q.
Conclusions: In a period of about 6 years, there was an important mortality of patients with ALS, with a higher prevalence of those with bulbar involvement at diagnosis. FEV1Q proved to be the best predictor of mortality among the analyzed variables, approaching on average 2. It is needed to replicate this analysis in a larger population before these results can be applied in the clinic practice.

Keywords: *FEV1Q. FEV1. FVC. Amyotrophic lateral sclerosis.*

CO 052. MACHINE LEARNING CLASSIFICATION OF PULMONARY HYPERINFLATION BASED ON BASELINE SPIROMETRIC PARAMETERS

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Introduction: Spirometry is the most accessible and widely used Respiratory Function Test (RFT). However, it does not allow for the evaluation of static lung volumes, such as residual volume (RV) or total lung capacity (TLC), which are essential to support the diagnosis of hyperinflation or pulmonary restriction. This study aimed to fill this gap by using the Catboost machine learning (ML) model to classify the presence of hyperinflation (abnormally elevated RV/TLC ratios).
Methods: This is a retrospective study with 8,138 baseline RFTs conducted at the Hospital da Luz Lisboa. The spirometric and whole-body plethysmography (WBP) parameters were subjected to the Catboost model using an 80-20 training-testing data split to classify the spirometries associated with increased RV/TLC values. For external model validation, an independent sample of 227 RFTs performed at the Hospitals of Luz Lisboa, Oeiras and Setúbal was collected. In the sample used for training and testing the model, the prevalence of RFTs with increased RV/TLC values was 24%, and this alteration was present in any spirometric pattern (normal, obstructive, restrictive, and mixed).
Results: The model showed good performance in the test sample, with an accuracy of 0.83, an area under the receiver operating characteristic curve (AUC) of 0.85, and an F1 score of 0.82. In the validation sample, the model maintained its performance with an accuracy of 0.85, an AUC of 0.86, and an F1 score of 0.84. This study demonstrated promising results with robust performance, both in the test sample and in external validation. However, there is a need to improve the negative predictive value to avoid false negatives and ensure accurate diagnoses for patients with hyperinflation.
Conclusions: The inclusion of more relevant parameters, reducing the entropy of the target variable in the training sample, and increasing the external validation sample can enhance the model's applicability in clinical contexts where the evaluation of non-mobilizable lung volumes is not possible.

Keywords: *Spirometry. Static lung volumes. Machine learning.*

CO 053. LUNG CANCER: FROM CLINIC TO THERAPEUTIC DECISION IN THE VERY YOUNG (< 45 YEARS) VS. THE VERY ELDERLY (> 85 YEARS)

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Introduction: Lung cancer mainly affects the elderly, and in most cases it is not possible to offer treatment with curative intent. Molecular markers show age-related differences. This fact, associated with the frailty found in the elderly population, inevitably limits the therapeutic options available. With this work, the authors intend to highlight the main differences in clinical presentation and therapy instituted in young people vs. elderly people with lung cancer.
Objectives: The clinical files of patients followed up in a Pulmonology Oncology consultation at CHUC diagnosed between 01/1/2018 and 12/31/2022 with primitive lung cancer with 45 and 85 years were consulted, the first being classified as group 1 and the seconds as group 2.
Results: We obtained a total of 97 patients, 48 young and 49 elderly. In group 1 (young people) the mean age was 41.7 ± 3.4 years; male in 60.4%; performance status of 1 in 60.4%; 31.3% were non-smokers and the majority (77.1%) in stage IV. In group 2 (elderly) the average age was 87.4 ± 2.4 years; male in 61.2%; performance status of 1 in 38.8%; 42.9% were non-smokers and the majority (75.5%) in stage IV. The most frequent histological subtype was adenocarcinoma, with a prevalence of 87.5% in group 1 and 67.3% in group 2. In the latter, the squamous subtype represents 24.5%, compared to group 2 in which it was registered only 1 case. With a positive molecular study, the ALK translocation was the most frequent in the young group (62.5%), while in the elderly group the EGFR mutation predominated (56%). As for PDL-1 expression, it was negative in 41.7% and 51.1% in groups 1 and 2, respectively. Regarding the therapeutic decision, chemotherapy (CT) was the therapeutic decision for 1st line in 33.3% in group 1 and 12.2% in group 2, in which the best supportive therapy (BST) was the 1st option in 44.9% of patients. Tyrosine kinase inhibitors (TKI) were used in 1st line by 25% in group 1 and 22.5% in group 2. 6.3% and 8.2% of groups 1 and 2 underwent first-line immunotherapy, respectively. In the young group, 5 patients underwent concomitant chemotherapy and radiotherapy (RT), compared to the elderly group, in which 4 patients underwent isolated RT.
Conclusions: In this work, in the young group we found a higher percentage of women and better performance status. In the elderly group, squamous histology and, in the molecular evaluation, mutation in the EGFR gene were more frequent. Regarding PDL-1 expression, the percentage difference between groups was not significant. With regard to first-line therapy, BST was the first option for most elderly people. This study highlights the need for a personalized assessment and decision, where age is definitely not negligible.

Keywords: *Lung cancer. Treatment. Young. Elderly.*

CO 054. CHARACTERIZATION OF ALK GENE FUSION PARTNERS IN LUNG ADENOCARCINOMA: A CROSS-SECTIONAL STUDY

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Introduction: The ALK gene codes for a protein called anaplastic lymphoma kinase. About 4-5% of people who have non-small cell lung cancer (NSCLC) have an alteration on chromosome 2 that leads to the fusion of the ALK gene with another gene (fusion partner), which possess potential oncogenic functions due to constitutive activation of ALK kinase. The most common ALK fusion partner is a gene called echinoderm microtubule-associated protein-like 4 (EML4) and results in the production of an EML4-ALK fusion protein. During the past decade, over 11 different variants of EML4 ALK have been identified in a variety of tumors, including NSCLC, digestive tract and breast cancer. The most common variant among EML4 ALK fusions is variant 1 (33%), followed by variant 3 (29%) and variant 2 (10%). It is a rare mutation most commonly seen in people who have never smoked or are light smokers, especially women of Asian descendants. Although more than 90 distinct fusion partner genes have been reported, treatment of ALK-rearranged cancers is decided without regard to which partner is present. There is little data addressing how the fusion partner affects the biology of the fusion or responsiveness to ALK tyrosine kinase inhibitors (TKIs). However, in some patients, the fusion partner it's not identified and that represents a particular situation not clarified in published literature regarding the prognosis and treatment response.
Methods: We conducted a cross-sectional analysis of a retrospective cohort with lung adenocarcinoma and ALK mutations detected by next generation sequencing (NGS) from 2017 to 2021, followed at Pneumology Department at Centro Hospitalar e Universitário de São

João. Our aim was to characterize the population, describe epidemiologic characteristics, staging at diagnosis and overall survival.
Results: Were included 47 patients, of which 25 (53.2%) were male and 22 (46.8%) were female with a mean age-at-diagnosis in years of 61.6 ± 11.7. Most patients (n = 28, 59.6%) were non-smokers, had no previous medical history of respiratory diseases (n = 39, 83%) and had no relevant environmental exposure (n = 28, 59.6%). Regarding cancer diagnosis, 14 (29.8%) patients were diagnosed with local disease, 9 (19.1%) patients were diagnosed with locally advanced disease and 24 (51.1%) with metastatic disease, with the most common sites of metastasis being bone, pleura, brain and liver. Of the 47 patients, in 15 (31.9%) the ALK fusion partner was not identified. Of the remaining, variant V6 was present in 14 (37.8%) patients, variant V3 in 13 (35.1%) patients, variant V5 in 3 (8.1%) patients, and both variant V8 and V2 were detected in 1 (2.7%) patient each. The mean overall survival in months (OS) was 43.9 ± 36.99 and the median progression free survival (PFS) in months was 26.9 ± 37.32.
Conclusions: This study analyzed lung adenocarcinoma patients with ALK mutations and identified EML4 as the most common fusion partner. Some cases had unidentified partners, posing challenges in prognosis and treatment response. The research emphasizes the need for further investigation to understand the impact of different fusion partners on outcomes.

Keywords: *Lung adenocarcinoma. ALK-fusion.*

CO 055. 2 YEARS OF IMMUNOTHERAPY IN MONOTHERAPY IN NON-SMALL CELL LUNG CANCER: WHAT COMES NEXT?

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Introduction: Lung cancer is the leading cause of cancer-related death. For this reason, in recent decades, there has been investment in new therapies, especially directed at specific molecular targets. There was thus a paradigm shift in the approach, especially of non-small cell lung cancer (NSCLC), with clinical trials demonstrating prolonged benefits of immunotherapy (IO) in monotherapy in patients who completed 35 cycles/2 years of treatment.
Methods: A retrospective analysis was carried out of the clinical process of the patients followed in an Oncological Pulmonology consultation at Coimbra University Hospital Center between January 1, 2016 and August 31, 2023, with the diagnosis of NSCLC and who completed two years of immunotherapy in 1st or 2nd therapeutic line. Demographic and clinical data, information regarding initiation of therapy, response to it, occurrence of toxicity, time until progression and death, in cases where this has occurred, were collected.
Results: We obtained a total of 25 patients, 22 male, with an average age of 63.0 ± 11.9 years; performance status (PS) of 1 in 80%; 20% non-smokers; the majority (96%) in stage IV. The most frequent histological subgroup was adenocarcinoma (84%). In 64% of the patients the expression of PDL-1 (programmed-death ligand 1) was greater than 50%. Pulmonary and bone metastases were the most frequent (48%). Chemotherapy (CT) was the first-line therapy in 64% of cases, with progression occurring in 25%. In the group that started 1st line therapy with immunotherapy (IO), 77.8% had a partial response (PR), 1 patient had a complete response (CR) and there was no case of disease progression. OI was second-line therapy in 87.5% of the patients who initially underwent CT, with pembrolizumab being the most used drug (85.7%). It should be noted that 2 of the patients who had progressed under 1st-line chemotherapy obtained PR with 2nd-line OI. Adverse effects occurred in 28% of patients, with colitis and pneumonitis being the most frequent (28.57%). To date, 28% of patients have died. Mean progression free survival (PFS) and overall survival (OS) were 39.6 ± 11.6 and 40.2 ± 14.1 months, respectively.
Conclusions: IO, more specifically 1st-line pembrolizumab in lung adenocarcinoma with PDL-1 expression, showed favorable results, with no progression seen in any of the analyzed cases, contrary to what was seen in the group that underwent 1st-line chemotherapy. line. It was also found that, even in patients who progressed under chemotherapy, IO enabled second-line PR. The PFS and OS allowed demonstrating that, despite the occurrence of adverse effects not being negligible, this therapy is beneficial in most cases.

Keywords: *Immunotherapy. Non-small cell lung cancer.*

CO 056. CLINICAL CHARACTERISTICS OF PATIENTS WITH NON-SMALL CELL LUNG CARCINOMA (NSCLC) WITH RET MUTATIONS

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Introduction: Genetic alterations in the RET gene are present in approximately 1% of patients with Non-Small Cell Lung Carcinoma (NSCLC), and due to the limited number of patients, knowledge about this group is limited. The objective of our study was to describe the clinical characteristics of this subgroup of patients, their mode of presentation, and clinical outcomes.
Methods: We conducted a retrospective analysis of patients with RET rearrangements identified by Next-Generation Sequencing (NGS) and diagnosed at a university hospital center between January 2017 and April 2023.
Results: We obtained data from 22 patients, with a slight predominance of females (n = 12, 54.5%), and a median age of 67 years (3,588). The Performance Status was 0 or 1 in 90.9% of the patients. Ten patients (45.5%) had a history of current or past tobacco exposure, with an estimated tobacco load of 35 pack-years. Regarding personal or family history of oncological pathology, 18.2% of the patients had personal history, and 22.7% had family history. Regarding tumor characteristics, the majority of patients had adenocarcinoma as the histological subtype, with one case showing combined histology of large cell neuroendocrine carcinoma with adenocarcinoma. In 13 patients (59.1%), PD-L1 expression was intermediate, and in 6 patients, it was high (> 50%). At the time of diagnosis, the majority of patients were at stage IV (n = 13, 59.1%), 4 patients (18.2%) were at stage I or II, and 5 patients (22.7%) were at stage III. The most frequent sites of metastasis were the lungs (n = 12, 54.5%) and bones (n = 6, 27.3%). Only 2 patients (9.1%) had central nervous system metastasis at the time of diagnosis. Regarding first-line therapy, surgery was chosen for 5 patients (22.7%), chemo-radiation therapy (QTRT) for 2 patients (9.1%), and supportive therapy for 5 patients (22.7%). Metastatic stage patients received first-line treatment with chemotherapy (n = 3, 13.6%), immunotherapy (n = 2, 9.1%), and tyrosine kinase inhibitors (TKI) in 5 patients (22.7%). Additionally, 2 other patients started TKI therapy in the second-line after disease progression. The most frequently used TKI was Selpercatinib in 5 patients, while the rest were treated with Pralsetinib. Overall, 7 patients (31.8%) experienced disease progression, most commonly in the thoracic region (n = 3), with a median progression-free survival of 11 months (4-41). By the end of the analyzed period, 13 patients (59.1%) had died, with a median overall survival of 8.0 months (0-33). The median follow-up time for all evaluated patients was 9.0 months (0-74). In the subgroup of patients who received TKI treatment (n = 7), the median follow-up time was 11.0 months (6-69), with death occurring in 3 patients, and the median overall survival was 9.0 months (8-11).
Conclusions: The analysis contributes to a better characterization of patients with NSCLC and RET mutation. However, due to the small sample size, it was not possible to obtain statistically significant

conclusions. More studies with larger samples are needed to better characterize subgroups of patients with NSCLC and rare molecular alterations.

***Keywords**: Non-small cell lung carcinoma. Ret mutation.*

CO 057. SMALL CELL LUNG CARCINOMA IN NONSMOKERS

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Introduction: Smoking is responsible for 80-90% of lung cancers worldwide. Among lung cancers occurring in non-smokers, the overwhelming majority corresponds to non-small cell lung carcinomas, with only 2% of small cell lung carcinomas (SCLC) occurring in non-smoking patients. Little is known about the pattern of occurrence and evolution of SCLC in non-smokers, as well as the involved risk factors. This study aimed to characterize patients diagnosed with SCLC who were non-smokers. **Methods:** We retrospectively reviewed non-smoking patients diagnosed with SCLC between January 2013 and July 2023. Data regarding demographic, clinical, and pathological characteristics was collected.
Results: We identified 12 non-smoking patients diagnosed with SCLC, of whom 10 were female (83.3%). The median age at diagnosis was 74 years (60-79), and the median follow-up time was 6.3 months (2.3-7.9). Concerning risk factors, 3 patients had passive tobacco exposure (25%), 3 worked in the textile industry (25%), and 5 had a history of respiratory disease (41.7%). Two patients had a family history of known neoplastic disease (16.7%). Regarding the diagnosis of SCLC, 1 patient was diagnosed in stage IA, 1 in stage IIIA, 1 in stage IIIC, 1 in stage IVA, and 8 patients were diagnosed in stage IVB. Liver and pleura were the most frequent sites for metastasis. Among patients in stage IV, 5 received first-line treatment with chemotherapy (41.7%), 2 with chemotherapy combined with immunotherapy, and 2 patients were provided with the best supportive care. Disease recurrence was observed in 6 patients (50.0%), and 7 patients died (58.3%), with a median overall survival of 6.3 months (2.3-7.9).
Conclusions: Small Cell Lung Carcinoma (SCLC) is a high-grade neuroendocrine carcinoma, being the most aggressive form of lung cancer with a 5-year survival rate of less than 10%. It is not an exclusive disease of smokers, making it essential to understand the pattern of occurrence and evolution in non-smoking patients.

***Keywords**: Lung cancer. Small cell lung carcinoma. Nonsmokers.*

CO 058. MULTIPLE PRIMARY LUNG TUMORS: A SINGLE-CENTER EXPERIENCE

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Introduction: The distinction between multiple primary lung tumors and intrapulmonary metastasis has implications in the treatment and prognosis of these patients. Molecular study through next-generation sequencing (NGS) tests is an important tool in the differential diagnosis. This study aimed to analyse demographic data and clinical characteristics of patients with multiple primary lung adenocarcinomas and compare their radiological and histopathological features.
Methods: A retrospective study that included all patients followed at a tertiary hospital center diagnosed with adenocarcinoma and presenting with synchronous or metachronous multiple lung lesions, subjected to biopsy and NGS analysis since 2017. The diagnosis of primary lung tumors was established in a multidisciplinary meeting based on molecular study (lesions with different NGS results). Demographic data, radiological and histopathological characteristics of the lesions, disease staging, treatment, and outcome were analysed.
Results: A total of 28 patients with a diagnosis of multiple primary lung adenocarcinomas were included and 56 lesions were analysed. Among these, 64.3% (n = 18) were male, with a median age of 64 (min 42 – max 83) years, 75% (n = 21) had a history of current or former tobacco use, and 21.4% (n = 6) had a history of other neoplasms. Lesions were synchronous in 78.6% (n = 22) of cases and metachronous in 21.4% (n = 6). Regarding their distribution, lesions were contralateral in 50% (n = 14), present in different lobes of the same lung in 32.1% (n = 9), and in the same lobe in 17.9% (n = 5) of cases. The radiological pattern of lesions was the same in 50% (n = 14) of cases. The predominant histopathological pattern differed between the two lesions in most cases (n = 19, 67.9%). The most frequent mutation was in the KRAS gene, followed by EGFR. Stage IA was the most common, observed in 71% of cases. Half of these would be classified as stage IV if one of the lesions were considered a metastasis. Both lesions underwent curative treatment in 23 cases. Disease progression/recurrence was observed in 7 patients, resulting in death in 4 cases. Among these, 4 had undergone initial curative treatment (2 surgery and 2 stereotactic radiotherapy). In total, there were 8 deaths (the aforementioned 4 and 3 unrelated to oncological disease). The median overall survival was 29 months.
Conclusions: Patients with multiple primary lung lesions are often subjected to radical treatment. Radiological and histopathological characteristics are usually insufficient to distinguish between these two entities, highlighting the importance of biopsy, molecular study, and multidisciplinary decision-making.

***Keywords**: Multiple primary lung tumors. Intra-pulmonary metastasis. Molecular study.*

CO 059. PULMONARY SARCOMATOID CARCINOMAS: FROM CLINICAL DATA TO THERAPEUTIC DECISION

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Introduction: Pulmonary sarcomatoid carcinomas are defined as poorly differentiated non-small cell carcinomas containing a sarcoma or sarcoma-like component (spindle and/or giant cells). They are rare tumours, accounting for less than 1% of all lung tumours, and usually present aggressively with a poor prognosis.
Objectives and methods: The aim of this study was to characterise the population of patients with pulmonary sarcomatoid carcinomas followed up in a tertiary hospital over the last 10 years. For this purpose, a data collection was performed through the hospital digital platform, which was subsequently analysed and interpreted.
Results: Since January 2013, 27 pulmonary sarcomatoid carcinomas were diagnosed in mostly male patients (n = 24; 88.9%), aged between 39 and 83 years (median 61 years). Of these patients, 44.4% (n = 12) were smokers at the time of diagnosis and most had a performance status ECOG = 1. Regarding histological classification, it was possible to observe that the majority (n = 19, 70.4%) were classified as pleomorphic carcinoma of the lung and of the patients with known PD-L1 quantification (only 59.3%), the majority (n = 9; 56.3%) showed an expression in > 50% of the cells. As for the molecular markers study (known only in 44.4% of patients), it was mostly neg-

ative, with only one patient ALK positive and another KRAS-G12C positive. After completing clinical staging, 23 patients (85.2%) had advanced disease (stage IIIB, IVA or IVB) and 4 patients were in a surgical stage (1 patient IB; 2 patients IIA and 1 patient IIIA). All cases were presented at a multidisciplinary team meeting and in 3 of them (11.1%) best supportive care was chosen ad initium. Of the 4 patients undergoing surgical treatment, 2 underwent adjuvant chemotherapy. The remaining 20 patients underwent first-line systemic therapy (1 patient under tyrosine kinase inhibitor (with Alectinib); 2 patients under immunotherapy (with Pembrolizumab) and 18 patients under chemotherapy (with platinum doublet with Paclitaxel or Pemetrexed)). Considering the whole population, a 3-month mortality after diagnosis of 29.6% was found. Overall survival at 6 months after diagnosis in this population was 63%, decreasing to 33.3% at 12 months and only 18.5% at 24 months (of the 5 patients with survival 24 months, all were treated with immunotherapy).
Conclusions: Although rare, pulmonary sarcomatoid carcinomas should be recognised by the pulmonologist, first and foremost due to their adverse prognosis and high rate of progression, which motivate a diligent response and guidance. In the future, there is still a need to better characterise this type of tumour from an anatomopathological and, above all, molecular point of view, with an intent to develop new therapies that could improve the current treatment paradigm for these neoplasms.

Keywords: *Lung cancer. Sarcomatoid carcinoma. Pleomorphic carcinoma.*

CO 060. STK11 AND KEAP1 GENE MUTATIONS AND RESPONSE TO IMMUNOTHERAPY IN NON-SMALL CELL LUNG CANCER

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Introduction: Immunotherapy has shown a significant improvement in overall survival and progression-free survival (PFS) in patients with metastatic non-small cell lung cancer (NSCLC). However, not all patients respond well to these treatments. Therefore, other predictive biomarkers for immunotherapy response have been explored, including mutations in the STK11 and KEAP1 genes. In essentially retrospective studies, it has been found that patients with co-mutations in KRAS, STK11, and/or KEAP1 have a worse response to immunotherapy.
Objectives: To assess the prevalence of mutations in the STK11 and KEAP1 genes in patients with metastatic NSCLC treated with immunotherapy, according to treatment response.
Methods: A retrospective descriptive analysis of a cohort of patients with metastatic NSCLC who initiated monotherapy immunotherapy between 12/2015 and 12/2018 at a tertiary hospital, divided into long responders (PFS 1 year) or short responders (PFS 3 months). Reflex evaluation of PDL1 expression and NGS panel, along with a retrospective evaluation of the presence of mutations in the STK11 and KEAP1 genes, were performed on all tumors. The prevalence of these mutations was analyzed in the two groups of patients.
Results: Among the 61 patients who met the inclusion criteria, only 38 (62.3%) had sufficient tumor DNA for some STK11/KEAP1 evaluation. Among these, 5 patients had an incomplete STK11 analysis, 12 had an incomplete KEAP1 analysis, and 3 had sufficient samples for STK11 evaluation only. The majority of patients were male (76.3%) with a median age of 60 [51; 67] years and ECOG 1 (60.5%). Adenocarcinoma was the predominant histological type (86.8%), with 55.6% showing PDL1 50% expression. 28.9% started immunotherapy as a first-line treatment, 39.5% as a second-line treatment, 18.4% as a third-line treatment, 10.5% as a fourth-line treatment, and 2.6% as a fifth-line treatment. It was found that 50% of patients were short responders and 50% were long responders. Among them, 24.2% (n = 8) had KRAS mutation, and all of these were short responders. STK11 gene mutation was found in 43.8% of long responders and 47.1% of short responders, while KEAP1 gene mutation was found in 25% of long responders and 18.2% of short responders. In the subgroup of patients with KRAS mutation, 62.5% had co-mutation with STK11, and none of the patients showed co-mutation with KEAP1. Only 3 patients had co-mutations of KEAP1 and STK11, of which 2 were long responders and 1 was a short responder.
Conclusions: The evaluation of STK11/KEAP1 mutations in material conserved for more than 5 years is unfeasible in over 1/3 of the patients, which raises the need to consider their inclusion in the standard NGS panel carefully. More than half of the long survivors had mutations in STK11 and/or KEAP1 without KRAS co-mutation, questioning whether the presence of these mutations only holds negative prognostic value in KRAS mutated patients. Due to the small size and sometimes incomplete evaluation of the STK11 and KEAP1 genes in this retrospective study, prospective studies are needed to draw more robust conclusions.

Keywords: *Immunotherapy. STK11. KEAP1. Metastatic non-small cells lung cancer.*

CO 061. THYMIC EPITHELIAL TUMORS – RETROSPECTIVE ANALYSIS

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Objectives: Thymic epithelial tumors (TET) are a heterogeneous and rare group of pathologies, including thymic carcinomas and thymomas, the latter of which may be associated with autoimmune pathologies. Their treatment and prognosis are controversial given the rarity of the disease and the evidence is based on small, mainly retrospective, series of patients. The authors aim to characterize the TET evaluated and treated at the Multidisciplinary Unit of Thoracic Tumors (UMTT) of the Hospital of Vila Nova de Gaia/Espinho.
Methods: Retrospective analysis of the morphological and clinical characteristics of TET evaluated at the UMTT from 2010 to 2023.
Results: 31 patients with TET followed at UMTT were identified, with a mean age of 64.2 ± 14.5 years and 51.6% (n = 16) male. Twenty-five (80.6%) were thymomas (four with associated Myasthenia Gravis) and 6 (19.4%) thymic carcinomas. Of the patients with thymomas, 20 (80.0%) underwent surgical resection, of which 6 (24.0%) underwent adjuvant radiotherapy. Resection was described as complete in 19 (95.0%) cases. One case of thymoma submitted to complete surgical resection (5.0%) recurred. According to the WHO histologic classification of thymomas, the majority were type AB (8 - 32.0%) or B2 (5 20.0%). Regarding the Masaoka-Koga staging of thymomas submitted to surgical resection, 9 (45.0%) patients were in stage I, 7 (35.0%) in IIA and 4 (20.0%) in IIB. The remaining 5 (20.0%) thymomas remained under surveillance and supportive therapy. Regarding TNM staging of the 6 patients with thymic carcinoma, one (16.7%) patient presented in stage IIIB and 5 (83.3%) in stage IV. Regarding their treatment, 3 (50.0%) underwent chemotherapy alone, 2 (33.3%) had chemo- and radiotherapy and one (16.7%) had surgery and adjuvant radiotherapy. The median follow-up time was 33 months (min 2; max 232) for thymomas and 35 months (min 2; max 103) for thymic carcinomas. During follow-up, recurrence was observed in 2 (6.4%) thymic carcinomas and one (3.2%) thymoma, and progression was observed in 3 (9.7%) thymic carcinomas and one (3.2%) thymoma. Seven (22.6%) of the patients in follow-up died (3 patients with thymoma and 4 with thymic carcinoma), and in 4 (12.9%) of them the cause of death was in the context of thymic carcinoma.

Conclusions: TET are a rare and heterogeneous group of diseases and therapeutic decisions should be taken systematically in a multidisciplinary setting. Complete surgical resection remains the gold standard of treatment for this setting of patients, playing a major role in their survival.

Keywords: *Thymoma. Thymic epithelial tumor. Masaoka-Koga.*

CO 062. TELEMONITORING IN SEVERE ASTHMA

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Introduction: Severe asthma is characterised by high instability and unpredictability in its evolution, and is often associated with exacerbations requiring medical care. Telemonitoring is a practice of remote patient monitoring, in which communication technologies and medical devices are used to collect patient health data remotely. These data are transmitted to healthcare workers, allowing continuous monitoring and analysis of the information, for clinical decision-making. An innovative telemonitoring programme for patients with severe asthma was implemented in a hospital in northern Portugal. This programme includes a telemonitoring platform, smartphones, remote monitoring devices (oximeter, tensiometer and thermometer), a personalised questionnaire and a team of healthcare workers composed of doctors and nurses. The aim of this study is to assess the effectiveness of the telemonitoring programme implemented.
Methods: Cross-sectional study with convenience sampling: all individuals included in the Asthma Telemonitoring Programme. Criteria for integration in the programme: previous diagnosis of severe asthma (GINA 2023 definition) and ability to use a smartphone with internet access as well as remote monitoring devices. Variables under study: epidemiological (gender and age) and clinical (diagnosis, pharmacological treatment, exacerbations and biometric parameters) during the study period: 02/11/2023 to 15/05/2023. Statistical analysis: SPSS 26.0. Ethical considerations: Data were collected from clinical files without identifying data, with anonymity.
Results: The sample consisted of 10 subjects, 30% (n = 3) male and 70% (n = 7) female with a mean age of 49.3 (± 8.41) years. 50% (n = 5) were on ICS/LABA/LAMA triple inhaler therapy, 30% (n = 3) budesonide/formoterol + tiotropium bromide and 20% (n = 2) fluticasone/vilanterol + tiotropium bromide. As a resource in SOS: salbutamol MDI in 50% (n = 5), formoterol/budesonide in 20% (n = 2) and terbutaline in 30% (n = 3). 362 device alerts appeared on the platform, of which 89.04% (n = 325) for O2 sat < 95%, 8.29% (n = 30) for HR > 100 bpm and 1.93% (n = 7) for temperature > 38ºC. There were 63 nursing teleconsultations, of which 28.57% (n = 18) were for clinical causes and the rest for lack of biometric records. These tele-consultations generated 38.89% (n = 7) of medical consultations in person within 24 hours, which allowed for early therapeutic intervention. No individual had the need to resort to the Emergency Service for respiratory causes nor was any hospitalization necessary for respiratory causes.
Conclusions: At the clinical level, the program of Telemonitoring of Severe Asthma proved to be effective in the early detection of exacerbations and in reducing the number of exacerbations requiring emergency care and hospitalization. It has improved disease management and control, through closer monitoring and reinforcement of self-care, providing patients with an enormous sense of safety and confidence. At an institutional level, it is a model of care that reduces health costs for asthma patients. This study shows the positive effects of telemonitoring in patients with severe asthma and proves to be innovative in the management of this type of patient.

Keywords: *Programme. Telemonitoring. Severe asthma.*

CO 063. THE EFFECTS OF BENRALIZUMAB ON STATIC LUNG VOLUMES AND AIRWAY RESISTANCE IN SEVERE EOSINOPHILIC ASTHMA: A REAL-WORLD STUDY IN PORTUGAL

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Introduction: Add-on biological therapies using monoclonal antibodies such as benralizumab (anti-IL-5R) are currently recommended by international guidelines to reduce exacerbations in severe eosinophilic asthma (SEA). Yet, few studies have assessed lung function related outcomes after the use of these therapies in SEA (i.e., patients with elevated blood/sputum eosinophil counts and airway inflammation). Our aim was to evaluate the effectiveness of benralizumab (approved by the European Medicine Agency since 2018) on lung volumes, air flow and airway resistance in SEA patients, 6 months after treatment initiation.
Methods: This is a real-world, observational, descriptive and multicentric study (Hospital Professor Fernando Fonseca and Hospital Santa Maria, Portugal), including a cohort of adult patients diagnosed with SEA, identified between January-June 2023. Data collected from medical records included demographics and disease characteristics. Spirometry and plethysmography were performed at baseline (T0) and after 6 months of treatment (T6) with benralizumab (30 mg dosing regimen) to assess: TLC (total lung capacity), RV (residual volume), FEV1 (forced expiratory volume in 1 second), FVC (forced vital capacity), mFEF25/75 (mean forced expiratory flow between 25% and 75% of FVC), ITGV (intrathoracic gas volume), Raw (airway respiratory resistance). Descriptive statistics with categorical variables were described as frequencies and continuous variables as mean and standard deviation (SD). Paired t-test and Cohen's d effect-size measure were calculated to compare the means of two measurements taken from the same individual and the standardized mean difference between groups (pre/post analysis) (d = 0.2 small, d = 0.5 medium, d = 0.8 large effect-sizes). Analyzes were performed in STATA/SE 15.1 (p-values below 5% considered statistically significant).
Results: Overall, 30 SEA patients were evaluated, mostly women (n = 18, 60.0%), with atopy (n = 22, 73.3%), mean age 58.4 years (SD 11.7), assisted by pulmonology (n = 19, 63.3%) or immunoallergology (n = 11, 36.7%) services. Mean eosinophilia at baseline was 1103.57 cells/l (SD 604.88; minimum-maximum 460-2400); after the use of benralizumab the count dropped to 0. Overall, lung function markedly improved during the study. After 6 months of treatment, significant increase ($p < 0.0001$) in FVC (15.3%), FEV1 (22.6%) and mFEF-25/75 (17.7%) were observed from baseline (Cohen's d between 0.77 to 1.10). ITGV, RV, RV/TLC and Raw significantly decreased ($p < 0.0001$) during the study period (-17.3%, -29.7%, -8.9%, 100.6%, respectively) (Cohen's d between -0.79 to -1.06). No differences in TLC measure between pre/post analysis were obtained ($p = 0.173$). No differences between sex were observed. Patients with more significant eosinophilia (> 900 cells/l; n = 15) presented better responses in FEV1 ($p = 0.001$) and mFEF-25/75 ($p = 0.007$).
Conclusions: The eosinophil depletion with add-on benralizumab led to significant improvements in SEA patients' respiratory function - namely static lung volumes, airflow and airway resistance, in real-life settings after 6 months. The significant deflating effect of benralizumab, exerted on the hyperinflated lungs of SEA patients, leads to a consequent amelioration of expiratory flow (increase FEV1 and mFEF-25/75) and air trapping (decreased RV/TLC). Taken together, our results suggest that the benralizumab

improves bronchial obstruction, lung hyperinflation and airway resistance. Further studies in a larger patient population are required to confirm these findings.

Keywords: *Eosinophilic severe asthma. T2 inflammation. Benralizumab. ANTI-IL5. Respiratory function.*

CO 064. BENRALIZUMAB EFFECTIVENESS IN PATIENTS WITH SEVERE EOSINOPHILIC ASTHMA, WITH AND WITHOUT CONCOMITANT CHRONIC RHINOSINUSITIS WITH NASAL POLYPS: THE BETREAT STUDY

Serviço Pneumologia, Centro Hospitalar e Universitário de Coimbra.

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Introduction: Severe eosinophilic asthma (SEA) in the presence of comorbid chronic rhinosinusitis with nasal polyps (CRSwNP) is usually more difficult to treat and control, with a more extensive eosinophilic inflammation. Benralizumab has shown to reduce exacerbations, oral corticosteroid (OCS) use and to improve asthma control for patients with SEA. However, real-world data on treatment response in patients previously with comorbid CRSwNP is lacking. This analysis from the BETREAT study aimed to describe the clinical outcomes with benralizumab in terms of asthma exacerbation, oral corticosteroid (OCS) use asthma control in patients with SEA with or without CRSwNP.
Methods: BETREAT is a multi-center, observational, retrospective study. In this analysis, patients with SEA were divided in two groups according to the presence or absence of CRSwNP. Baseline (12 months before index date) clinical and laboratory characteristics were collected prior to benralizumab treatment initiation (index date). Change in annualized exacerbation rate (AER), maintenance OCS (mOCS) use and asthma control (ACT and CARAT) were collected for both groups at 24-months follow-up.
Results: A total of 71 patients were included in the analysis, 22 (31.0%) with CRSwNP. At baseline, patients with CRSwNP had a higher median blood eosinophil count (900 vs 510 cells/µL, higher annual exacerbation rate and mOCS use. Mean baseline AER was 3.62 and 2.90 in patients with and without CRSwNP, reducing to 0.44 and 0.52, respectively, at 24-months (relative reduction [RR]: 87.8% and 82.1%). Most patients in both groups remained free of exacerbations until the 24-months follow-up, 59.1% of those with CRSwNP and 53.1% of patients without CRSwNP. The proportion of patients with mOCS use decreased from 63.6% at index to 40.0% at 24-months in patients with CRSwNP and from 44.9% to 24.5%, respectively, in patients without CRSwNP. Among patients using mOCS at baseline mean (SD) daily dose was 21.9 mg/day for patients with CRSwNP and 16.7 mg/day for patients without CRSwNP; for those patients still using mOCS at 24months, mOCS daily dose was 20.4 mg/day and 12.9 mg/day for patients with and without CRSwNP, respectively. Between the closest date to index and 24-months, the proportion of patients achieving symptom control according to ACT varied from 33.3% to 76.2% in patients with CRSwNP and from 9.1% to 60.6% in patients without CRSwNP. Within the same study period, the proportion of patients achieving symptom control according to CARAT varied from 0% to 47.4% in those with CRSwNP and from 12.5% to 66.7% in patients without CRSwNP.
Conclusions: Patients with SEA treated with benralizumab for up to 24 months experienced substantial improvements in AER, mOCS use and asthma control, regardless of the presence or absence of CRSwNP.

Keywords: *Severe eosinophilic asthma. Benralizumab. Chronic rhinosinusitis with nasal polyps. Real-world.*

CO 065. BENRALIZUMAB EFFECTIVENESS IN BIOLOGIC-NAÏVE AND BIOLOGIC-EXPERIENCED PATIENTS WITH SEVERE EOSINOPHILIC ASTHMA: THE BETREAT STUDY

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Introduction: Benralizumab has shown to reduce exacerbations, oral corticosteroid (OCS) use and to improve asthma control for patients with severe eosinophilic asthma (SEA). However, real-world data on treatment response in patients previously treated with other biologic therapies are scarce. This analysis from the BETREAT study aimed to describe the clinical outcomes with benralizumab in terms of asthma exacerbation, oral corticosteroid (OCS) use asthma control in patients with SEA with or without prior biologic use.
Methods: BETREAT is a multi-center, observational, retrospective study. In this analysis, patients with SEA were divided in two groups regarding their 12-months history of previous biologic therapy: biologic-naïve and biologic-experienced. Baseline (12 months before index date) clinical and laboratory characteristics were collected prior to benralizumab treatment initiation (index date). Change in annualized exacerbation rate (AER), maintenance OCS (mOCS) use and asthma control (ACT and CARAT) were collected for both groups at 24-months follow-up.
Results: A total of 73 patients were included in the analysis, 49 (67.1%) were biologic-naïve. The main cause for discontinuation of previous biologic was lack of efficacy (91.7%). The majority of patients were treated with either omalizumab (50.0%) or mepolizumab (45.8%). Mean baseline AER was 3.02 and 3.29 in biologic-naïve and -experienced patients, reducing to 0.39 and 0.69, respectively, at 24-months (relative reduction [RR]: 87.1% and 79.0%). Most patients remained free of exacerbations until the 24-months follow-up, 53.1% of biologic-naïve and 58.3% of biologic-experienced patients. The proportion of patients with mOCS use decreased from 44.9% at index to 14.6% at 24-months in biologic-naïve patients and from 58.3% to 52.2%, respectively, in biologic-experienced patients. Among patients using mOCS at baseline mean (SD) daily dose was 21.7 mg/day for biologic-naïve patients and 17.6 mg/day for -experienced patients; for those patients still using mOCS at 24-months, mOCS daily dose was 22.6 mg/day and 12.1 mg/day for biologic-naïve and -experienced patients, respectively. Between the closest date to index and 24-months, the proportion of patients achieving symptom control according to ACT varied from 26.7% to 77.1% in biologic-naïve patients and from 12.5% to 47.4% in biologic-experienced patients. 90.9% of biologic-naïve and 76.2% of biologic-experienced patients had an improvement in symptom control matching or exceeding the minimal clinically difference in ACT (3 units) from baseline to 24-months. Within the same study period, the proportion of patients achieving symptom control according to CARAT varied from 0% to 38.7% in biologic-naïve patients and from 20.0% to 45.0% in biologic-experienced patients. 55.6% and 66.7% of biologic-naïve and 76.2% of biologic experienced patients had an improvement in CARAT score 3 units from baseline to 24-months.
Conclusions: Both biologic-naïve and -experienced patients with SEA treated with benralizumab for up to 24 months had substantial improvements in AER, mOCS use and asthma control.

Keywords: *Severe eosinophilic asthma. Benralizumab. Real-world.*

CO 066. CLINICAL OUTCOMES IN SEVERE EOSINOPHILIC ASTHMA PATIENTS TREATED WITH BENRALIZUMAB IN REAL-WORLD SETTING: BETREAT STUDY

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Introduction: Benralizumab has been shown to reduce exacerbations, oral corticosteroid (OCS) use and to improve asthma control for patients with severe eosinophilic asthma (SEA). It is indicated as add-on maintenance treatment in adult patients with SEA inadequately controlled despite high-dosage inhaled corticosteroids plus long-acting -agonists. In-depth knowledge of real-world profile of patients with SEA being treated with benralizumab is needed. The BETREAT study aimed to describe demographic and clinical characteristics, background treatment patterns of SEA patients treated with benralizumab, and to assess clinical outcomes during up to 24-months follow-up after initiation of benralizumab.
Methods: BETREAT is a multi-center, observational, retrospective study. SEA patients aged > 18 years that were treated at 16 investigational sites and had their first benralizumab dose between July 2019 and October 2020 were included upon informed consent. Baseline (12 months before index date) clinical and laboratory characteristics were collected prior to benralizumab treatment initiation (index date). Change from index in exacerbations, maintenance OCS (mOCS) use and asthma control (ACT and CARAT) were assessed at 24-months follow-up.
Results: A total of 74 patients were included in the study, 73% were female. Most patients (75.0%) were diagnosed with asthma at 18 years of age or older. At least one comorbidity was reported in 91.9% of patients, with chronic rhinosinusitis with nasal polyps (29.7%), allergies (39.2%) and respiratory infections (35.1%) as the most frequent respiratory comorbidities. Obesity, hypertension and type 2 diabetes were present in 45.9%, 43.2% and 16.2% of patients, respectively. Mean blood eosinophil counts (BEC) (+SD) was 729.07 ± 651.81 x103 cells/L and the majority of patients (62.0%) had BEC above 400x103 cells/L. Most patients (89.2%) had at least one asthma-related exacerbation and the mean (SD) number of exacerbations per patient was 3.12 (2.20). The majority of patients (95.9%) had received ICS+LABA and half of patients received mOCS. Most patients (66%) were naïve to biological therapy. Of those with previous biologic experience, 50.0% received omalizumab and 45.8% mepolizumab. The main cause for discontinuation of previous biologic treatment was lack of clinical efficacy (91.7%). Overall treatment persistence with benralizumab was very high, with only one patient discontinuing treatment. Benralizumab treatment reduced mean (SD) annualized exacerbation to 1.00 (2.20) (relative reduction 85%) and most patients (61.6%) remained free of exacerbations until the 24-months follow-up. Considering patients with mOCS use at index (23.5%), 45.7% were no longer using mOCS at 24-months follow-up. Between the closest date to index and 24-months, the mean (SD) CARAT score varied between 15.1 (5.1) and 21.0 (6.1). The proportion of patients achieving symptom control according to CARAT varied from 4.3% to 40.4%. Within the same period, mean ACT (SD) varied between 12.9 (4.6) and 20.4 (4.1). The proportion of patients achieving symptom control according to ACT varied from 4.0% to 67.3%
Conclusions: In this real-world cohort of SEA treated with benralizumab there was a reduction in exacerbation rates, OCS use and led to clinically important improvements in PROs. This study complements available randomized trial evidence on the clinical outcomes with benralizumab in a high-risk, hard-to-treat, SEA patient population.

Keywords: *Severe eosinophilic asthma. Benralizumab. Real-world.*

CO 067. CLINICAL OUTCOMES IN SEVERE EOSINOPHILIC ASTHMA PATIENTS

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Introduction: Biological therapies have been changing paradigms around severe asthma treatment. Several studies showed benefits in forced expiratory volume in 1 second (FEV1) with different drugs. There is lack of evidence showing the impact on forced vital capacity (FVC), forced expiratory flow 25-75% (FEF25-75), airway resistance (reff), total lung capacity (TLC), residual volume (RV) and carbon monoxide diffusion capacity (DLCO).
Objectives: To determine the impact on lung functional after 6 and 12 months of biological therapy in patients with severe asthma.
Methods: Multicentric cross-sectional study, including patients from two hospitals followed up in a severe asthma consultation under biological therapy. Data were collected from the Asthma Control Test (ACT) questionnaire and lung function tests after 6 and 12 months of treatment. Results are presented as mean and standard deviation for a normal distribution; median and interquartile range for non-normal distribution. Comparison between continuous variables was performed using the paired t-test or the Wilcoxon test, respectively. Spearman Correlation was used to assess the correlation between variables.
Results: A total of 89 patients were included (under mepolizumab 47, omalizumab 32 and benralizumb 10), mean age 52 years (± 13), 80% female. Mean lung functional values before treatment were: FEV1 63% (± 22), FVC 82% (± 17), FEF25-75 27% (16-41), TLC 111% (± 15), RV 170% (± 128), Reff 203% (± 88), DLCO 82% (± 19), FeNO 33 ppb (14-64). After 6 months of treatment there was a statistically significant improvement in the values of FEV1 72% (± 24) ($p < 0.001$), FVC 88% (± 17) ($p = 0.003$), FEF25-75 43% (± 28) ($p = 0.005$) and airway resistance Reff 145% (± 54). In the remaining lung functional values there was no statistically significant improvement. After 12 months of treatment there was a statistically significant improvement for FEV1 71% (± 22) ($p < 0.001$), FVC 89% (± 17) ($p < 0.001$) and FEF25-75 44% (± 30) (< 0.001). There were no statistically significant differences between the lung functional assessment at 6 and 12 months of treatment. There were no statistically significant differences between the improvement in FEV1 or FVC and the different biological therapies. After 12 months of treatment the median improvement in FEV1 was 155 mL (-80 - 532) and in FVC 155 mL (-180 - 493). This lung functional improvement showed a statistically significant correlation with the median improvement in the ACT (9 (7-12)) ($p = 0.033$, = 0.287 and $p = 0.012$, = 0.338 respectively).
Conclusions: This study demonstrated that biological therapy improved FEV1, FVC, FEF25-75 and airway resistance values. The improvement of these parameters may contribute to symptomatic improvement. As shown in other studies, there was a statistically significant improvement after 6 months of treatment.

Keywords: *Biological therapies. Severe asthma. Lung function.*

CO 068. WHERE ARE THE SUPER-RESPONDERS IN SEVERE ASTHMA? – APPLICATION OF THE EXATO SCALE

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Introduction: In recent years, therapeutic offers for severe asthma have made it possible to aim for the so-called remission of the disease/status of superresponders. The standardization of the use of objective scales for this evaluation is a necessity. The EXATO scale, recently developed, is a tool available for this purpose. It is divided into 4 categories: no response, partial response, good response or complete response/superresponder and includes 4 vari-

ables: number of exacerbations, ACT, dose of systemic corticosteroid and FEV1. The FEOS score (FEV1, exacerbations, oral corticosteroids, symptoms score), which varies between 0 and 100, is another tool available to quantify this response.
Objectives: To identify asthmatics who are superresponders to biological therapy, using the EXATO scale, in a cohort of patients followed up in a functional unit for severe asthma and to verify its agreement with the FEOS score.
Methods: We analyzed 58 patients with at least 1 year of treatment with anti-IL5/IL5R and anti-IL4R. We applied the EXATO scale at 12 months of treatment and analyzed the change in the 4 variables that integrate it over 1 year, every 4 months, through hierarchical linear modelling. We also analyzed the concordance (association) between the EXATO scale and the FEOS score in the classification obtained at 12 months, using the chi-square and Cramer's V as an indicator of the effect size.
Results: There was a significant change over 1 year of treatment in all variables. We verified a significant decrease in the number of exacerbations (average of 0.82 exacerbations every 4 months), being more accentuated between 0 and 4 months. Significant linear increase in ACT (on average 1.02 every 4 months). Significant linear decrease in OCS dose (on average 0.64 every 4 months). Significant increase in FEV1 (on average 0.11 every 4 months) being more pronounced between 0 and 4 months. In the application of the EXATO scale at 12 months of treatment, of the 58 initial patients, 16 were excluded due to lack of data. Thus, of the 42 patients evaluated, 2% had no response, 2% had a partial response, 7% had a good response and 88% had a complete response. Attending the criteria for disease remission after 12 months of treatment, which includes the absence of symptoms (we considered ACT > 20) and exacerbations, stable pulmonary function and absence of systemic corticosteroids; we found that, of the patients classified as superresponders, 65% fulfilled these criteria. The chi-square indicated a significant association between the classifications obtained by the EXATO and FEOS scales, with this association having a large size (Cramer's V = 0.69), indicating strong agreement. We found that all patients with scores greater than 80 on the FEOS score were classified as superresponders on the EXATO scale, and that the majority of patients (75%) classified as superresponders on the EXATO scored more than 60 on the FEOS scale.
Conclusions: The EXATO score is a very informative and easy to use tool for evaluating the response to biological therapy, which makes it a useful tool to apply in clinical practice.

Keywords: *Severe asthma. Biologics. Super-responders. EXATO. FEOS.*

CO 069. IMPACT OF HOME ADMINISTRATION OF BIOLOGICALS ON SEVERE ASTHMA CONTROL: A REAL-LIFE STUDY

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Introduction: The Asthma Control Questionnaire (ACT) and Control of Allergic Rhinitis and Asthma Test (CARAT), along with a history of exacerbations, peripheral eosinophil count, and assessment of spirometric parameters, are widely used tools for monitoring disease control in asthma patients. The emergence of biological agents in severe asthma has led to promising results as targeted therapy in recent years. Despite being traditionally administered in a hospital setting, there has been a trend towards changing this paradigm. In fact, the safety and efficacy of subcutaneous self-administration at home for selected biological agents have been demonstrated by several studies.
Methods: A retrospective observational study was conducted based on the review of electronic medical records of all patients undergoing home self-administration of biological therapy for severe asthma or eosinophilic granulomatosis with polyangiitis (EGPA) at the Pulmonology and Immunology Department until August 2022. The results of ACT and CARAT questionnaires, respiratory functional tests, exacerbations, and peripheral eosinophil count were compared for 1 year and 6 months before and after the start of home biological administration. Repeated measures analysis was performed, and statistical significance was considered for $p < 0.05$.
Results: Thirty patients under biological treatment were identified, with 2 having EGPA and the remaining having severe asthma. Among them, 19 (63.3%) self-administered the therapy at home, with a median duration of 15.7 months (9.9-17.3) in this regimen. The mean age was 54 ± 10 years, and 15 (78.9%) were female. Twelve patients (63.2%) were on Mepolizumab, and the rest (n = 7, 36.8%) were on Benralizumab. Additionally, 4 (21.1%) were on systemic corticosteroids. Descriptive analysis of variables used to infer asthma control at the 4 time points (1 year before, 6 months before, 6 months after, and 1 year after transitioning to home biological administration). There were no statistically significant differences over time in CARAT score ($p = 0.202$) or ACT score ($p = 0.603$), peripheral eosinophil count ($p = 0.362$), FVC ($p = 0.124$), FEV1 ($p = 0.297$), FEV1/FVC ($p = 0.882$), and positive bronchodilation tests ($p = 0.392$). There was a statistically significant difference between the two groups in the exacerbation parameter, which was lower after home biological administration; however, the absolute number of exacerbations was low (between 0 and 1) in both groups.
Conclusions: The results suggest the non-inferiority of home biological therapy administration compared to hospital administration concerning asthma control. Despite the limitations of sample size and study design, these real-world results align with other published studies, emphasizing the effectiveness of this therapeutic regimen.

Keywords: *Asthma. Biologic agents. At-home treatment.*

CO 070. ALLERGY TO HYMENOPTERA – SENSITIZATION AND SYMPTOMATOLOGY BY INHALATION

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Introduction: Hymenoptera venom allergy affects 5% of the general population. For an IgE-dependent hypersensitivity reaction to occur, prior exposure is necessary, either directly through sting, or through antigenic exposure via inhalation or digestive route.
Objectives: To determine which are the predictors of the development of respiratory symptoms with the inhalation of hymenoptera antigens, in patients with allergy to these insects.
Methods: Observational retrospective cohort study, analyzing patients followed at the CHTMAD Immunoalergology Consultation for allergy to hymenoptera, from June 2020 to June 2021. Statistical analysis performed with SPSS Statistics25.
Results: 63 patients were included, 41 (65.1%) male, with a mean age of 41.5 ± 15.5 years. Fifty-one patients (80.9%) were beekeepers and 8 were farmers (12.7%). Seventeen patients were diagnosed with rhinosinusitis, 10 with asthma and 15 had a history of atopy. Fifty patients (79.4%) were followed for allergy to bee, 10 (15.9%) for allergy to wasp and the rest to poles. The most frequent symptoms with the sting were urticaria (76.2%; n = 48), pruritus (50.8%; n = 32) and angioedema (49.2%; n = 31). Respiratory symptoms such as dyspnea (66.7%; n = 42), wheezing (31.7%; n = 20), oropharyngeal tightness (25.4%; n = 16) and cough (23.8%; n = 15) were also common. With regard to previous reactions to the anaphylaxis episode, 42 patients (66.7%) had stinging symptoms: 35.7% (n = 15) with a mild local reaction, 9.5% (n = 4) with an exuberant local reaction and 54.7% (n = 23) with systemic reaction. Fifteen patients previously

had rhinitis (86.7%; n = 13), conjunctivitis (46.7%; n = 7), wheezing (33.3%; n = 5) and dyspnea (26.7%; n = 4), with the inhalation of hymenopteran antigens. Of these, only 5 presented symptoms with inhalational exposure, having never been stung before. It was found that patients who developed coughing (OR 6.64; p = 0.005) and wheezing (OR 3.17; p = 0.069) with the sting were more likely to experience symptoms with inhaled exposure to hymenoptera antigens. In addition, with inhalation exposure, beekeepers more frequently had respiratory symptoms (OR 13.81; p = 0.01) and asthmatics were more likely to develop wheezing (OR 11.54; p = 0.006) and dyspnea (OR 10.97; p = 0.001). At baseline, patients had a mean bee IgE of 26.0 ± 42.5 kU/L, wasp IgE 9.6 ± 19.1 kU/L and polystes IgE 8.5 ± 9.3 kU/L L. Patients who experienced symptoms with inhalation exposure had higher bee IgE values (p = 0.008).
Conclusions: Some patients developed an anaphylactic reaction the first time they were stung, having previously only presented respiratory symptoms (namely cough, wheezing and dyspnoea) with inhalation. It was found that beekeepers, asthmatics and patients who developed coughing and wheezing from a hymenopteran sting were more likely to experience respiratory symptoms from inhalational exposure. These patients also had higher levels of IgE at baseline, reflecting greater sensitization. This work demonstrates that inhalational exposure to hymenoptera should not be undervalued, both as a means of inducing allergy and as a triggering factor for symptoms in asthmatic patients.

Keywords: *Hymenoptera. Allergy. Anaphylaxis. Asthma.*

CO 071. MODEL OF CARE FOR SEVERE ASTHMA PATIENTS – AN EXPERT CONSENSUS RECOMMENDATIONS

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Introduction: Although the emergence of new models of care and biological drugs has enabled further tailored therapeutic approaches to patients with severe asthma (SA) – a heterogeneous chronic respiratory condition – more complex treatments require additional strategies to be effectively implemented in practice. Severe Asthma Multidisciplinary Units (SAMUs) are increasingly plea as value-added services for a person-centeredness management of SA as they allow the access to personalized multifaceted care approaches aiming at improving patients' outcomes. However, the development and unified implementation of SAMU is still challenging in several regions worldwide. Our aim was to evaluate the perception on the barriers and opportunities of SAMUs implementation among a wide range of clinical experts in Portugal.
Methods: This was designed as a 2-phase cross-sectional evaluations of a set of 16 evidence-based statements (previously defined by a scientific committee) that were assessed by experts in SA (pulmonologists, allergists, and a range of other clinical specialists). During each cross-sectional assessment, experts expressed their agreement with each statement in a 3-point Likert scale (1-'agree'; 3-'disagree'). Results of the first survey were shared with the participants, subjected to debate, and further scored by the panel during the second round. Descriptive statistics with categorical variables described as counts and frequencies were performed (STATA/SE 15.1).
Results: Overall, 101 experts (n = 44; 43.6% allergists, n = 44; 43.6% pulmonologists, n = 13; 12.9% other specialties), mostly attending physicians (n = 88; 87.1%) participated in the study. Less than half of them (n = 41; 40.6%) work in a SAMU or are members of the National Specialists in Severe Asthma Network (n = 44; 43.6%). Statements 1, 2, 9 and 16 - defining SAMU's goals and proposing a minimum set of implementation requirements following international protocols and recommendations to manage and properly registering patients - obtained full agreement (95%, 98%, 96% and 96% respectively) among participants. Nonetheless, around 11% of experts disagree that a SAMU can be created in any hospital center in Portugal (statement 3). Although most participants believe that a SAMU should have an organizational chart (statement 6; 97% consensual) and promote scientific advancement by engaging clinical trials (statement 15; 96%), the exact composition of the multidisciplinary team still seems controversial (disagreement of 9.2% and 6.2% in items 4 and 5, respectively). Yet, although experts agree that both clinical and humanistic outcomes should be evaluated by means of validated questionnaires (item 10; 95% agreement), debate on the access to complementary precision diagnostic tests or further interventional procedures for SA still exist (disagreement of 5.2% and 8.9% in statements 7 and 8, respectively). There are also some barriers regarding the implementation model of a SAMU and its performance/quality indicators (statement 13; disagreement 5.1%).
Conclusions: Experts in SA agreed on a minimum set of requirements for the standardization and optimization of SAMU in Portugal. However, challenges regarding the implementation of this management model, including the definition of a core of human and technical resources, needs to be addressed.

Keywords: *Severe asthma. Quality of care. Multidisciplinary care. Multidisciplinary units.*

CO 072. THE RELATIONSHIP BETWEEN BLOOD EOSINOPHILS AND PSYCHOPATHOLOGICAL SYMPTOMS IN ASTHMA PATIENTS

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Introduction: Asthma is a heterogeneous disease with a variety of clinical manifestations, including psychopathological ones, such as anxiety and depression, which may be associated with worse control of the disease. The objective of this work is to analyze the relationship between blood eosinophils and psychopathological symptoms in asthmatic patients.
Methods: The target population included adult patients with a confirmed asthma diagnosis followed up in a Pulmonology consultation at a tertiary hospital for at least 6 months. Asthma control was assessed using the Asthma Control Questionnaire (ACQ), while the level of blood eosinophils was determined within 7 days prior to the consultation. The assessment of psychopathological symptoms was performed using the Brief Symptom Inventory 18 (BSI 18), which assesses three dimensions of symptoms: anxiety, depression and somatization. Each subscale consists of six items and the score of each subscale is given by the sum of these items. The Global Severity Index corresponds to the general level of the individual's psychological distress and results from the sum of all items in the questionnaire.
Results: The sample included 93 patients, 29 with < 150 eosinophils/uL and 64 with > 150 eosinophils/uL.
Conclusions: Increased peripheral blood eosinophils in patients with asthma appear to be associated with more symptoms of anxiety and depression.

Keywords: *Asthma. Eosinophils. Psychopathological symptoms.*

CO 074. CYSTIC FIBROSIS – A CALL FOR NEW APPROACHES

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Introduction: Cystic fibrosis (CF) is an autosomal recessive disease caused by mutations in the cystic fibrosis transmembrane conduc-

tance regulator (CFTR) gene. More than 2,000 mutations have been reported worldwide, but not all of which have been proven to cause disease. The fact that most research is conducted in developed countries has made the molecular diagnosis of this disease difficult in individuals from under-developed countries, who are invariably underrepresented in the studies carried out.
Case reports: Case 1: 31 years old female patient originally from Sao Tome & Principe, presented with history of bronchiolitis requiring invasive mechanical ventilation (IMV) in childhood and recurrent respiratory infections in adulthood. She has diffuse varicose bronchiectasis, more pronunced in the upper lobes, and chronic methicillin-susceptible *Staphylococcus aureus* (MSSA) infection. There is no evidence of gastrointestinal affection. These clinical conditions lead to chronic obstructive pulmonary syndrome (FEV1 41%). Due to frequent exacerbations, she is under azithromycin and inhaled antibiotics with colistimethate sodium and tobramycin. The diagnosis of CF was made at the age of 26 after a positive sweat test (ST) (63 mmol/L). However, the extended genetic study identified merely one disease-causing mutation [2307insA], with contradictory data in the literature regarding the rest. Case 2: 36 years old male patient, African descendant, with a history of poor weight status progression and steatorrhea since childhood. The hypothesis of CF was raised at the age of 28 after hospitalization for a respiratory infection that led to the performance of ST (116 mmol/L) and subsequent genetic evaluation. Nevertheless, it was only possible to identify a mutation in one of the alleles [F508del]. Additionally, patient suffers from exocrine pancreatic insuficiency (EPI), CF-associated liver disease and central cylindrical bronchiectasis with chronic *Pseudomonas aeruginosa* (PSAE) infection. He is currently on inhaled tobramycin and aztreonam and azithromycin due to frequent exacerbations. In spite of therapeutic measures, he maintains a poor nutritional status (BMI 16 kg/m^2) and severe respiratory obstruction in the functional assessment (FEV1 48%). Case 3: 23 years old female patient, born in Cape Verde, with recurrent pancreatitis and respiratory infections since childhood. The diagnosis of CF was assumed at 13 years of age after positive ST (120 mmol/L) and genetic assessment with only one disease-causing mutation [R334W/(TG)10]. She has EPI, CF-related diabetes (CFRD) and bilateral varicose bronchiectasis (more prominent in the apical segments) with chronic pulmonary infection to PSAE and methicillin-resistant *Staphylococcus aureus* (MRSA). Samples with *Burkholderia cepacea* are also described in the past. Functionally, she presents a moderately severe obstructive syndrome (FEV1 56%). She is currently under CSI and with all other medical therapy optimized.
Conclusions: An inconclusive genetic study does not exclude the diagnosis of CF. These cases highlight the importance of characterizing the CFTR mutational spectrum and the adjustment of molecular testing according to ethinicity and geographical origin of population. The access to health care remains one of the main determinants of the prognosis of this disease. In the future, the issue of eligibility for CFTR modulators will be discussed due to the increasingly frequent presence of “rare mutations”.

Keywords: *Cystic fibrosis. Genetics. Under-developed countries.*

CO 075. DEPRESSION AND ANXIETY IN CYSTIC FIBROSIS – A RETROSPECTIVE STUDY

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Centro Hospitalar Barreiro Montijo.

Introduction: Studies have shown that patients with cystic fibrosis (CF) have a high prevalence of anxiety and depression. However, the results vary according to the methods used and the location of the studies.
Objectives: We aimed to determine the prevalence of depression and anxiety in the adult population with CF in the south of Portugal (regions of Lisbon and Vale do Tejo, Alentejo and Algarve).
Methods: A retrospective study was carried out in a Portuguese CF Reference Center. Depressive and anxious symptoms were assessed using questionnaires that patients completed during visits to the center: Patient Health Questionnaire 9 (PHQ-9) and Generalized Anxiety Disorder 7 (GAD-7). Additional information on age, sex, genotype and therapy was obtained by consulting the clinical file. Statistical analysis was performed using the SPSS IBM® program, Version 29.
Results: Forty-nine patients were evaluated from March 2022 to January 2023. They had a mean age of 32 ± 11 years, with a slight predominance of females (51%). Forty-two patients (86%) had the F508del mutation, 13 of which were homozygous. Twenty-eight patients (57%) were medicated with Elexacaftor/Tezacaftor/Ivacaftor (ELX/TEZ/IVA). Twenty patients (41%) had scores consistent with anxiety on the GAD-7. Of these, 80% had mild anxiety and 20% moderate. In the PHQ-9, 17 cases of depression (35%) were detected, of which 65% were mild depression, 23% moderate, 6% moderately severe and 6% severe. It was also found that the PHQ-9 score was significantly lower in the group of patients under ELX/TEZ/IVA ($p < .05$), with no differences observed on the GAD-7. There were also no differences in questionnaire scores between genders.
Conclusions: In this study, a high prevalence of anxiety and depression was observed in patients with CF. Patients under ELX/TEZ/IVA had less depressive symptoms than the rest, which is possibly due to the improvement in the respiratory manifestations of the underlying disease. The diagnosis, treatment and psychological approach to mental illness are fundamental in the population with CF, given the prognostic value and impact on quality of life. Our small sample and the retrospective nature of the study prevent the generalization of these results, requiring more research on anxiety and depression in CF, as well as on the possible effect of the new CFTR modulators.

Keywords: *Cystic fibrosis. Depression. Anxiety. CFTR modulators.*

CO 076. THE IMPACT OF CFTR MODULATORS ON SUBFERTILITY IN WOMEN WITH CYSTIC FIBROSIS

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Introduction: In recent decades, due to advances in therapies, there has been an increase in life expectancy and quality of life of patients with Cystic Fibrosis (CF). With this, fertility became a frequent concern in these patients. CFTR (Cystic Fibrosis Transmembrane Regulator) modulator therapies show promising results in improving lung disease; however, there are still few data about its impact on fertility and the safety of its use in pregnancy.
Methods: Sixteen female patients aged over 18 years are being followed up at the Reference Center for CF at the Centro Hospitalar e Universitário de Coimbra, 8 of which have experienced pregnancy. Two women became pregnant naturally prior to the diagnosis of CF. Three patients became pregnant without treatment with CFTR modulators, one naturally and two using assisted reproductive thecnologies. The remaining pregnancies occurred under therapy with CFTR modulators. One of the patients had two pregnancies: one using assisted reproductive technologies, prior to therapy with modulators and another conceived naturally already under ivacaftor/tezacaftor/elexacaftor. The remaining three patients also became pregnant naturally after starting treatment with ivacaftor/tezacaftor/elexacaftor. None of the patients used contraceptive methods prior to pregnancy.
Results: Of the total of 9 pregnancies, one is still ongoing, without complications so far. Of the 8 completed pregnancies, no relevant

complications related to CF were recorded during pregnancy or delivery and the babies were born healthy even in the case of patients who became pregnant under therapy with CFTR modulators, who chose to maintain treatment. The patients maintained FEV1 stability and did not experience severe exacerbations or that required hospitalization.
Conclusions: The use of CFTR modulators appears to benefit fertility in patients with CF. However, the mechanisms by which it affects fertility are still unknown, making it relevant to advise these patients on family planning and contraception. In addition, there is no information regarding the safety of its use during pregnancy and breastfeeding, the challenging decision of whether or not to maintain therapy with CFTR modulators in these phases remains up to the patient and the attending physician.

Keywords: *Cystic fibrosis. Fertility. CFTR modulator therapies.*

CO 077. IMPACT OF CFTR MODULATORS THERAPIES IN ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS

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Introduction: Cystic fibrosis (CF) is a genetic disease caused by mutations in the gene that encodes the protein Cystic Fibrosis Transmembrane Regulator (CFTR), an epithelial ion channel involved in the transport of chloride and bicarbonate on the surface of cells, regulating salt and water balance. Its absence/dysfunction results in the dehydration of secretions, translating into a multisystemic disease, which manifests itself at the pulmonary level by bronchiectasis, secondary to chronic inflammation and infection. Although the predominant microorganisms in the airways are bacteria, fungi play a major role in the progression of lung disease, with Aspergillus fumigatus being the most frequently isolated. Allergic Bronchopulmonary Aspergillosis (ABPA) is a hypersensitivity response, mediated by Th2 and IgE, to Aspergillus fumigatus. CFTR modulators have revolutionized disease progression by mproving/normalizing CFTR expression, function and stability.
Case reports: We present the cases of 5 patients with CF and history of ABPA, three males. The mean age is 27.0 ± 9.3 years and the mean age at diagnosis was 14 ± 8.2 years. The average value of the sweat test was 102.0 ± 20.1 mmol/L. Regarding the genetic study, 3 patients had delF508/delF508, one had delF508/R334W and finally, one patient had G542X/G85E. The mean number of ABPA episodes was 3.0 ± 1.3, and were treated with corticosteroid therapy, some cases with itraconazole/voriconazole, and one case with inhaled amphotericin and omalizumab. The 5 patients started triple modulator therapy with ivacaftor/tezacaftor/elexacaftor (ELZ/TEZ/IVA), a mean of 19 ± 5.3 months ago. The mean values of immunoglobulins (Ig) prior to the start of ELZ/TEZ/IVA were: total IgE 411.0 ± 235.7 kU/L, Aspergillus fumigatus IgE 3.7 ± 2.6 kU/L, Aspergillus fumigatus IgG 102.0 ± 70.8 mgA/L. The average of the highest value of total IgE that the patients presented, prior to the beginning of ELZ/TEZ/IVA, was 826.0 ± 1,127.6 kU/L. At the start of modulator therapy, only one patient was under therapy for ABPA, having discontinued inhaled amphotericin 3 months after starting ELZ/TEZ/IVA and corticosteroids after 6 months. After starting ELZ/TEZ/IVA, the average values of the Igs were: total IgE 76.0 ± 127.6 kU/L, Aspergillus fumigatus IgE 3.5 ± 2.3 kU/L, Aspergillus fumigatus IgG 60.1 ± 46.8 mgA/L. The mean value of eosinophils was 237.0 ± 178.6/L and 200.0 ± 98.0/L, before and after starting the modulator therapy, respectively. Three patients presented isolation of Aspergillus fumigatus in the microbiological examination of sputum, with an average of 5 ± 1.7 isolations. After starting the ELZ/TEZ/IVA, 3 isolations were obtained from only one patient. The patients are stable, with no further episodes of ABPA or any targeted therapy.
Discussion: CF treatment with CFTR modulators had revolutionized the disease phenotype. Despite studies demonstrating that these therapies are associated with significant changes in the airway microbiome, it is still unknown what is their impact on microbial colonization rates, namely colonization by Aspergillus fumigatus, and consequently on ABPA. In the patients presented, the initiation of ELZ/TEZ/IVA led to a decrease in total IgE and Aspergillus fumigatus IgE and IgG and the absence of new episodes of ABPA, probably due to the improvement in mucociliary clearance and the eventual attenuation of the immune response to microorganisms.

Keywords: *Cystic fibrosis.* Aspergillus fumigatus. *Allergic bronchopulmonary aspergillosis. CFTR modulator therapy.*

CO 078. INCIDENCE AND CASE FATALITY RATES OF ADULTS HOSPITALISED WITH INVASIVE PNEUMOCOCCAL DISEASE IN PORTUGAL, 2017-2018 – THE SPHERE STUDY

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Introduction and objectives: Invasive pneumococcal disease (IPD), caused by *Streptococcus pneumoniae*, is the most severe form of pneumococcal disease, primarily affecting children < 5 years and adults 65 years. All forms of this disease have a significant morbidity and mortality, and vaccination is considered the primary intervention to reduce them. This study aimed to determine the incidence and fatality rates for IPD among hospitalized adult patients in mainland Portugal.
Methods: This was a retrospective, multicentric, and cross-sectional study based on secondary data collection from electronic hospital databases of 7 centers in mainland Portugal. The study included adult patients (18 years old) hospitalized with IPD between 2017-2018.
Results: A total of 395 adult patients were included in the study, with a majority being male (61.8%) and aged 65 years (55.4%). Among the participants, 26.3% were current smokers and 17.4% heavy alcohol consumers. Majority of patients (72.2%) had at least one medical condition of interest, namely chronic cardiac disease (27.1%), diabetes mellitus (25.6%), and chronic respiratory disease (20.5%). Bacteremic pneumonia was the most frequent clinical manifestation of invasive infection (80.0%). *S. pneumoniae* serotype information was not available for any patient. Vaccination status was unknown in 64.3% of individuals, while only 4.8% of total had been vaccinated against *S. pneumoniae*. The average length of hospitalizations was 16.8 ± 18.7 days, with 95 patients (24.1%) requiring intensive care unit (ICU), for an average of 11.0 ± 11.0 days. Global mortality during hospital stay was 16.5%, and was more probable in patients who required ICU admission (36.8%). Overall, the global incidence rate of IPD was found to be 0.93 cases per 1,000 hospitalized adults, with a global case fatality rate of 16.5 deaths per 100 hospitalized adults with IPD.
Conclusions: This study provides real-world evidence on the incidence and fatality rates of IPD in mainland Portugal as reflected in the number of hospitalizations, ICU admissions, length of stay and mortality and emphasizes the need for effective management strategies. This data highlights the need for increased vaccination coverage, especially among those 65 years, and the identification of S. pneumoniae serotypes.

Keywords: *Invasive pneumococcal disease. Incidence rate. Case fatality rate. Vaccination.*

CO 079. A RARE CAUSE OF BRONCHIECTASIS: THE SENIOR-LKEN SYNDROME

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Introduction: Senior-Lken syndrome is a rare autosomal recessive genetic disorder belonging to the group of ciliopathies and affects 1 in 1,000,000 individuals. Currently, less than ten cases are described in the literature. Eyes and kidneys are the most affected organs, with retinitis pigmentosa or Leber congenital amaurosis, and nephronophthisis, respectively.
Case report: A 61-year-old woman referred to the bronchiectasis outpatient appointment for diffuse cylindrical and varicose bronchiectasis. Since her 20's, she complained of nyctalopia and progressive decrease of visual acuity, and was diagnosed with pigmentary retinopathy. At the same time she had bilateral otosclerosis, surgically approached. She also has a history of chronic kidney disease since 34 years-old with unknown etiology, under hemodialysis and in active list for kidney transplant since 54 years-old. Other medical history included arterial hypertension, valvular cardiopathy and more recently a monoclonal gammopathy of undetermined significance. Familiar antecedents were irrelevant. A genetic study identified a c.397G > T p.(Glu133*) variant, probably homozygous in the SDCC4G8 gene, and the diagnosis of Senior-Lken Syndrome was established. Regarding respiratory history, two years ago she had a hospital admission for haemoptysis, and infected bronchiectasis were diagnosed. Bronchofibroscopy revealed a blood clot in the medium lobar bronchium and susceptible Escherichia coli and the filamentous fungi *Paecilomyces variottii* were identified in the bronchial aspirate. The cytologic exam was negative for neoplastic cells. These findings together with a consolidative image in the angiography CT scan were suspicious for a pulmonary mycetoma, and treatment with itraconazole was performed. Since then the patient is stable with respiratory secretions controlled, under respiratory kinesitherapy, and without new episodes of haemoptysis.
Discussion: So far, there are no reports of meaningful bronchiectasis in patients with Senior-Lken syndrome. In fact, ciliopathies are a possible cause of bronchiectasis. Although primary ciliary dyskinesia is the most common ciliopathy, other syndromes that impair ciliary function are described, including Senior-Lken syndrome. As a direct consequence, these individuals at more prone to severe respiratory infections due to the impairment of airway clearance mechanisms. Thus, respiratory involvement, namely bronchiectasis, in a patient with kidney and ocular involvement in a context of the rare Senior-Lken syndrome must be investigated.

Keywords: *Senior-Lken syndrome. Ciliopathy. Bronchiectasis. Hemoptysis.*

CO 080. CHARACTERIZATION OF THE BRONCHIECTASIS CONSULTATION AT CENTRO HOSPITALAR DE LEIRIA FOR 6 MONTHS.

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Centro Hospitalar de Leiria.

Introduction: Bronchiectasis is a chronic lung disease characterized by abnormal and irreversible bronchial dilation, leading to chronic inflammation and long-term impairment of respiratory function. The etiology of bronchiectasis includes chronic respiratory infections such as pneumonia and tuberculosis, hereditary diseases, as well as other conditions like autoimmune and congenital respiratory tract disorders. Risk factors include smoking, immunodeficiencies, gastroesophageal reflux, aspiration, among others. In Portugal, there has been an increase in the incidence and prevalence of this condition in recent years, affecting all age groups. The Bronchiectasis consultation is conducted by Pulmonologists, and it is not universally available in all hospitals. This consultation is essential for managing a disease that often arises in the context of multiple pathologies. The following is a casuistic report of the Bronchiectasis consultation at the Pulmonology Service of Centro Hospitalar de Leiria for the period from January to June 2023, including patient characteristics such as gender, age, medical history, risk factors, etiology of bronchiectasis, microbiology, number of exacerbations, instituted therapy, and influenza and pneumococcal vaccination. Data were collected from patients' medical records and analyzed using Microsoft Excel.
Methods: A total of 116 patients were observed, comprising 54 men and 62 women. The average age was 56 years. The majority of patients, around 31% (36), were in the age group of 61 to 70 years. It is worth noting that 4.3% (5) of the patients were in the age group of 18 to 30 years. On average, patients had 2 consultations per year. Out of the 116 patients analyzed, 25 (21.6%) were former smokers, and 7 (6%) were active smokers, with an average packyears of 25.3. Regarding medical history, asthma and COPD were the most prevalent, with 30.1% (35) having asthma and 14.7% (17) having COPD. Some isolated important medical histories were also noted, such as severe asthma under immunomodulator therapy, Scimitar Syndrome, poliomyelitis, Trisomy of chromosome 14, among others. The 116 patients were also evaluated for their lung function based on the most recent spirometry results. The analyzed data showed an average FEV1 of 68%, an average FVC1 of 82.3%, and an average Tiffeneau index of 64.4%.
Results: From the analysis, it was found that the most common etiology is post-infectious, representing 56.9% of the patients, of which 36.4% were cases of bronchiectasis following Mycobacterium tuberculosis infection. The second most common etiology is idiopathic, representing 36.2% of the analyzed patients. In recent sputum culture, the most frequently isolated microorganisms were *Pseudomonas aeruginosa*, representing 17.2% of the patients, *Haemophilus influenzae*, 11.2% of the patients, and *Staphylococcus aureus*, 5.2% of the patients. Patients were also analyzed regarding their chronic therapy, with 3.4% of them using inhaled Colistin, and 8.6% using Azithromycin. The number of exacerbations per year, antibiotic therapy used during exacerbation, and immunizations were also studied.

Keywords: *Bronchiectasis. Consultation. Colonization.*

CO 081. RELATIONSHIP BETWEEN FLAME RETARDANTS AND RESPIRATORY HEALTH- A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

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Introduction: Chronic respiratory diseases are a dealing cause of death and disability worldwide. Their prevalence is steadily increasing and the exposure to environmental contaminants, in which Flame Retardants (FR) are included, is being considered as a possible risk factor. Despite the widespread and continuous exposure to FRs, the role of these contaminants in chronic respiratory diseases is yet not clear. This study aims to systematically review the association between the exposure to FR and chronic respiratory diseases.
Methods: Searches were performed using the Cochrane Library, MEDLINE, EMBASE, PUBMED, SCOPUS, ISI Web of Science (Science and Social Science Index), WHO Global Health Library and CINAHL EBSCO. Analytical, observational, and epidemiological studies (cohort, case-control, and cross-sectional studies) reporting associa-

tions between chronic respiratory diseases and different types of FR or their metabolites quantified in environmental or biological matrices were included. Random-effects meta-analysis were used to summarise the numerical effect estimates.
Results: Among the initial 351 articles found, only 7 fulfilled the inclusion criteria and were included (5 cross-sectional and 2 cohort studies). No statistically significant increase in the risk for chronic respiratory diseases with exposure to FR was found and therefore there is not enough evidence to support that FRs pose a significantly higher risk for the development or worsening of respiratory diseases. However, a non-significant trend for potential hazard was found for asthma and rhinitis/rhinoconjunctivitis, particularly considering urinary organophosphorus FRs (PFR) including TNBP, TPHP, TCEP and TCIPP congeners/compounds. Most studies showed a predominance of moderate risk of bias, therefore the global strength of the evidence is low.
Conclusions: The limitations of the studies here reviewed, and the potential hazardous effects herein identified highlights the need for good quality large-scale cohort studies in which biomarkers of exposure should be quantified in biological samples.

Keywords: *Flame retardants. PBDES. Organophosphorus flame retardants. Respiratory diseases. Asthma. COPD. Rhinitis. Rhinoconjunctivitis.*

CO 082. KNOWLEDGE, BELIEFS AND ATTITUDES ABOUT ELECTRONIC CIGARETTE USE IN PEOPLE UP TO 40 YEARS OLD

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Introduction: According to the World Health Organization (WHO) eight million deaths are caused by smoking annually. Electronic smoking devices (ESDs) are the new face of the smoking epidemic among young people in Brazil and other countries. Therefore, it is necessary to understand their beliefs, knowledge and their consumption pattern, to promote effective preventive public policies.
Objectives: To understand the behaviors involved in the use of ESDs. In addition, we sought to identify consumption patterns, associated behaviors and identify current beliefs about these products.
Methods: Qualitative research on the knowledge/use of electronic cigarettes, made available online through Google Docs and disseminated mainly among university students at UFOP, with completion stimulated in person and by varied online interactions. An attempt was made to apply it on both sides of the Atlantic in the expectation of being able to contrast possible differences, but the summer vacations in Portugal made it difficult to obtain more responses.
Results: 900 people responded, 9 of them in Portugal. Most (75.1%) were aged 17-24 years, another 25.9% were aged 25-39 years. Among the participants, 53.8% were women and 45.8% men. Of these, 58.6% are white, 29.7% brown, 10.7% black and 1% yellow. In addition, 9.7% have literacy (1st degree or 2nd degree), 74.7% incomplete higher education, 15.5% complete higher education or postgraduate degree. Of the respondents, 44.5% are current smokers or have smoked various products at some time. Among current smokers, 37% are daily users and 43.2% non-daily users. 15% of ESDs users made daily use of the product. In addition, 47.4% said they had used ESDs before. 29% acquired them at social events and 20.2% through WhatsApp. Regarding the frequency of use, 68% answered that they only use ESDs when using alcohol. 52.3% believe that it does more harm than the common white cigarette. In addition, 3.5% answered that ESDs do not have nicotine, while 96.5% believe that they do. About 78.2% of respondents answered ''yes'' or ''maybe'' if they would like to quit smoking, with the top three products of interest in quitting being the straw cigarette (59.2%), the electronic cigarette (35.3%) and the regular cigarette (23.1%). 13.6% of respondents claimed to have already tried to quit smoking ESDs without success, with 44.7% having made one attempt and 55.3% having tried two or more times. **Conclusions:** The prohibited commercialization of ESDs by Anvisa in Brazil does not prevent their utilization in the country. Although a little more than half of the participants believe that the electronic cigarette is more harmful than the common one, its use still occurs. A significant number of people stated that they only use this device with the consumption of alcoholic beverages and a relevant portion of the participants showed interest and registered difficulty in stopping using ESDs. It is of great relevance to understand the beliefs and motivations involved in the use of ESDs, for the elaboration of preventive campaigns and other effective actions.

Keywords: *Electronic cigarettes. Smoking. Nicotism. Young.*

CO 083. THE PRESS DEBATE FOLLOWING THE ANNOUNCEMENT OF THE PORTUGUESE NEW TOBACCO BILL: A DESCRIPTIVE AND THEMATIC ANALYSIS

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Introduction and objectives: The World Health Organization (WHO) emphasizes that the tobacco industry (TI) is the vector of the pandemic, through marketing, advertising and promotion strategies, in addition to interfering/obstructing tobacco control policies. The solution to reduce the impact of this pandemic is not in the health sector, but in the political will to implement multisectoral public prevention policies, aligned with the WHO Framework Convention on Tobacco Control (FCTC). It also requires civil society activism with governments and policymakers. In May/2023, the Ministry of Health (MoH) announced a proposed Tobacco Law comprising: 1) extension of smoke-free policies to outdoor environments and all enclosed public spaces (tobacco + vaping); 2) reinforcement of the ban on TI advertising, promotion and sponsorship; 3) restriction of tobacco supply at points of sale and vending machines, ban on tobacco sales and vaping at music and youth festivals; 4) transposition of the European Directive on heated tobacco, banning flavors, additives and mandating health warnings with text and image. After the press release, a media debate ensued. The Government backed down, removing some measures, especially the supply restriction, and added exceptions and moratoria. In order to identify the various actors and their discourses, a narrative and thematic analysis was conducted.
Results: The actors identified were journalists, parliamentary deputies, minister of health and secretary of state for health promotion, health professionals, mainly physicians, business associations and IT. The predominant discourse was one of controversy and opposition to the law. Journalists defended smokers' right to free choice and freedom, criticizing the intervention of an ultra-protective state. Some parliamentarians criticized the measures to restrict the supply and extend smoking environments to outdoor spaces, calling them "excessively prohibitionist", "abusive and intrusive" or "too restrictive"; and also opposing the regulation of heated tobacco by calling for a "harm reduction" strategy. In addition, they justified it with legal principles such as violation of the right to liberty and proportionality. Business associations (tobacco retailers, restaurants) strongly opposed, claiming possible economic losses and increased tobacco smuggling. The same arguments were used by IT, which asked to be involved in the political nego-

tiation of the law. Health professionals defended the proposed measures, elucidating the public health evidence supporting them and warning of TI interference, either in opinion articles or quoted and/or interviewed in articles written by journalists. The MoH justified the rollback of the law with economic arguments and equitable access to tobacco products, failing to exercise its duty to educate society and policymakers about the public health evidence.
Conclusions: Opposition to the law was the winning discourse. The arguments used and some of the actors are identified by researchers as discourse/groups allied to IT. These findings and the Government's backtracking by weakening and delaying the legislation constitute a clear violation of FCTC Article 5.3.

***Keywords**: Tobacco control. Public health. Tobacco industry.*

CO 084. COMPARATIVE EVALUATION OF POST-OPERATORY LUNG FUNCTION AFTER ROBOTIC AND VATS ANATOMIC RESSECTIONS

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Objectives: One of the goals of lung anatomic resections (segmentectomy or lobectomy) performed with minimally invasive techniques, either robotic (RATS) or thoracoscopic (VATS), is to allow patients a better recovery from their procedure, with less pain, less time with chest tubes, better recovery of lung function and therefore a faster return to active life. We aim to compare lung function tests, before and after surgery, of patients submitted to anatomic ressections performed by RATS and VATS.
Methods: Our 7-year experience, from June 2016 until June 2023, with RATS was 156 surgeries, 132 of them were lung surgery We retrospectively analised lung function tests, pre-operative and at 3 months post-op, of 45 patients submitted to anatomic resections (25 segmentectomies and 20 lobectomies) by RATS. We then compared the actual values with the predicted post operative values for the procedures in question. This population was then compared with 50 anatomic resections (31 segmentectomies and 19 lobectomies) performed by VATS, in the same period, at our institution. Statistical analysis, was performed with STATA 16.
Results: The mean baseline and post-op values of FEV1, DLCO, TLC and FVC in our RATS and VATS group were not significantly different. When comparing the mean post operatory values of FEV1 and DLCO with the Predicted Post-operative (PPO) they were in both groups better that the expected values, but no difference was shown between the two surgical approaches.
Conclusions: Both minimally invasive approaches have shown similar results in post-operative lung function at 3 months and in both cases results are better that the ones predicted by the formulas used to calculate the PPO values.

***Keywords**: Robotic surgery. Rats. Lung function. Anatomical resections.*

CO 085. SURGICAL APPROACH TO THORACIC ENDOMETRIOSIS: A 10-YEAR RETROSPECTIVE ANALYSIS IN A CENTRAL HOSPITAL

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Introduction: Thoracic endometriosis is defined by the presence of endometrial tissue in the lung or pleura and can manifest clinically by pneumothorax (more frequently), hemothorax or catamenial hemoptysis. It appears mostly in the right hemithorax. Histopathology of a biopsy lesion during menstruation is the gold standard for diagnosis. The combination of hormonal and surgical treatment is a therapeutic option for this pathology in order to prevent recurrence.
Objectives and methods: The objective of this study is to characterize patients diagnosed with thoracic endometriosis undergoing surgical treatment. This is a retrospective analysis of the last ten years of patients operated on at the Department of Thoracic Surgery at Hospital de Santa Marta. Data were obtained from clinical files.
Results: Over the last ten years, fifteen patients with thoracic endometriosis underwent surgical treatment, all female, with a mean age of 37.4 years (26 - 48 years). The main antecedents were diagnosed endometriosis (46.7%, n = 7), smoking habits (26.7%) and previously treated pulmonary tuberculosis (13.3%, n = 2). Thoracic endometriosis manifested itself through pneumothorax in 86.7% (n = 13) and hemothorax in 13.3% (n = 2) of patients, occurring on the right in all cases (100%, n = 15). With regard to surgical treatment, all patients underwent video-assisted thoracoscopic surgery (VATS); regarding pneumothorax, 92.3% (n = 12) underwent pleurodesis, 92.3% (n = 12) atypical pulmonary resection (APR), 38.5% (n = 5) pleurectomy, 23.1% (n = 3) pleural biopsy, 23.1% (n = 3) diaphragmatic implant biopsy and 7.7% (n = 1) diaphragmatic orifice repair; in the case of hemothorax, 50% (n = 1) underwent decortication and 50% (n = 1) pleural biopsy, RAP and pleurodesis. The main surgical findings were diaphragmatic fenestrations in 73.3% (n = 11), pleural implants in 26.7% (n = 4) and diaphragmatic implants in 20% (n = 3) of the cases. As for histology, only 20% (n = 3) of the samples collected during surgery showed the presence of endometriosis. In the postoperative period, the mean time under thoracic drainage was 4.2 days and the mean hospital stay was 8.3 days. Of the patients submitted to surgery, 33.3% (n = 5) relapsed, of these 60% (n = 3) operated on in our center and the remaining 40% (n = 2) operated on in other hospitals, being later re-operated on in our center, no evidence of new recurrence to date; the median time to relapse was 2.6 years (5 months - 6 years); Of these patients who relapsed, 20% (n = 1) were on hormone therapy, while the remaining 80% (n = 4) had discontinued it.
Conclusions: In this analysis, it was found that thoracic endometriosis is an entity that appears in women of reproductive age. The VATS approach allows not only the diagnosis but also the treatment of this pathology. It was verified that the histological diagnosis is not always possible, in which case it can be presumed based on the anamnesis, imaging and visualization of the endometrial lesions, highlighting the diaphragmatic fenestrations. The combination of surgical treatment and hormone therapy prevents recurrence, and the latter should not be discontinued.

***Keywords**: Thoracic endometriosis. Catamenial pneumothorax. Catamenial hemothorax.*

CO 086. EXTRACORPOREAL MEMBRANE OXYGENATION AS A BRIDGE TO LUNG TRANSPLANTATION – OUTCOMES OF THE PORTUGUESE TRANSPLANTATION CENTER

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Introduction: Lung transplantation (LTx) is a final treatment option for end-stage lung disease under optimized medical therapy. The

increasing number of procedures allowed a temporal division into ERA1 (2001-2015) with less than 25 transplants/year and ERA2 (2016-2023) with more than 25 transplants/year. Extracorporeal Membrane Oxygenation (ECMO) is a technique with concurrent growing use for pre-transplant support. This study aims to analyze survival outcomes and outcomes in patients undergoing LTx with ECMO as a bridge.
Methods: From June 2001 to January 2023, 355 lung transplants were performed. Twenty-one of these patients had ECMO support as a bridge to transplantation. Eight (38%) were male and 13 (62%) female, with a mean age of 41.5 years (minimum 13; maximum 60). Diagnoses included: interstitial lung disease (52.4%); cystic fibrosis (CF) (14.3%); non-CF bronchiectasis (9.5%); ARDS due to COVID-19 infection (9.5%) and lung re-transplantation (14.3%). Eighteen patients underwent bilateral transplantation, one both bilateral and renal and two unilateral. All were adapted to VV ECMO, with a mean duration of 34 days (minimum 3; maximum 203), with 3 admitted in pre-LTx list already under ECMO. Eleven were switched to VA intraoperatively and three left the operating room without ECMO support.
Results: Of the 21 patients, nine cases of primary graft dysfunction (PGD) and five cases of acute rejection were observed in the immediate postoperative period. During this period, thoracic complications occurred in 17 patients, the most prevalent being atrial fibrillation (33%) and hemothorax (24%). Extra-thoracic complications were identified in 18 patients, the most common being iatrogenic leukopenia and acute kidney injury. Until discharge, 19 patients had respiratory infections, three of which developed into septic shock. In the initial 12 months of follow-up, five patients had graft dysfunction. Mortality was 41% (7 patients), all happening within four months of transplantation. The most common cause of death was PGD (67%). Overall survival was 81% in the first month, 71% in the third month and 58.8% in those who completed one year of follow-up. Taking into account only ERA2, this survival is 80%, 75% and 63.5% respectively. There were no significant differences at one month and three months compared to patients not requiring ECMO as a bridge, but survival at one year was significantly lower in patients on ECMO ($p = 0.029$). A marginal divergence between the two groups was observed for ERA2 alone, but it was not statistically significant ($p = 0.087$).
Conclusions: The increased number of transplants performed and the rising utilization of ECMO as a bridging procedure for LTx reinforces the feasibility of this technique, with no major impact on survival and acceptable results in carefully selected patients. However, results should be cautiously evaluated, given the small sample size and further research is required into the use of this type of support.

Keywords: *Lung transplant. Bridge. ECMO. Outcomes.*

CO 087. ECMO AS BRIDGE DO LUNG TRANSPLANT: THE INTENSIVE CARE PERSPECTIVE

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Introduction: Lung transplant is an established treatment for patients with advanced chronic non-malignant lung disease, with an increasing number of lung transplants being performed worldwide, Portugal included. The Lisbon Central Hospital – Centro Hospitalar Universitário Lisboa Central – performed 355 lung transplants from January/2001 to January/2023. Extracorporeal Membrane Oxigenation (ECMO) is a cardiopulmonary support that is becoming increasingly used. In respiratory failure it allows oxygen supply on refractory hipoxemia and also a less agressive ventilation, reducing morbimortality. Due to organ shortage, there is an increasing number of people waiting for lung transplantation, and it is essential do develop new approaches in order to reduce morbimortality during the waiting process. Although ECMO devices have been used in lung transplantation programmes, only a few studies include a large number of patients and data about long term survival.
Methods: Among the 355 lung transplants, 73 took place on the last 2 years. 21 patients from the 355 (6%) have been submitted to ECMO as bridge to transplant. Those patients came from Intensive Care Units all over the country. 9 of those patients came from our unit, and of them, 1 received ECMO in the beginning as a bridge to recover but, due to non recovery of its respiratory function, was referred to lung transplantation. 3 patients died while waiting for lung transplant. The main diagnosis of the 9 patients that received a lung transplant were n = 5 to interstitial lung disease, n = 2 to bronchiectasis (1 due to cystic fibrosis and 1 non cystic fibrosis), n = 1 due to lung fibroelastosis and n = 1 due to Granulomatosis. VV-ECMO was the main support used until lung transplant (1 of the patients was converted to VAV-ECMO). The duration of ECMO-support until transplant ranged from 7 to 203 days (with a median time of 21 days). The majority (n = 6) of patients needed 2 oxygenation membranes until the transplant. In terms of cannulation, 6 patients had "fem-fem" VV ECMO cannulation and 6 had femoral-jugular configuration.
Results: This analysis is only referred to ECMO support until transplant.
Conclusions: Although there are significant risks related with ECMO, this technique allows physical rehabilitation in the awake patient. 3 month-survival rates after lung transplantation of patients that received ECMO as bridge to transplant are similar to those without ECMO support. On our 9 patients the 3 month-survival rate after lung transplantation was of 88%.

Keywords: *VV-ECMO. Lung transplantation. Bridge to transplant.*

CO 088. TUBERCULOSIS IN CRITICALLY ILL PATIENT AT INTENSIVE CARE UNIT: A CLINICAL CASE

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Case report: 42-year-old man, from Guinea-Bissau, living in Portugal for a few months, construction worker, with relevant personal history of arterial hypertension and unspecified liver disease that led to hospitalization for three months in his country. Admitted to the Emergency Department with weight loss, progressively worsening fatigue and cough with hemoptoic sputum. After etiological investigation, *Mycobacterium tuberculosis* was identified in the bronchoalveolar lavage by nucleic acid amplification test (negative microscopic examination), leading to the diagnosis of disseminated tuberculosis: pulmonary and pleural affection (empyema, pulmonary nodules and right lung cavitation), central nervous system (parietal space-occupying lesion with vasognic brain edema and midline shift) and probably also liver (hyperbilirubinemia and transaminases elevation with no other identified cause). Due to difficult control of the pulmonary focus, it was necessary to place a chest drain in the operating room under anesthesia, where he had an episode of vomiting during mobilization with consequent aspiration pneumonia in the left lung. As a consequence, a worsening of the respiratory point of view led to admission to the Intensive Care Unit (ICU), with the patient being initially under high-flow oxygen therapy but later requiring invasive mechanical ventilation (IMV) due to severe acute respiratory distress syndrome. In view of this scenario, several questions arise about the particularities of the management of critically ill patients with tuberculosis in the ICU, leading to a lack of information and specific recommendations for this group of

patients, starting in the use of non-invasive ventilation and IMV. There is also a constant need for aerosol generating procedures, such as endotracheal suction and bronchoscopy, leading to an increased risk of disease spreading. There are also several challenges from the therapeutic point of view, starting in anti-tuberculosis drugs dose adjustment in situations of kidney and liver failure.
Discussion: Gastrointestinal disorders often identified in these patients make it difficult to administer and properly absorb drugs – most of it available only in peroral formulations, leading to higher risk of inadequate drug levels and inadequate control of the disease, increasing risk of multidrug-resistant tuberculosis. This case is intended to report the experience of managing a critically ill patient with tuberculosis, addressing the difficulties identified and the solutions found to overcome them, in order to guarantee the best level of care without compromising health professionals safety.

Keywords: *Tuberculosis. Critically ill patient. Intensive care.*

CO 089. THE HOSPITAL SCORE AND LACE INDEX AS PREDICTORS OF 30-DAY READMISSION IN RESPIRATORY PATIENTS

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Introduction: Hospital readmissions are common. Validated risk assessment tools such as the HOSPITAL score and LACE index have been developed to identify patients at high risk of hospital readmission so they can be targeted for interventions aimed at reducing the rate of readmission. This study aims to evaluate the utility of HOSPITAL score and LACE index for predicting hospital readmission or death within 30 days in a large-sized university hospital.
Methods: All adult patients who were admitted to the Pulmonology Department from January to September of 2022, were retrospectively evaluated to determine if the HOSPITAL score and LACE index were significant predictors of hospital readmission within 30 days. Data were collected from consultation of clinical electronic records and statistical analysis was performed with SPSS® software.
Results: 222 discharges were analysed after exclusion of patients who died during the hospital stay, were transferred to another hospital or left against medical advice (25 cases). There was a predominance of males (58.6%) and the mean age was 64.2 years. The majority (81.1%) of patients were admitted through the emergency department. The median duration of stay was 14 days. The most prevalent main diagnosis were: pneumonia (20.72%); exacerbation of COPD (13.6%); lung cancer (11.71%); pneumothorax (9.01%); ILD (8.56%); exacerbation of bronchiectasis (7.21%). Of the patients included, 35 (15.7%) were readmitted to the same hospital within 30 days and 11 (4.95%) died in the same period. Both HOSPITAL score and LACE index were significantly higher in readmitted patients ($p < 0.02$). On logistic regression, only HOSPITAL was significant concerning the association with readmission but the determination of the area under the ROC curve yielded a value of 0.67. In turn, the LACE index showed a good association with mortality after discharge with a ROC value of 0.77.
Conclusions: The HOSPITAL score may be superior to the LACE index to identify patients at higher risk of hospital readmission within 30 days, but LACE index showed superiority in identifying the risk of death after discharge. The authors feel that there is a need for the development of tools to predict patients at risk for early hospital readmission or death in the respiratory population, as most scores already developed focus, mainly, on COPD patients.

Keywords: *HOSPITAL score. Lace index. Readmission. Death.*

CO 090. STILL ABOUT THE PANDEMIC – IMPACT OF SARS-CoV-2 ON THE DIAGNOSTIC WORKUP AND FOLLOW UP OF SUSPECTED LUNG CANCER PATIENTS

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Introduction: The COVID-19 pandemic forced unprecedented challenges on healthcare systems around the world. Besides the direct impact of the disease itself, clinicians were also confronted by procedural difficulties, and likewise patients' access to medical healthcare was heavily impaired. Consequently, disease burden also reflected on other pathologies such as lung cancer, possibly bringing to a halt recent diagnostic and therapeutic advances.
Objectives: We aimed to assess the impact of the COVID-19 pandemic on lung cancer diagnosis and management.
Methods: Retrospective study including all patients newly diagnosed with lung cancer between January 2019 and December 2020 in a tertiary center. Two groups were then established: a control group, comprising patients diagnosed before the pandemic, and a study population, including patients diagnosed during the nationally implemented emergency/calamity states (lockdown months). t-Student and Mann-Whitney tests were applied for continuous variables and the chi-square test was used to compare categorical variables.
Results: A total of 447 patients were diagnosed with lung cancer during the two years, 242 in 2019 and 205 in 2020. Of all patients diagnosed in 2020, 49% (n = 102) were referred to follow up during the lockdown months (versus 147 patients in the same timeframe of 2019). Mean age at the time of diagnosis was 66.7 ± 11.3 years. Most patients were male (67.8%) and were either smokers or former smokers (71.7%). While most patients diagnosed outside of the lockdown period were referred from primary care/other specialties (83%; n = 88), more than half the patients diagnosed during the pandemic were referred from either the emergency department and/or after hospital admission (55.6%; n = 55; $p < 0.001$). Patients referred during the pandemic had a significantly worse ECOG-Performance Status (17.2% prevalence of ECOG 3-4 versus 4.7% in patients diagnosed outside the lockdown period; $p = 0.004$) and were more likely to be symptomatic prior to referral (66.7% of incidental imaging findings outside the pandemic versus 33.3% during COVID-19; $p < 0.001$). Overall, most patients were diagnosed using transthoracic lung biopsies (58%; n = 119), although during the pandemic this proportion was significantly lower (67 versus 48.5%; $p = 0.007$); on the contrary, the number of patients diagnosed using ultrasound-guided procedures was significantly higher during the pandemic (8.3 versus 2.9%; $p = 0.009$). The were no significant differences concerning tumor histology between groups, with lung adenocarcinoma being the most prevalent (n = 139), followed by squamous cell lung cancer (n = 29) and small cell lung cancer (n = 18). The proportion of patients with advanced-stage disease was significantly higher in the pandemic subgroup (78.8% versus 50.9%; $p < 0.001$) and, as expected, this translated into a significantly lower proportion of patients proposed to curative-intent treatment (32.3 versus 67%; $p < 0.001$) and higher rates of best supportive care (11.1 versus 2.8%, p =.019). The cumulative burden resulted in higher mortality rates for the subgroup diagnosed during the pandemic, despite the more recent diagnosis (74.7 versus 59.4%; $p = 0.020$).
Conclusions: Delay in patient referral and overall diagnostic/staging workup led to a significantly higher mortality rate and overall higher morbidity for patients diagnosed with lung cancer during the SARS-CoV-2 pandemic, hindering some of the advances of the previous years in this field.

Keywords: *COVID-19. Lung cancer. Staging. Diagnosis.*

CO 091. DELAYED PNEUMOTHORAX AFTER COVID-19 IN A SMALL PORTUGUESE GROUP OF ADULTS

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Introduction: In COVID-19 pandemic, a great number of complications during treatment of acute phase was observed, such as pneumothorax frequently associated with invasive and non-invasive ventilation. Delayed occurrence of pneumothorax after recovery from the infection is less commonly reported, especially in non-ventilated patients.
Objectives: The purpose of our study was to determinate if there was any risk factor associated with the development of pneumothorax after COVID-19 recovery and observe the chronology of presentation.
Methods: We selected all cases of spontaneous pneumothorax in the Pulmonology department of Hospital Santa Maria – Centro Hospitalar Universitário de Lisboa Norte during the period between January 2021 and August 2022 and observed our population retrospectively. All patients who did not present SARS-CoV-2 infection were excluded, after verifying the information on the national platform for infectious disease notification (SiNAVE). Other relevant pulmonary conditions were excluded by examining CT-scan, alfa1antitripsin level and medical history. We identified a group of 15 patients with the described characteristics.
Results: All our patients had asymptomatic to mild illness. Of the observed population, 67% were males (n = 10). Mean age was 36 years (19-84y), all individuals were Caucasians and 13% (n = 2) were active smokers. 74% (n = 12) had no history of previous pneumothorax, 13% (n = 2) had already been affected by pneumothorax during acute phase of SARS-CoV-2 infection and 13% (n = 2) had a previous episode before SARS-CoV-2 infection, without any evident etiology. Median interval between SARS-CoV-2 infection and the occurrence of pneumothorax was 70 days (19-120d). Our population immunization status against SARS-CoV-2 was: 53% (n = 9) vaccinated with full scheme, 33% (n = 5) with only 1 administration and 14% (n = 2) not vaccinated. For what concerns treatment, 53% (n = 8) underwent collocation of thoracic tube, 47% (n = 7) were admitted for clinical and radiological monitoring, and none needed surgical intervention. Only one patient suffered a recurrence after hospital discharge and needed further treatment undergoing atypical pulmonary resection.
Conclusions: We found no obvious risk factor for the occurrence of delayed pneumothorax, such as severity of primary infection, immunization status or smoke habits. With a great number of SARS-CoV-2 infections every year, it is important to study and understand medium- and long-term sequelae of this disease.

Keywords*: Pneumothorax. COVID-19.*

CO 092. INSPIREGBS – INSPIRATORY MUSCLE TRAINING IN PEOPLE WITH GUILLAIN-BARRÉ SYNDROME: A FEASIBILITY STUDY

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Introduction: Guillain-Barré syndrome (GBS) is a rare immune-mediated peripheral nerve disease often preceded by infections. Respiratory muscle weakness is a common complication in GBS patients, leading to decreased vital capacity, weakened coughing ability, atelectasis, and pulmonary infections. Inspiratory muscle training (IMT) has been widely used to enhance inspiratory muscle strength and pulmonary function in various diseases, however, its application in GBS is unknown. Our study aimed to assess the safety, feasibility, and preliminary effectiveness of an IMT protocol - InspireGBs - in people with GBS.
Methods: A pre/post feasibility study was conducted. Feasibility of InspireGBs was determined by participant recruitment/retention, adherence, time spent in each session and adverse events. Secondary outcome was inspiratory muscle strength. InspireGBs was informed by well-designed studies involving patients with chronic obstructive pulmonary disease and spinal cord injury and clinical experience of the researchers. It consisted of three sets of 10 breaths, separated by quiet breathing for 1 min, performed twice daily, 5 days a week for 6 weeks. Participants were asked to comfortably be sat on a chair with back support with a hip angle of 90°, upper limbs resting on the table, and feet on the floor, while using a nasal clip. Initial resistance was set at 50% of participant's baseline maximal inspiratory pressure (PImax) and increased weekly by 10% of the measured PImax if tolerated; otherwise, an increment of 5% was conducted. Tolerance to the IMT was measured using the modified Borg score for "difficulty to breathe through the device". All sessions were supervised by a trained physiotherapist familiarised with IMT and GBS rehabilitation.
Results: Fourteen patients with GBS were screened and assessed for eligibility and 11 proceeded to the intervention (63% male; 639 years). One participant was lost due to health-related problems. Ten participants completed the intervention and were included in the final analysis for feasibility and inspiratory muscle strength. Recruitment and retention rates were high (100% and 91% respectively). Excellent adherence rates (96%) were obtained with no reported adverse effects. Sessions lasted from 4 to 6 minutes. The PImax improved (median:39 [26.5-50]cm/H2O vs 61 [56.3-64.5]cm/H2O; p = 0.005).
Conclusions: This feasibility study provided valuable information on the implementation of an IMT protocol for people with GBS integrated in their rehabilitation program. InspireGBs is a feasible and safe intervention with high adherence, and it may improve inspiratory muscle function when added to usual inpatient rehabilitation care. A randomized controlled trial is now needed to strengthen these findings.

Keywords*: Guillain-Barré syndrome. Inspiratory muscle training. Respiratory rehabilitation.*

CO 093. RECOVERY OF OPTIMAL VITAMIN D IMPROVES RESPONSIVENESS TO PHOSPHODIESTERASE-5 INHIBITORS THERAPY IN PULMONARY ARTERIAL HYPERTENSION

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Introduction: Vitamin D (vitD) deficiency is highly prevalent in patients with pulmonary arterial hypertension (PAH). Moreover, PAH-patients with lower levels of vitD have worse prognosis. We demonstrated that in animals with PAH and severe deficit of vitD, restoring vitD levels to an optimal range partially improves some pathophysiological features of PAH. Also, recent evidence suggests that vitD deficiency may cause insufficient response to phosphodiesterase-5 inhibitors (PDE5i), such as sildenafil, in some patients with PAH, a possibility that remains to be tested. Thus, in this study, we hypothesize that the recovery of optimal vitD levels in experimental PAH might help to improve responsiveness to PDE5i therapy.
Methods: Male Wistar rats were fed a vitD-free diet for five weeks and then received a single dose of Su5416 (20 mg/Kg) and were exposed to vitD-free diet and chronic hypoxia (10% O2) for three weeks to induce PAH. Following this, vitD deficient rats with PAH were housed in room air and randomly divided into two groups: (a) daily tadalafil therapy (oral; 10 mg/kg) + continued vitD-free diet (n = 9) or (b) daily tadalafil therapy (oral; 10 mg/kg) + single oral

dose of 50,000 IU/Kg of vitD plus standard diet (n = 9) for four weeks. Animals were then used for exercise capacity evaluation, invasive haemodynamic, pulmonary vascular remodelling and contractility analysis, and sample collection. Temporal evolution of cardiac (dys)function was assessed by echocardiography.
Results: Recovering optimal levels of vitD improved pulmonary endothelial function, measured by an increase in the endothelium-dependent vasodilator response to acetylcholine. It also increased the vasodilator response to sildenafil. Moreover, pulmonary small artery (< 55 µm) remodeling was decreased in vitD-restored group, as measured by a decline in mean lumen/total ratio and mean medial thickness. In a cardiac morphometric analysis, vitD treatment attenuated increases in both right ventricle (RV) and right atrial hypertrophy, as well as the fulton index (RV/LV+S). VitD supplementation also significantly improved the exercise capacity with increases seen in distance run, evaluated by endurance tests in a treadmill set. RV catheterization showed that vitD did not decreased the RV dysfunction, evaluated by end-systolic and end-diastolic pressure. Similar to the RV, no alterations were observed in pulmonary artery pressures. However, serial echocardiographic analysis revealed an improved pulmonary flow in the vitD-restored group, where pulmonary artery acceleration time normalized to ejection time ratio (PAAT/PAET) and pulmonary artery velocity-time integral (PAVTI) were increased. It also improved tricuspid annular plane systolic excursion (TAPSE).
Conclusions: Altogether, these data suggest that in animals with PAH treated with tadalafil, restoring vitD levels to an optimal range improves some pathophysiological features of PAH. Therefore, in addition to recovery of optimal vitD status being indicated to restore calcium homeostasis in those PAH patients with severe deficiency, it might help to improve responsiveness to PDE5i.

Keywords: *Vitamin D. Pulmonary arterial hypertension. Phosphodiesterase-5 inhibitor. Hypoxia-sugen.*