



SPECIAL ARTICLE

Portuguese Journal of Pulmonology: year-in-review 2009

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Abstract

The *Portuguese Journal of Pulmonology* is progressively achieving an important status in Portuguese medical literature. The present editors thought it would be an enriching task to revise the main topics published during 2009. The invited members of the Editorial Board covered and commented the most relevant articles and gave us an important picture of the quality of the science it was published in Portuguese Pulmonology.

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PALAVRAS-CHAVE

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Resumo

A *Revista Portuguesa de Pneumologia* (RPP) tem como um dos seus principais objectivos o de contribuir de forma significativa e relevante para a literatura médica portuguesa. Os presentes editores consideraram que seria importante a análise e comentário da informação mais relevante publicada em cada uma das áreas da Pneumologia no passado ano de 2009. Os membros do Conselho Editorial convidados fizeram uma avaliação e evidenciaram os artigos mais relevantes publicados na RPP.

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Obstructive sleep apnoea syndrome

Obstructive Sleep Apnoea Syndrome (OSAS) shows a high prevalence and morbidity, which makes it a growing public health problem.¹ This syndrome is frequently associated with daytime hypersomnia and complaints of non-refreshing sleep.¹

Franco and coworkers² performed an analytical, longitudinal study which enrolled 20 patients with moderate to severe OSAS (AHI > 15/h) diagnosed by in-lab polysomnography to evaluate the efficacy of continuous positive airway pressure (CPAP) therapy on daytime somnolence, measured by Epworth Sleepiness Scale (ESS).

All patients answered the cited questionnaire before and one month after CPAP treatment.

The patients were divided in two groups, the compliers (n = 10) and the non compliers (n = 10) to CPAP. Both groups were similar in what concerns age, body mass index (BMI) and ESS score.

The former presented a decrease of ESS from 15.5 to 11.7 and the latter a decrease from 15 to 13, being the statistical significance only reached in the compliant group.

Despite the small sample size, this study showed a significant reduction in daytime somnolence in patients with moderate to severe OSAS who used CPAP.

Beyond hypersomnia, and linked to it, OSAS patients have an increased risk of traffic accidents, a frightening consequence of the disease.³ Aguiar M. et al.⁴ studied a group of consecutive OSAS patients, seeking to analyse differences in demographics, symptoms, sleep study characteristics and quality of life. The authors asked to 163 patients at their first clinical interview if they had road traffic accidents and divided them into two groups concerning that issue: Group 1 (with road traffic accidents; n = 74) and Group 2 (without road traffic accidents; n = 89). Both groups were identical in age, sex and BMI. Group 1 presented higher values of daytime sleepiness measured by ESS, AHI and lower values of quality of life measure by FOSQ questionnaire.

Results can be argued as they are based on patients subjective statements, nevertheless the study is very interesting and the authors concluded that sleepier and more severe OSAS patients should be earlier diagnosed and treated in order to reduce road traffic accidents risk.

REM-related sleep disordered breathing (REM-SDB) is an obstructive sleep apnoea syndrome (OSAS) subcategory, defined as AHI in REM sleep ≥ 5 , AHI in non-REM sleep (NREM) ≤ 15 /h and AHI REM/NREM $\geq 2^5$ and being 10 to 36% of total OSAS population.

Loureiro CC and colleagues⁶ studied 19 patients with REM-SDB diagnosed by in-lab polysomnography in what concerns their demographic, clinical and sleep study characteristics. The authors found that these patients, compared with OSAS ones, were, on average, less obese, less sleepy, more frequently women and showed high prevalence of anxiety disorders, compared to general and OSA populations.

The studied patients showed, also, a reduction in total amount of deep sleep, an increase in REM sleep and their sleep efficiency were at the normal lower limit.

So, these subgroup of patients have singularities that must be carefully looked and searched not to fail the diagnosis.

Chronic obstructive pulmonary disease

In 1995, the *Portuguese Journal of Pulmonology (PJP)* published an article introducing the PNEUMOBIL Project,⁷ which aimed to increase the awareness of COPD (Chronic Obstructive Pulmonary Disease) and the use of spirometry for its early diagnosis, in Portugal.

Due to actual lack of knowledge of this disease and its insufficient diagnosis, this project was recreated as PNEUMOBIL-2,⁸ with the scientific sponsorship of *Portuguese Society of Pulmonology (SPP)*, GOLD (Global Initiative for Obstructive Lung Disease) and *Escola Superior de Tecnologias da Saúde de Lisboa*. The logistics were sponsored by *Boehringer Ingelheim* and *Pfizer*.

The study was performed between May 2007 and May 2008, being enrolled 5324 smokers or ex-smokers, aged 40 or more years old, who performed spirometry and fulfilled the respiratory questionnaire adapted from *American Thoracic Society (MRC-DLD)* questionnaire. The authors found a high prevalence of bronchial obstruction, defined as Tiffeneau Index < 70, among recruited individuals (25%) and 95% of them were not aware of the disease. The majority of the patients were classified as GOLD 1 or 2.

The authors concluded that Portuguese population is not aware of COPD and that there is a lack of spirometry use towards its diagnosis.

COPD is no longer considered as a respiratory disease, but a systemic one,⁹ characterized by systemic inflammation, oxidative stress, both secondary to arterial blood gas changes and both leading to muscular derangements and atrophy.

Brasil Santos and coworkers¹⁰ performed a descriptive, prospective and transversal study to evaluate the correlation between bronchial obstruction and resting capillary lactate concentration, resting cardiac rate and the walked distance in the 6 min walking (6-WT) test as also to evaluate the correlation between bronchial obstruction and the arterial blood gas values, desaturation during 6-WT and cardiac rate after that test.

Ninety one patients were randomly enrolled from the COPD patients pool observed during the year of 2004 in the *Hospital Universitário de Brasília*. No correlation was found between bronchial obstruction and resting capillary lactate concentration. The bronchial obstruction and the pCO₂ related with a worse performance in 6 min walking test.

The 6 min walking test (6-WT) is a low cost, simple and reproducible test assessing the functional capacity in COPD patients, having a strong association with O₂ consumption during the daily life activities of these patients.¹¹ Rodrigues and coworkers¹² designed an observational, transversal study, enrolling 30 COPD patients on pulmonary rehabilitation programme in an university brazilian hospital, aimed to determine which of these variables: FEV₁, daytime and night time paO₂ and the quadriceps strength better correlated with the distance walked in the cited test.

Quadriceps strength was the only studied variable that correlated with the distance walked. For each quadriceps strength kg, the patients walked, on average, 5.9 m.

The authors stated the importance of muscular quadriceps strength in COPD patients, concluding that pulmonary

rehabilitation plays a major role in these patients treatment.

The use of the new information technologies could reach a better and more effective management of home care in chronic diseases. The REALITY (Representative Evaluation of Evolving Remote Home-Based Patient Monitoring Delivery) project was run in three European countries, including Portugal, and aimed to evaluate the impact of home telemonitoring in chronic patients. In our country 51 patients with chronic respiratory failure, followed in H. Pulido Valente, Lisboa (n = 38) and H. Espírito Santo, Évora (n = 13) were enrolled as also 21 patients with moderate/severe persistent asthma followed in H. Espírito Santo.¹³

Exclusion criteria were: patient and/or carer illiteracy, lack of home telephone line and patient carrying a cardiac pacemaker.

Patients had several morning tasks as: record the best of three peak expiratory flow (PEF) measurements, the last night sleep quality, ECG and oximetry (if applicable), and evening ones as: answer questions concerning respiratory symptoms, chronic and rescue medication use, daily hours of oxygen therapy use (if applicable), need of non-scheduled or emergency medical appointments and daily cigarette consumption (if applicable). Once a week, patients should answer questions on how often they went out and EQ-5D quality of life questionnaire. This programme lasted 9 months.

Eighty percent of RCF patients felt more/much more supported and 75% would use this system in the future as also 81% of the asthmatic patients. All the investigators considered this service useful and would like to see it on field in the future. The authors considered the home telemonitoring as a positive tool to home chronic patients follow up.

Tobacco smoking

Tobacco smoking is the main etiological factor of disease in the world. It is estimated, by the World Health Organization, that about 14% of the burden of disease in wealthier countries is attributable to smoking,¹⁴ and cardiovascular, cancer and respiratory disorders are the most frequent consequences.¹⁵

Nevertheless, in a retrospective analysis of medical records of 526 outpatients in follow-up for smoking cessation at a tertiary hospital in Portugal, Aguiar et al.¹⁶ found respiratory, psychiatric and cardiovascular diseases as the most frequent pathologies in 52.1%, 46% and 14.6% of the sample, respectively.

A similar profile was found by Rosendo et al.¹⁷ using files from 3 General Practice (GP) Centres in Coimbra, where, from the 224 randomly interviewed patients, 50% of the smokers had co-morbidities, in which cardiovascular and psychiatric disorders were also the most frequent.

The low incidence of cancers among these populations may be explained by a young average age of the samples, 39.4 years old in the smoking patients from the latter study and 45.5 years old in the hospital patients.

Regarding the starting age of smoking, a questionnaire carried out in a population of 1770 adolescents in four Porto schools and published by Damas et al.¹⁸ revealed

an average at the age of 15, similar to the reported data in the outpatient analysis, under 15 years old,¹⁶ although in the GP study the mean starting age of smoking was 17.2 years old, approximately the same age presented in the 2005-2006 National Health Survey, published by Machado et al. in the PJP,¹⁹ with a starting age of 17 years in men and 18 in women.

Interestingly, according to this fourth National Survey for Health,¹⁹ 20.9% of the Portuguese population are smokers (male: 30.9% female: 11.8%), with the highest prevalence of regular smoking males observed in the Azores (31%), where also were found the youngest start-age smokers (15 years) and the highest daily average consumption, both in males (23 cigarettes) and in females (16 cigarettes). The highest rate of women smokers occurred in Lisbon (15.4%).

Regarding the burden of disease attributable to smoking in Portugal, Borges et al.¹⁴ estimate that 11.2% of disability adjusted life years (DALYs) and 11.7% of deaths are related to this habit, being still very unequal the gender distribution of this data: 15.4% DALYs and 17.7 deaths in men and 4.9 DALYs and 5.2% deaths in women.

Nevertheless, in the assessment made in a student population in the north of Portugal,¹⁸ from the 194 adolescents smokers (11.1% of the sample submitted to the confidential self administered questionnaire) the majority were female—101, corresponding to 5.8% of all students—showing that primary prevention, which is essential against this epidemic, must target teenage girls.

It is also relevant to have strong legislative support, namely to avoid exposure to second-hand smoke, that might be responsible, among other consequences, for more frequent infections and asthma exacerbations in adolescents and younger age groups.

In this context, Areias et al.²⁰ showed that, only two months after the implementation of the new legislative ban on smoking (since January 2008), from a population of 96 asthma outpatients in a reference hospital in Lisbon, 39.6% of the sample reported positive changes with improved performance of daily life activities, decrease in symptoms and lesser resort to prn medication, in which 81.6% were no longer exposed to passive smoking.

These results point out the importance of legislation, of a correct preventive approach and other measures, as well as the standing in improving motivation to quit smoking, reducing the cost of therapy and spreading information about the advantages of abandoning this deleterious habit.

Techniques

Interstitial lung diseases (ILD) remain an important diagnostic challenge for the pulmonologist. Usually the clinical behavior and lung involvement by the disease, are progressive and diffuse. The non invasive diagnostic interventions are often insufficient. Even, minimally invasive interventions show, sometimes, poor efficiency on the correct identification of the pathology we seek.

The more or less the disease progression assumes an acute behavior, more likely the patient could be on dependence of a ventilator support that could end on invasive ventilation in a intensive care unit. The PJP published two studies^{21,22}

during the year of 2009 where the authors discussed the place and the importance of surgical lung biopsy (SLB) on the diagnosis of ILD. Both studies evaluated different clinical situations where the selection of the SPB, to obtain the diagnosis, was done only by the incapacity, by other means, to obtain the correct evaluation of the pathological process.^{23,24}

The results point out, in both the studies, an excellent diagnostic efficiency, 95%^{21,22} with a discrete morbidity and with no intervention related mortality.^{21,22} The kind of the diagnosis obtained in each of the studies are quite different according with the setting they were done.^{21,22}

In one of the studies patients were under invasive ventilation and the intervention was guided by the emergency to identify an alternative therapeutic option.²¹ In this study the SLB results could change the treatment strategy in 8/ 19 patients.²¹ Unfortunately, only four out of the eight patients could, in time, benefit from this change,²¹ raising the question of intervention precocity.

A quick and accurate diagnosis with the less possible morbidity is a permanent challenge to the clinician. Mediastinal masses are frequent motive of pulmonologist referral but, to achieve the diagnosis is sometimes difficult. The traditional diagnostic strategies involved more or less invasive surgical interventions,²⁵ but nowadays the diagnosis may need only minimally invasive interventions in an outpatient clinic regime.²⁶

Mauro Zamboni et al.²⁷ published during 2009 in the PJP their experience on the diagnosis of mediastinal masses using cutting needle "Trucut" CT image oriented. The patient selection criteria are very important in order to avoid technique associated complications: lesions from 3 to 10 centimeters, mediastinal anterior location (93%), no more than 2 centimeters deep from the chest wall.²⁷ Using "Trucut" 18 gauge needle they got an excellent diagnostic efficiency in 49/ 56 patients (88%) with no associated morbidity.²⁷

Lung cancer

Lung cancer remains the more frequent cancer, globally, in the world from the last decades.²⁸ During 2008 it represented the most important cause of death by cancer (18.2% from total causes).

Luís Alves et al. published an epidemiological study²⁹ with the objective to evaluate the Portuguese lung cancer mortality trends from 1955-2005. They drew a possible relationship between the smoke habits profile of the Portuguese population using a model "smoking epidemic" from Lopez A. et al.³⁰ Using this model they assumed a straight relationship between population smoking habits prevalence and lung cancer occurrence, using lung cancer mortality rates. Despite all diagnostic and therapeutic developments, we must accept our incapacity to change, globally, the natural history of the disease; so, we could accept lung cancer mortality rates a good estimate of lung cancer incidence rate.³¹ Using these assumptions, in Portuguese population, this study point out stabilization in lung cancer mortality rates among male, and a slight, and persistent, increase in female gender.²⁹ According with the model of "smoking

epidemic" these figures could be compatible with the third stage of Lopez A. et al.,³⁰ and we could expect, in next decades, to observe a decrease in global Portuguese lung cancer mortality rates if the tendencies of population smoke habits were maintained.

The tumor in the airways is a frequent occurrence during the evolution of many tumors³² although, the most frequent malign neoplastic involvement had respiratory origin. Even when, the cure of the disease wasn't the main goal, local treatment is fundamental for the symptomatic control that could represent, for the patient, a life saving procedure. Besides the global strategies for the treatment of neoplastic disease there are many local treatment modalities we use to control the progression of the disease inside the airways and the associated symptoms, dyspnoea, cough and haemoptysis.³³ Endoluminal high dose rate brachytherapy using Ir¹⁹² inside the airways is one of these local treatments.³⁴ In the study published by Maria Fortunato et al.³⁴ the authors describe their experience with this kind of intervention presenting seven patients, with different oncological pathologies, in which this modality of treatment was performed. Global results were fair, they got symptomatic control in 6/ 7 treated patients. After a follow up of seventeen months 3/ 7 patients were alive, one of them, without evidence of the disease.³⁴ The progression of the disease was the main reason for patients' death, although in one case, dead was associated to the occurrence of a severe haemoptysis, six months after the treatment.³⁴

Tuberculosis

In 2009 the PJP published three original papers on tuberculosis (TB), that answer some important issues on the subject: prevalence of MDR-TB, the evaluation of a new diagnostic tool and review of clinical patterns of TB in children admitted in a Pediatric Department.

Perdigão et al.³⁵ analyzed the transmission, drug susceptibility and characteristics of a study population from a Central Lisbon's Hospital and concluded that no significant TB outbreak was detected among the patients attending this hospital, although a considerable proportion of the isolates belonged to the "Lisboa family" and approximately 27% of all cases were probably due to recent transmission. They only found four MDR-TB strains (3 from the "Lisboa family"). However this data poses a serious public health problem and measures are necessary to contain them. They suggest that susceptible Lisboa strains should also be monitored, especially those infecting HIV positive individuals, to prevent the acquisition of resistance.

It can be criticized by the fact that of all cases were hospitalized patients and may not represent the national epidemiological trend. MDR-TB prevalence in its study is twice higher than national prevalence. However, a similar study from these researchers pointed to similar data.³⁶

In another study, Perdigão J³⁶ genotyping isolates and combining with mutational results, found that Lisboa strains, are responsible for the majority of the MDR-TB. Extensive drug-resistant tuberculosis (XDR-TB), MDR strains also resistant to one intravenous second line antituberculosis

drug and a fluoroquinolone (FQ) were highly prevalent among the MDR-TB isolates (53%). This study confirms the high prevalence of MDR-TB and the increasing prevalence of XDR-TB in Lisboa, which alerts for the need of new strategies to stop transmission.

The paper of Macedo et al.³⁷ aimed to determine the sensitivity of the new MTBDRplus[®] assay in comparison to classical mycobacteriological methods. This study indicated that this assay is a rapid, user-friendly and highly sensitive test for detection of resistance directly from sputum samples. It is a relevant paper, since it pointed out to the availability of a new rapid and accurate diagnostic tool of MDR and XDR-TB. Its dissemination through TB clinics should allow a more rapid and correct therapeutic.

Leite AL et al.³⁸ reviewed retrospectively clinical data of all TB patients admitted in a Pediatric Department from 2000 to 2007. Twenty three patients, aged from 6 months to 16 years old were admitted, 78% with pulmonary tuberculosis and 22% extra-pulmonary tuberculosis. So, even though tuberculosis in children has dramatically decreased in the last decade in our country, probably related to the decreased of TB patients, TB in a child must still be kept in mind as a diagnosis in children, even if vaccinated, particularly when there is a history of contacts and forces us to proper surveillance of contacts of patients with active TB. It also alerts us to the need for new methods of diagnosis of TB infection, rapid and sensitive, enabling us to identify early those children at risk for developing a TB disease. It also alerts us for the need of new vaccines as one of the research priorities in tuberculosis. I also recommend a recent State of the Art on Childhood Pulmonary Tuberculosis.³⁹

Pleural effusions

One paper by Soares P et al.⁴⁰ retrospectively reviewed the clinical records of 118 inpatients less than 18 years old admitted with parapneumonic pleural effusion, during 7 years, in order to characterize these patients and to establish possible prognostic factors on admission, as well as to correlate treatment options with the outcome. The authors concluded that respiratory distress, loculations, empyema, low pH in pleural fluid, glucose or proteins in pleural fluid, high lactic dehydrogenase level in pleural fluid and high serum C-reactive protein were associated with a worse prognosis. Another conclusion of the authors was that pleural drainage and/or surgery can shorten hospital stay and improve outcome. This paper suggests these comments: 40% of patients admitted with loculated pleural effusions points to a late diagnosis of this complication; clinicians may be aware of that possibility in children with pneumonia that runs with respiratory distress, prolonged fever and insufficient response to correct antibiotic therapy. Hernández-Bou Set al.⁴¹ reported the use of antigen assays to detect pneumococcus in pleural fluid as a quick and sensitive diagnostic method, and a valid alternative to PCR and should be used to improve etiologic diagnostic. Finally, thoracoscopy has a good effectiveness in management of children with parapneumonic pleural effusion at the fibrin purulent stage accordingly to Freitas Set al.⁴² and should be considered in selected patients.

Asthma

In a recent editorial of the European Respiratory Journal, bronchial asthma—when referred to the paediatric ages—was considered “the illness of our time”.⁴³ But we are all aware of its importance also in adulthood, not only by its prevalence, but also by the high percentage of non-controlled patients. In spite of all this knowledge, in 2009, bronchial asthma did not receive a particular attention of the Portuguese pulmonologists. In fact, on this item, only three original articles were published in the PJP, and only one of the studies was done in Portugal.

It is not the moment, and the place, to discuss this (notorious) lack of interest. But it must be stated.

This fact strikes our attention especially as one of the studies reports the asthma hospital admissions and mortality in Portugal, in a eight years period (2000-2007).⁴⁴ The mean annual admission rate observed was not particularly high, being even lower than the one observed in another studies. However, almost half (48.7%) of the admitted patients were aged under 19 years. Along this period of time there was only a slight decrease in these admissions. And the asthma hospital mortality was not reduced.

It is generally accepted that a very low percentage of asthmatics can not have their disease controlled. It means that the large majority (90%-95%) of these patients can control it, and that they can have very high patterns of quality of life and, consequently, that the costs of the illness can be substantially reduced.

The above mentioned article emphasizes the most that needs to be done and how it is absolutely essential the real involvement of the pulmonologists.

The lack of asthma control is often associated with the underdiagnosis and undertreatment of related diseases, such as rhinoconjunctivitis, subject that is focused in another article.⁴⁵ In this are reported the results from a study of the association of rhinoconjunctivitis and asthma in an adolescent population of Recife (Brazil). It makes evident the high prevalence of asthma and rhinitis in this group of adolescents, what was also stated in previous studies, namely those of the ISAAC phases in Portugal. But it also calls our attention for the high number of underdiagnosed cases, as “65.1% of the patients were unaware of the symptoms” and, specially, for the association of rhinoconjunctivitis with the more severe asthma symptoms.

The important conclusion is that to control the latter the former must be also controlled.

The third study correlates symptoms with spirometric parameters, in a group of elderly asthma patients.⁴⁶ Notwithstanding its methodological limitations, otherwise discussed by the authors, this work shows the lack of relation between the clinical findings and the functional evaluation. This fact is known, and it can be observed not only in the asthmatic patients but also in the ones with other respiratory diseases, and it has been stated in several studies.

For this reason it is advisable that the functional evaluations must be performed periodically, and their results must be compared, when it is possible, with the basal ones. The periodicity should be, for the advanced age groups, at least once a year.

Infection

Hospital admissions for respiratory diseases continue to increase. In 2008, 73 880 patients were admitted to Portuguese hospitals, with respiratory disease as the primary diagnosis. This figure represents an increase of 14.8% compared with admissions in 2003; the primary diagnosis of pneumonia in hospitalized patients in 2008 increased by 18.9% compared to 2003, these patients being responsible for more than 350,000 days of hospitalization.⁴⁷

In 2009, the PJP published 33 original articles of which 10% (3 articles), referred to infectious pulmonary diseases. These articles, confirm the importance of the identification of the etiologic agent in the largest possible number of cases, because of significant benefits for the patient (as demonstrated also by reducing the time of hospitalization, reduction of comorbidities in patients and in some cases even reducing mortality).

In the article "C-reactive protein and severity of acute bronchiolitis"⁴⁸ S Costa et al., in a retrospective study carried out in 176 children aged between 0 and 36 months, in S. Joao Hospital (Porto), intended to demonstrate the value of C-Reactive Protein (CRP) as a marker of severe bronchiolitis. Given its feature as a marker of acute inflammation, there could be relationship between the value of CRP and markers severity of acute bronchiolitis, suggesting that CRP could have prognostic value in children hospitalized for bronchiolitis. The objective was not fully achieved and more studies (particularly prospective ones), studying the effect of associated infections and with more strict criteria for Bronchiolitis are warranted. Despite these limitations it seems of great importance that each department revise their attitudes, because it could be a good starting point not only for improving the care but also for the preparation of consistent, prospective studies.

In the study *The lung abscesses: review of 60 cases*,⁴⁹ Luisa Magalhaes et al. suggest that lung abscesses are difficult to characterize, with antibiotic resistance constituting a problem in its therapeutic approach. The authors started from the definition of the lung abscesses as cavities that arise in the lung parenchyma, presenting a greater or lesser amount of necrotic tissue inside, appearing in predisposed individuals such as patients with chronic lung disease or obstruction secondary to cancer and patients most at risk of aspiration (patients with abnormal neurological status, intravenous drug users, patients with alcoholism, pathology of the pharynx and oesophagus, neuromuscular disease). In a review article published in 2008 in the PJP⁵⁰ Ana Moura Gonçalves, et al. studied of the main causative agents, from the diagnostic methodology to the therapeutic approach in lung abscesses. In the 60 cases of Santo António Hospital (Porto) evaluated in 2000/ 2005 it was intended to assess the time to diagnosis, identification of the microbial agent and risk factors. Most of the patients had comorbidities, all patients were treated with antibiotics and 7 patients died.

The average hospital stay was (27.5 days). The prevalence was higher among males by larger number of associated risk factors, including alcoholism and lung tumours.

Patients at admission had a mean duration of symptoms of 23 days, with 6 out of 14 patients with neoplasm of the lung that was unknown at the time of admission. It was possible to identify a microorganism in 46% of cases (*Pseudomonas*

aeruginosa, *Saureus* and methicillin-resistant *Acinot obacter baumannii* as the most common). Only one patient did not perform thoracic CT but only 53% of patients carried out bronchoscopy, which may have influenced the identification of the microbial agent.

Organ transplantation now represents the best replacement therapy for patients with chronic terminal illnesses. Although the kidney is the most transplanted organ in our country, transplantation of other solid organs has gradually grown in recent years, including liver and heart.

Acute rejection still persists as the main cause of early loss in organ transplantation, although its incidence has declined with the advent of new and potent immunosuppressants. With increased patient survival, several authors have demonstrated the prevalence and importance of immunological complications or not, late, many of them secondary to the use of immunosuppressants, representing an important risk factor for graft loss. by Patricia Caetano Mota et al.⁵¹ evaluated in a retrospective study patients admitted to the Renal Transplant Unit, at S. João Hospital (Porto) with the diagnosis of respiratory disease in a period of 12 months. Thirty six patients were included, in which the most commonly used immunosuppressants were prednisolone and mycophenolate mofetil with cyclosporine (38.9%) or tacrolimus (22.2%) or rapamycin (13.9%). In 86% of patients infectious respiratory illness emerged, including pneumonia in most cases, opportunistic infections, lung abscesses and tracheobronchitis in a limited number of cases. Microbial agents were identified in 22% of cases and five cases had iatrogenic disease by rapamycin. Infection was the major complication in transplant patients, and bacterial and opportunistic agents the most frequent. The authors emphasized the importance of a good monitoring of serum levels of rapamycin and other potentially toxic immunosuppressive drugs.

Data from this study confirm that the published literature with particular reference to a Portuguese study by Agostinho Costa et al.,⁵² confirming the need for a quick diagnostic approach, which can often go through invasive methods, a factor which may prove is important in establishing a therapy as early as possible and also determining the sharp decline in mortality, both also in the temporal profile of lung infection.

So to increase the success of transplantation all revisions made to treatment of our patients, resulting guidelines will lead to an earlier detection of infection and the development of new therapies to overcome antimicrobial resistance they arise.

Physiopathology

As there is a worldwide increase in the elderly population, there have been many publications analysing the effects of aging on pulmonary function. It is thought that the respiratory system is the one which ages faster, due to a higher degree of exposure to environmental pollutants over the years. However, undertaking regular exercise can slow the age-related decline in lung function.⁵³ Ruivo et al.⁵⁴ performed a study to compare the respiratory pattern in healthy non-smoker adults and the elderly to confirm the

effects of aging on lung function. Lung function parameters (forced vital capacity—FVC, forced expiratory volume in one second—FEV₁, peak expiratory flow rate and maximum voluntary ventilation) and expansion of the chest were studied in 35 individuals male and female in each age group. Both male and female elderly subjects had lower lung function testing scores than the adult subjects, with this difference more pronounced in females. Expansion of the chest in females was the parameter most inversely correlated with age. These results confirmed differences in the respiratory patterns of healthy adults and the elderly, suggesting that age has impact on lung function, with a gender influence on the degeneration process, which is not consensual in the literature. In this study, the differences in male and female subjects could be related to differences in height and weight of both genders.

It is known that heart failure is associated with respiratory alterations, however the impact of these changes on functional performance of patients with this diagnosis has not been well studied. Di Naso et al.⁵⁵ performed a transversal study with 42 patients with heart failure and analysed these parameters: maximum inspiratory pressure (P_{Imax}), FVC, FEV₁, distance covered in the six-minute walk test, New York Heart Association functional class and the physical functioning domain of the Short Form-36 Quality of Life Questionnaire. The authors showed that P_{Imax} and FVC correlated positively with the six-minute walk test and the physical functioning domain score of the Short Form-36 and negatively with functional capacity. Also, FEV₁ had a positive correlation with the six-minute walk test and a negative one with functional capacity, but had no correlation with SF-36. This study demonstrated that lung function and inspiratory muscular force correlated with functional capacity in patients with heart failure. Nevertheless, it has some limitations, like the small sample size and diverse heart failure aetiology.

Botelho et al.⁵⁶ carried out a very interesting study which was awarded the Robalo Cordeiro prize. They intended to develop and validate a non-invasive method for assessing lung deep lymphatic chains (LDLC) by nanoradioliposomes aerosolised modulated on the *Bacillus subtilis* spore wall. They chose this microorganism because it is an human airways saprophyte. The aim was to produce a nanoradioliposome formulation that can mimic the dynamics of preferential removal of spores by LDLC and present the ideal properties as a tracer for molecular imaging studies. From seven liposomal formulations tested, the formulation-F was the one that demonstrated physicochemical and radiopharmaceutical properties that made it an ideal candidate for molecular imaging studies of the LDLC *in vivo*. Nanoradioliposomes of the formulation-F after radioactive labelling were administered as aerosols to 20 *Sus scrofa* and it was possible to visualize lymph nodes and deep lymphatic lung network. This formulation also displayed stability and toxicity profiles compatible with their human use. This study showed that it is possible to produce nanoradioliposomes targeting specific organs or tissues with diagnostic and therapeutic purposes.

Conflict of interest

Authors declare they don't have any conflict of interest.

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