



SCIENTIFIC ASSEMBLY UPDATE

Selected clinical highlights from the 2012 ERS congress in Vienna

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ABSTRACT: This article reviews a selection of scientific presentations at the 2012 European Respiratory Society Annual Congress in Vienna, Austria. The best abstracts from the groups of the Clinical Assembly (Clinical Problems, Rehabilitation and Chronic Care, Imaging, Interventional Pulmonology, Diffuse Parenchymal Lung Disease, and General Practice and Primary Care) are presented and discussed in the context of the most up-to-date literature. The reviewed topics especially deal with the areas of chronic obstructive pulmonary disease (acute exacerbations, comorbidities, prognosis and rehabilitation), the diagnosis and management of idiopathic pulmonary fibrosis, sarcoidosis, endobronchial techniques in emphysema, functional imaging and issues in respiratory medicine relevant for the primary care setting, including aspects related to end-of-life care and palliation.

KEYWORDS: Chronic obstructive pulmonary disease, end-of-life, idiopathic pulmonary fibrosis, interventional pulmonology, primary care, rehabilitation, sarcoidosis

The 2012 European Respiratory Society (ERS) Annual Congress was held in Vienna, Austria. This meeting is the largest worldwide in the field of respiratory medicine, with around 20 000 attendees each year. This year, a total of 5241 abstracts were submitted to the Congress of which 76% were accepted (874 from the Clinical Assembly) and presented during the scientific sessions by research groups from all over the world. In addition, outstanding lectures based on the most recent literature updates were presented in the symposia sessions during the Congress.

Although such a broad programme cannot be reviewed exhaustively, the present article discusses the most relevant topics and presentations from the Congress, including breakthrough reports and studies of particular interest to most of the healthcare professionals in the area of respiratory medicine. Hot topics and selected abstracts presented at the Congress from the scientific groups of the Clinical Assembly (Clinical Problems, Interventional Pulmonology, Diffuse Parenchymal Lung Disease, Chest Imaging, General Practice and Primary Care, and Rehabilitation and Chronic Care) are discussed in the context of recent literature.

UPDATES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Among the most relevant topics discussed at the ERS Congress in Vienna were acute management,

diagnosis and characterisation of chronic obstructive pulmonary disease (COPD) patients.

Episodes of exacerbation in COPD

The optimal dose and duration of systemic glucocorticoid therapy for acute exacerbations of COPD is still unknown. A recent review analysed data from seven studies and 288 patients, with treatment course varying among 3–15 days [1]; despite the fact that shorter periods were not associated with a significant increase in treatment failure, no conclusive evidence was obtained to recommend change in clinical practice due to the wide confidence interval around the estimate effect.

LEUPPI *et al.* [2] designed a multicentre trial including 304 patients with acute exacerbations of COPD admitted to hospital. They received 40 mg of prednisone daily for either 5 or 14 days in a placebo-controlled fashion. The time to the next exacerbation at 180 days did not differ between groups both in the intention-to-treat and the per-protocol analyses, thus allowing them to conclude that 5-day treatment with systemic steroids is non-inferior to the longer period with regard to re-exacerbation rate in the following months.

In a web database including 15 821 patients from 13 European countries, ROBERTS *et al.* [3] broached the sex differences on COPD admission. They

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have shown that the proportion of nonsmoker females was three-fold higher than in males (9.6% *versus* 3.4%), but the proportion of current smokers was significantly higher (37.5% *versus* 28.3%; $p < 0.001$). Although females were more likely to die in hospital (5.5% *versus* 4.7%; $p = 0.018$), they had less coloured sputum at admission (53.5% *versus* 56.3%; $p < 0.001$), received less steroids and antibiotics, and had a lower rate of comorbidities (1.3% *versus* 1.7%; $p < 0.001$). The same database was analysed by LOPEZ-CAMPOS *et al.* [4] to evaluate the patient's repeated admission rate during 90-day follow-up and the clinical features and outcomes, such as mortality. Factors associated with multiple admissions were current smoking habit (OR 0.69), forced expiratory volume in 1 s (FEV1) (OR 0.99) and arterial oxygen tension (OR 1.003).

The problem of readmissions was also tackled by McCLINTOCK-TIONGCO *et al.* [5] in a population of patients (around half female) with 577 consecutive episodes. Time of readmission was not predicted by age, number and type of comorbidities, length of stay, rate of readmission, white blood cell count and C-reactive protein levels. However, patients who died were older (76 ± 8 *versus* 70 ± 11 years; $p = 0.03$), and had higher systemic inflammatory pattern.

The cardiovascular risk during acute exacerbations of COPD was addressed by four interesting studies. In the first of these, authors assessed the arterial stiffness by means of the aortic pulse velocity in 55 consecutive patients, while in a stable state, at exacerbation and 3, 7, 14 and 35 days thereafter [6]. Patients with an infectious exacerbation (namely positive sputum culture or positive PCR for bacteria and human rhinovirus) had a greater increase in arterial stiffness from the stable state, which maintained at a higher rate in the recovery period. URBAN *et al.* [7] evaluated the endothelial dysfunction by means of the flow-mediated dilatation technique and the systemic inflammation, in 28 consecutive patients. During exacerbation, patients showed a mean C-reactive protein value of $7.0 \text{ mg}\cdot\text{L}^{-1}$, leukocyte count of $9.7 \times 10^3 \text{ cells}\cdot\text{mL}^{-1}$ and flow-mediated dilatation of $6.8 \pm 3.6\%$ indicating a severe endothelial dysfunction. This pattern progressively returned to normal once the clinical stability was reached, thus suggesting that systemic inflammation may play a key role in worsening the endothelial function. QUINT *et al.* [8] studied the impact of acute exacerbations of COPD on survival after acute myocardial infarction in 1063 consecutive patients, 10% of whom had more than one episode per year. After adjusting for confounding factors (smoking and sex) and stratifying by age, mortality was greater in frequent exacerbators, and in patients who had exacerbations in the 2 months preceding the myocardial infarction. The level of cardiac troponin T at admission day in hospitalised patients was reported by SOYSETH *et al.* [9] in a population of 50 consecutive patients with acute exacerbations of COPD and 124 patients with stable COPD. The geometric mean of troponin T in acute exacerbations of COPD was around five-fold higher than in stable controls (25.8 *versus* $4.5 \text{ ng}\cdot\text{L}^{-1}$, respectively), thus suggesting a possible role of this biomarker in the diagnostic definition of acute exacerbations of COPD.

Comorbidities and prognosis in COPD

The link between osteoporosis and cardiovascular disease in COPD patients was underlined by ROMME *et al.* [10]. In their

study, computed tomography (CT) measured by bone radiodensity and its relationship with coronary artery calcification score (by the Agatston and MESA (Multi-Ethnic Study of Atherosclerosis) scores from the CT scan) were assessed in the ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints) study cohort. Bone radiodensity correlated with age ($r = 0.267$, $p < 0.001$), FEV1 ($r = 0.08$, $p = 0.010$), body mass index, BODE (body mass index, airflow obstruction, dyspnoea, exercise capacity) index, and the Agatston and MESA scores ($r = -0.252$, $p < 0.001$ and $r = -0.197$, $p < 0.001$, respectively). Low bone radiodensity may be associated with high coronary artery calcification score and adverse clinical outcome.

In a follow-up survey, HAARMANN *et al.* [11] investigated if the increased sympathetic nerve activity (microneurographic recordings) was associated with elevated morbidity and mortality in COPD patients. Significant increase in muscular sympathetic nerve activity was found in patients who were hospitalised or deceased compared to those who lived without hospitalisation (60.3 *versus* $40.5 \text{ burst}\cdot\text{min}^{-1}$; $p = 0.022$), thus increased sympathetic nerve activity is probably associated with elevated risk of morbidity/mortality in this population.

The link between bacterial colonisation and airways inflammation was investigated by SINGH *et al.* [12], who assessed the bacterial load of *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae* by quantitative PCR in the sputum of 18 consecutive patients with stable COPD. The degree of airway inflammation was recorded by interleukin (IL)-1 β and IL-8 levels (ELISA). Inflammation was higher with increasing bacterial load in the sputum, thus suggesting the probable importance of infection in the COPD pathogenesis.

Anaemia is known to be common in chronic diseases, but data on the effects of anaemia are still scarce and inconclusive in the COPD population. Due to this, LAINSCACK *et al.* [13] reviewed the ECLIPSE study cohort and included 123 patients with haemoglobin measurement both at baseline and at least once during the 3-year follow-up. Anaemic individuals were older, had greater functional limitations (lower 6-min walking distance, higher Medical Research Council dyspnoea score and BODE score, and worse St George's Respiratory Questionnaire) and systemic inflammation, and were more likely to die during the follow-up (24% *versus* 9%) than those with normal haemoglobin.

Finally, STOLZ *et al.* [14] evaluated the role of serum pro-adrenomedullin, a stable peptide of the precursor of adrenomedullin, in predicting the risk of death in COPD patients. They prospectively studied 638 stable subjects in pulmonary tertiary hospitals from eight European countries. The death rate from any cause or from respiratory disease at 24 months and from respiratory disease was higher in patients with higher pro-adrenomedullin levels. The addition of this biomarker to the BODE index improved its performance in predicting mortality, even suggesting a possible role of pro-adrenomedullin in predicting the risk of death in the COPD population.

REHABILITATION AND CHRONIC CARE

Multiple interesting abstracts representative of the updated and relevant topics in the area of rehabilitation and chronic care were presented at the ERS Congress in Vienna. The best studies in this area were presented in two sessions. New data were especially presented on the characterisation of metabolic abnormalities and exercise-induced changes in skeletal muscles of COPD patients and healthy elderly subjects. Novel data on changes of physical activity in the COPD population over a longitudinal observation were also presented.

Lower limb muscle dysfunction and intramuscular abnormalities occur frequently in people with COPD [15, 16] and may, at least in part, be caused by a significant reduction in daily physical activity [17]. POLKEY *et al.* [18] showed that people with COPD had significantly prolonged phosphocreatine recovery time and lower nadir intramuscular pH in the quadriceps muscle as compared to healthy elderly subjects, while biceps brachia muscle metabolism was not different between groups. These results suggest that anaerobic metabolism is confined to the quadriceps muscles in COPD and that the objectified daily arm activities will most probably be preserved in people with COPD compared to healthy elderly subjects.

GIAVEDONI *et al.* [19] reported a reduced mitochondrial density in the vastus lateralis muscle of COPD patients compared to healthy elderly subjects, in particular in patients who also have an abnormal low fat-free mass index. These results expand our understanding of the complex underlying intramuscular mechanisms that may contribute to a lower muscle oxidative capacity in COPD patients, as described previously [17].

Our current knowledge about the effects of exercise-based pulmonary rehabilitation on intramuscular abnormalities in COPD patients are limited [20]. GOUZI *et al.* [21] reported a blunted muscle angiogenic response following a 6-week exercise training programme in patients with COPD compared to sedentary healthy elderly subjects. The underlying reasons for the impaired muscle angiogenic response remain to be determined before new therapeutics can be considered. Indeed, skeletal muscle gene and protein expression of pro- and anti-angiogenic factors should be studied following acute exercise and prolonged exercise training to better understand training-induced angiogenesis [22]. Moreover, the possible influence of muscle oxidative stress and/or low-grade systemic inflammation on exercise-induced angiogenesis warrants further research.

HEINZELMANN *et al.* [23] showed small but significant increases in quadriceps muscle capillarisation following a 3-week inpatient pulmonary rehabilitation programme, in particular in patients with the highest degree of airflow limitation. Even though these preliminary data show early intramuscular changes, exercise-based pulmonary rehabilitation programmes of a longer duration have been shown to result in even greater intramuscular changes [20, 24]. Moreover, the sustainability of intramuscular changes following exercise-based pulmonary rehabilitation remains to be determined in COPD patients.

Physical inactivity has been shown in COPD patients compared to healthy elderly subjects [16]. Nevertheless, the changes in physical activity over time have not yet been reported in people with COPD. WASCHKI *et al.* [25] presented

new data on the change in objectified physical activity over 3 years in these patients. On average, total daily energy expenditure, physical activity level and steps per day decreased significantly compared to baseline across all stages. Obviously, the determinants of physical activity decline and its clinical relevance remain to be elucidated. Nevertheless, these novel data confirm the need for interventions, such as an exercise-based pulmonary rehabilitation programme [26], an exercise counselling programme [27] or simply after motivational support [28], to achieve sustainable physical activity behaviour change in COPD patients.

CHEST IMAGING

Over the past years the paradigm of medical imaging has shifted from gaining pure morphological information to a combination of morphological and functional information. Functional imaging is more and more frequently achieved in COPD patients by CT and magnetic resonance imaging (MRI). Moreover, ¹⁸F-2-fluoro-2-deoxy-D-glucose-positron emission tomography (¹⁸FDG-PET) imaging for assessment of inflammatory diseases and the noninvasive pressure assessment by MRI are being more frequently studied.

Morphological and functional imaging

CT is the technique of choice for noninvasive assessment of the lung. However, with broad availability of multi-slice CT scanners the classic high resolution-CT (HRCT) technique is less frequently applied as shown by a European survey [29]. Most institutions (77%) acquire a volumetric dataset with reconstruction of thin slices (<3 mm). Expiratory scans or scans in the prone position were performed only upon demand by a majority of the respondents (58% and 59%, respectively).

Inhalation of toxins for multiple hours per day, such as using biomass as fuel during food preparation, may lead to signs and symptoms of COPD. HRCT findings of 20 patients with biomass COPD were compared to findings in 34 patients with tobacco-smoke COPD [30]. Biomass COPD caused primarily pure forms of emphysema (either centrilobular or panlobular) compared to tobacco-smoke COPD. The emphysema index was significantly worse in tobacco-smoke COPD, thus suggesting that tobacco smoke may be more aggressive and lead to more parenchymal destruction than other forms of inhaled toxins.

Insights in regional lung function were gained by MRI. By using hyperpolarised Helium-3 it was possible to directly visualise the ventilation in 10 COPD patients [31]. A spectrum of normal, delayed or no ventilation was found. This information was then matched with the MRI perfusion datasets, thus showing areas with delayed ventilation (caused by collateral ventilation, partial obstruction, lung hyperinflation or a mixture of such mechanisms) and maintained perfusion, and other areas with no perfusion. This was the first study demonstrating the possibility of direct visualisation of the local match/mismatch of ventilation/perfusion.

Imaging of the lung parenchyma using MRI still remains challenging. In 12 COPD subjects the MRI signal of the lung parenchyma was correlated to the CT-derived lung density and a good linear agreement was found ($r^2=0.8$) [32]. The patients were examined by MRI a second time, 1 week apart, and a high repeatability was found. Data suggest that it might

be possible to use MRI for monitoring lung parenchymal changes in COPD.

Other imaging techniques

¹⁸FDG-PET is an interesting technique for assessment of functional information, based on glucose metabolism. This metabolism is increased in oncological and inflammatory diseases. In COPD patients this feature can be used to study inflammation of the peripheral airways. Indeed, the activated neutrophils accumulate ¹⁸FDG, and ¹⁸FDG uptake was increased by 9% in current smokers as compared to never-smokers [33]. Chronic inflammation in smokers leads to the development of centrilobular emphysema. In 10 COPD patients the ¹⁸FDG uptake correlated well with the corresponding pulmonary function test results and CT-based densitometry results [34].

MRI is also an important tool for assessment of the right ventricular heart function; however, right heart catheterisation is mandatory for pressure and output assessment. In 65 patients with pulmonary hypertension, right heart catheterisation and MRI were performed within 12 h [35]. The predicted (by the derived equation: mean pulmonary artery pressure = 33.4 + (right ventricular end-diastolic mass index ($\text{g}\cdot\text{cm}^{-2}$) \times 1.21) - (pulmonary artery average velocity ($\text{cm}\cdot\text{s}^{-1}$) \times 0.99)) and the invasively measured mean pulmonary artery pressure were strongly correlated ($r^2=0.74$; $p<0.0001$). In another study, 55 patients with COPD-associated pulmonary hypertension were investigated by cardiac MRI and followed for a period of 44 months [36]. Stroke volume, as assessed by phase contrast flow measurements in the main pulmonary artery, was a good predictor of mortality, with the cut-off of $<40\text{ mL}\cdot\text{m}^{-2}$ being a strong predictor of adverse outcome.

Taken together, these new data encourage the use of MRI assessment of the right heart to provide useful information on the presence and the progression of COPD-associated pulmonary hypertension.

INTERVENTIONAL PULMONOLOGY

Interventional bronchoscopy gets more and more interesting. This year, two main fields were covered in the abstract presentations, namely potential indications of new techniques

in the field of obstructive lung diseases and the use of endobronchial ultrasound (EBUS).

Obstructive lung diseases

Evidence that endoscopic lung volume reduction may contribute to the management of patients with COPD is accumulating. Notwithstanding, the various approaches require different patient's conditions, and indications must be strictly followed to achieve the expected benefits. Therefore, treatment algorithms are necessary to identify the ideal candidate for each technique. Patients fulfilling the inclusion criteria with severe emphysema (severe COPD, HRCT, body plethysmography, diffusing capacity measurements and 6-min walk test) are selected by those measurements to the different modalities [37].

The therapeutic strategies may vary in patients with severe emphysema and reversible blocking techniques, or irreversible non-blocking techniques can be distinguished. The application of these techniques is dependent on the emphysema distribution and the degree of collateral ventilation. Fissure integrity is a clear predictor of success for strategies involving endobronchial valves (Pulmonx, Neuchatel, Switzerland and Olympus Medical, Tokyo, Japan) [38]. A catheter-based measurement, the Chartis system (Pulmonx), can be helpful to evaluate the degree of collateral ventilation [38]. In a symposium held during the ERS Congress, unpublished data from a European multicentre trial were presented showing that a response rate of 80% to seek fissure integrity can be achieved with the help of Chartis [39].

Data from the European VENT (Endobronchial Valve for Emphysema Palliation Trial) trial [38] demonstrated that, in patients undergoing lobar occlusion, FEV1 and quality of life score (St George's Respiratory Questionnaire) improved dramatically at 6 months (table 1). The main complication of this procedure was the risk of pneumothorax; however, early data suggest that this adverse event might also be a predictor of the success of the procedure [40].

Another approach is the implantation of lung volume reduction coils (PneumRx, Inc., Mountain View, CA, USA), consisting of a nitinol wire of preformed shape that results in parenchymal compression and volume reduction. DESLEE *et al.* [41] reported that patients may have a greater benefit with this

TABLE 1 Results of the European VENT (Endobronchial Valve for Emphysema Palliation Trial) at 6 months

	Complete fissures [#]			Control
	Lobar occlusion	No lobar occlusion	p-value	
Subjects n	20	17		19
Δ FEV1 %	26 \pm 24	6 \pm 12	0.004	3 \pm 14
Δ cycle ergometry workload W	8 \pm 15	0 \pm 14	0.10	-3 \pm 7
Δ 6-min walk distance %	22 \pm 38	-2 \pm 19	0.03	19 \pm 54
Δ St George's Respiratory Questionnaire point	-10 \pm 15	-2 \pm 14	0.2	3 \pm 15

Data are presented as mean \pm SD, unless otherwise stated. FEV1: forced expiratory volume in 1 s. [#]: n=56. Reproduced from [38].

technique, especially those selected for having homogeneous emphysema [42].

Finally, updates with an alternative method, the use of bronchoscopic thermal vapour ablation (Uptake Medical, Seattle, WA, USA), were presented this year [43]. It seems that a so-called heterogeneity index is important to select the most accurate patient; the severity of induced inflammation seems to be an important factor for the success of this technique.

Endobronchial ultrasound

Worldwide, the EBUS technique is accepted as the new gold standard for diagnosing and staging mediastinal lesions, especially in the era of targeted therapy for lung cancer, and new insights were discussed during the ERS Congress. Molecular testing of EBUS-transbronchial needle aspiration (TBNA) samples obtained from mediastinal and hilar lymph nodes is feasible, with a high adequacy rate (92%) [44]. Rapid-on-site evaluation and cell block techniques was also discussed. The cytological diagnosis of lymph node metastases depends on many variables such as the number of passes made at each station, access to rapid-on-site evaluation or type of sample processing. When comparing the different options for specimen handling, it was reported that the cell block technique has a high correlation with cytology, but adds only few new diagnoses. Moreover, access to rapid-on-site evaluation avoids nearly 47% of TBNA procedures, based on a positive predictive value of 100% [45]. Therefore, most centres are currently shifting to the cell block approach.

Complications of EBUS-TBNA remain low despite a more precise evaluation and a growing number of procedures. Most complications are associated with the modality of conscious sedation (over-sedation requiring antidotes or failed sedation), usually not related to EBUS *per se* (bronchospasm). No long-term adverse effects were observed following EBUS-TBNA [46].

DIFFUSE PARENCHYMAL LUNG DISEASES

Advances in idiopathic pulmonary fibrosis (IPF), sarcoidosis and lung involvement in systemic diseases were discussed in much detail at the ERS Congress in Vienna.

Idiopathic pulmonary fibrosis

In recent years, pathogenetic mechanisms leading to lung derangement, honeycombing and definitive lung failure were more deeply understood. Alveolar stem-cell exhaustion and abnormal activation of proliferative pathways are the key elements involved [47, 48]. Genetic studies of familial and sporadic cases of IPF have recently allowed to assimilate a proportion of IPF cases to telomeropathies [49], including lung cancer [50].

Progresses have been made in the understanding of the natural course of this heterogeneous disorder. A simple-to-use staging system for IPF based on sex, age and physiology (GAP index) has been shown to be helpful in improving prognostication, guiding management and facilitating research [51], whereas addition of data obtained by CT scan does not improve the predictive value of the GAP index [52]. Endoscopic biopic procedures seem to obviate, in the majority of cases, the need for surgical biopsy to assess the usual interstitial pneumonia pattern [53]. The therapeutic options for IPF are still an area of active research. Analysis of physiological parameters and of

long-term survival in patients treated with pirfenidone included in the long-term extension RECAP study (following the phase III, randomised pivotal trials CAPACITY) further confirmed the utility of this drug [54]. Some encouraging data are inferable by the phase II study using an anti-connective tissue growth factor monoclonal antibody [55] or by using recombinant thrombospondin during acute exacerbations of IPF [56].

To evaluate the current practice of IPF management in the context of recent 2011 international guidelines, COTTIN *et al.* [57] conducted a survey among lung specialists in France. Out of 1456 pulmonologists, 35% were involved in the management of IPF patients and 36% discussed the cases with radiologists and pathologists. One-third of pulmonologists working in the community referred patients to specialised centres. The guidelines were known by 67% of specialists involved in IPF, with 84% of them considering this document appropriate for practice. Overall, this survey showed that, despite awareness of international IPF guidelines, multidisciplinary discussion and early diagnosis need to be improved through the network of expert centres.

Sarcoidosis

The most important challenges in patients with sarcoidosis relate to the accurate assessment of pulmonary and extrapulmonary organ involvement, and treatment options in difficult cases. Although it may not be a generalisable approach, ¹⁸F-DG-PET, if appropriately indicated, can provide valuable information and contribute to optimise treatment [58]. Whole-body MRI has been shown to provide additional information regarding extrapulmonary organ involvement, and depicted manifestations of extrapulmonary sarcoidosis in 38% of cases in an unselected cohort [59]. Abnormal whole-body MRI findings correlated with high clinical scores. In particular, abnormal skeletal findings correlated with decreased lung volumes and might, therefore, be a marker of general disease activity.

A 16-week therapy using bosentan for pulmonary arterial hypertension-associated with sarcoidosis resulted in a significant reduction in mean pulmonary artery pressure and pulmonary vascular resistance as compared with placebo. Sustained changes were reported in patients with a forced vital capacity <70% of predicted, confirming that even advanced parenchymal lung disease may respond to vasodilator therapy [60].

The link between *Tropheryma whipplei* bacteria and histologically confirmed sarcoidosis was retrospectively assessed in 56 patients [61]. *T. whipplei* RNA was detected by PCR in formalin-fixed and paraffin-embedded specimens in two (3.6%) out of 56 subjects, suggesting the hypothesis that it might play a role in the pathogenesis of sarcoidosis.

Lung involvement in systemic diseases

Pulmonary involvement in patients with Marfan syndrome, an autosomal connective tissue disorder caused by mutations in the gene coding for the extracellular matrix protein fibrillin 1, has been reviewed by CERVERI *et al.* [62]. Both lung function and CT scan were considered highly relevant for the assessment of this condition. Out of 14% of patients who reported a history of pneumothorax, 11% had radiological

signs of emphysema and 32% had apical blebs. Only 37% of them had normal lung function, with restrictive or obstructive patterns in 19% and 44% of them, respectively.

Patients with coexisting granulomatosis with polyangiitis and Crohn's disease were reported by VASZAR *et al.* [63]. Four patients were identified in the Mayo Clinic (Scottsdale, AZ, USA) medical records in whom the diagnosis of Crohn's disease preceded that of the systemic vasculitis [63]. Chest imaging showed pulmonary nodules, with necrotising granulomatous inflammation and segmental vasculitis at histopathological examination. The authors suggested that this association may not be a coincidental finding, and may be suspected in the event of pulmonary abnormalities in patients with Crohn's disease, or the presence of granulomatous colitis in patients with granulomatosis with polyangiitis (Wegener's).

GENERAL PRACTICE AND PRIMARY CARE

In the field of general practice and primary care, several sessions during the Primary Care Day at the ERS Annual Congress reported on: recent insights on the importance of multimorbidity; the challenge of establishing an early but valid diagnosis, even in the setting of scarce resources; and on how to organise an appropriate disease management programme for patients with asthma or COPD.

Importance of multimorbidity and early diagnosis

LISSPERS *et al.* [64] presented an 11-year epidemiological register study, describing the natural history of >21 000 COPD patients from Sweden between 1999 and 2009. During this period, COPD was, to a larger extent, first diagnosed in primary care (from 59% to 81%), while the mean age at diagnosis decreased by 7 years from 73 to 66 years and the exacerbation rate from 3.0 to 1.3 exacerbations per patient per year. Co-diagnosis of diabetes increased from 12% to 19%, heart failure from 16% to 26%, and lung cancer from 0.94% to 1.47%, while the mean life expectancy was 8.3 ± 6.8 years shorter than for the average Swedish population. HEEREMA-POELMAN *et al.* [65] investigated the adherence to a maintenance exercise programme after pulmonary rehabilitation, which amounted to 73.3% and 63.3% after 6 and 12 months, respectively. Predictors for drop-out were poorer for lung function ($p=0.021$), longer duration of rehabilitation ($p=0.018$) and higher levels of depressive symptoms ($p=0.025$) as assessed by the Hospital Anxiety and Depression Scale.

In a huge effort, APTE *et al.* [66] investigated over 204 000 Indian patients visiting 7 400 randomly selected doctors across 22 states for a 1-day point-prevalence study. No less than 50% of patients presented with respiratory symptoms, 25% with gastrointestinal symptoms and 18% cardiovascular symptoms. Extrapolating these results, respiratory symptoms may account for at least 20 million patient visits per day in India. HARRIS *et al.* [67] evaluated the validity of spirometric testing performed in the community in 405 patients with abnormal screening spirometry and adults with a history of smoking, followed by repeat spirometry in the hospital pulmonary function laboratory. Out of 405 patients, 82% had obstructive spirometry, with 45% having moderate obstruction, while 32% and 11% were found to have severe and very severe COPD,

respectively. The mean FEV₁ was slightly higher when the spirometry was performed in the community (1.52 L) than in a pulmonary function laboratory (1.49 L), confirming earlier findings [68].

Finally, LOPEZ-GIRALDO *et al.* [69] studied lung function abnormalities (by spirometry, diffusing capacity of the lung for carbon monoxide, blood gases and body plethysmography) in 63 patients with heart failure and preserved left ventricular ejection fraction. Lung function was abnormal in 88% of patients; 30% had evidence of airflow limitation, 16% had a restrictive pattern, 82% an altered diffusion capacity, and 67% had unexpected significant hypoxaemia. These findings suggest a very high rate of lung abnormalities in patients with subclinical heart failure.

Disease management

In a systematic review, BOLAND *et al.* [70] investigated whether disease management programmes for COPD are cost-effective. Disease management decreases the risk of hospitalisation and healthcare costs substantially, but more studies on total costs and cost-effectiveness in different settings are still needed. SUNDH *et al.* [71] found that scheduling an extra visit to an asthma/COPD nurse following an exacerbation decreased the risk of re-exacerbations in 775 COPD patients during a 4-year follow-up. Therefore, they recommended close co-operation between healthcare professionals to prevent acute exacerbations of COPD in primary care. SYK *et al.* [72] presented the results of a randomised controlled multicentre trial assessing exhaled nitric oxide fraction (FeNO)-guided anti-inflammatory treatment in nonsmoking asthmatics (aged 18–64 years) with perennial allergy and regular inhaled corticosteroid treatment. In this primary care study, adjustment according to FeNO and for a given use of inhaled corticosteroids led to an improved asthma control questionnaire score and to a significantly lower cumulative incidence of acute exacerbations driven by a reduction in moderate episodes. Finally, in Thailand, BOONSAWAT *et al.* [73] reported that the "Easy Asthma Clinic Network" was effective in reducing, by almost 60%, the rate of hospitalisation for asthma, mainly due to usage of simplified asthma guidelines. The authors further emphasised the important role of nurses and pharmacists [73].

OTHER SELECTED CLINICAL PROBLEMS

Further to pulmonary rehabilitation, the ERS Rehabilitation and Chronic Care Group also presented several aspects of chronic care, including the end-of-life. VASKE *et al.* [74] reported novel data regarding end-of-life fears, which occurred in ~50% of 132 COPD patients entering an inpatient rehabilitation programme. Biomedical variables and mental status did not explain the variance for fear of dying and fear of death when dyspnoea-related fear was included in a multiple regression model. These data suggest that psychotherapeutic interventions for people with COPD may influence their fear of dying. Moreover, JANSSEN *et al.* [75] examined 1-year changes in the patients' preferences regarding the place of death among 265 patients with advanced chronic diseases (COPD, heart failure and renal

failure). During 1-year follow-up, a majority of the patients changed their preference for the place of death, with only 40% eventually dying where they had previously indicated as preferred. Data suggest that it is not possible to prepare advance directives concerning the preferred place of death.

KAUFMAN *et al.* [76] interestingly evaluated the role of nerve transplantation in the management of symptomatic diaphragm paralysis. The study included 30 patients presenting with chronic, phrenic nerve injuries following surgery, chiropractic manipulation, trauma or anesthetic block and failing to improve during 6 months of conservative management. Reversal of diaphragm paralysis was clearly demonstrated in 77% of patients, and the surgical intervention was free of pulmonary or cardiac complications. Thus, phrenic nerve transplantation should be considered as a therapeutic option in the management of symptomatic diaphragm paralysis in selected patients.

STATEMENT OF INTEREST

Conflict of interest information can be found alongside the online version of this article at www.erj.ersjournals.com

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