

Preface

Chronic obstructive pulmonary disease (COPD) is a world-wide problem that is increasing in prevalence. COPD is a chronic lung disease characterised by persistent airflow limitation that is not fully reversible. COPD is the third leading cause of death world-wide. It is a heterogeneous disease, with multiple aetiological factors, clinical phenotypes and comorbidities. Acute exacerbations and progressive decline in lung function contribute to symptoms and outcomes. It is vitally important that we develop a deeper understanding of this complex chronic disease, in order to enhance the preventive and therapeutic strategies for patients with COPD, with the ultimate goal of effective management using a “personalised medicine” approach.

This ‘Hot Topics in COPD’ Supplement of the *Journal of Thoracic Disease* addresses innovative and emerging areas at the leading edge of our understanding of COPD, in the fields of pathogenesis (microbiome, biomarkers, inflammation), diagnosis (spirometry, imaging) and treatment (guidelines, self-management, pulmonary rehabilitation, anxiety and depression, oxygen therapy, lung transplantation and other emerging therapies). We thank the authors who, as leading researchers in these areas, have contributed state-of-the-art reviews and perspectives of these critical topics.

The lung microbiome

The lung was previously thought to be a sterile organ in health; however, this is now known not to be the case. The bacterial communities present in the normal lung, collectively called the lung microbiome, have important implications for patients with COPD. Chambers and colleagues (1), in their invited perspective, alert us to the potential role of the lung microbiome in COPD, particularly in pathophysiology, cellular and molecular biology, and clinical phenotypes. Their article calls for a greater appreciation of the impact of altered microbial diversity in the lung, through the use of novel culture-independent techniques to identify all of the microbes present in COPD lung. In this way, patterns of bacterial diversity can be better understood in COPD, with a view to developing treatment approaches that would rebalance bacterial communities in the lung.

Emerging biomarkers for COPD

Given the complexity of COPD as a chronic disease, the development of biomarkers would be useful for detecting the presence of COPD, characterising COPD phenotypes, and monitoring response to treatment. Shaw and colleagues (2) have catalogued the remarkably large number of biomarkers associated with various aspects of the pathogenesis and clinical manifestations of COPD. When focussing particularly on predicting the rate of disease progression, the numbers of biomarkers are far fewer. Their review appraises the current knowledge about radiological, sputum, blood, exhaled breath and other biomarkers for COPD, including those linked to response to air pollution or ageing.

Insights into chronic lung inflammation

COPD is characterised by persistent and excessive inflammation, both in the lungs and systemically. In their review, Bozinovski and colleagues (3) argue that specific mediators fail to turn off the excessive inflammation that is present in COPD. This has implications for the recruitment and survival of inflammatory cells within the airways, leading to a heightened and prolonged chronic inflammatory response. They provide evidence that multiple mediators converge on a central receptor system (ALX/FPR2) of the N-formyl peptide receptor family. Future non-steroid-based treatments targeting inflammation could therefore be developed (including analogs that stimulate this receptor), to promote resolution of chronic inflammation in the lung.

Advances in spirometry

The spirometric measures of FEV₁ and FVC remain the cornerstone of the diagnosis of well-established COPD. The underutilisation of spirometry in primary care can delay the recognition of COPD. This in turn can delay advice to avoid

aggravating factors such as smoking and can delay commencement of therapy, thereby contributing unnecessarily to the burden of this disease. Extensive small airway disease can develop before traditional spirometric indices become abnormal. An interesting new approach to the early recognition of small airways disease described Johns and colleagues (4) involved measuring indices of curvature of the expiratory limb of the flow-volume loop. It has yet to be shown whether intervention at this early stage can reverse the pathological processes or slow the rate of progression of the airways or parenchymal involvement.

Functional lung imaging

A number of imaging modalities are available to characterise the structure of the lung, to define morphological abnormalities in COPD. However, advancing imaging techniques are now being used to identify physiological consequences of COPD i.e., both structural and functional changes. Stephen Milne and Greg G. King (5) describe CT- and nuclear medicine-based techniques, as well as highly novel approaches such as micro-CT, synchrotron imaging, optical coherence tomography and electrical impedance tomography. As these techniques are developed further and applied clinically, greater accuracy will be available to measure lung mechanics and ventilation/perfusion abnormalities in COPD, to increase our understanding of lung pathophysiology, enable subphenotyping of COPD, and to monitor changes with treatment.

Improving uptake of clinical guidelines for COPD

Adherence to treatment guidelines has been shown to be surprisingly suboptimal by clinicians treating patients with COPD. The production of management guidelines involves an inherent assumption that compliance with the recommendations contained in such guidelines will produce tangibly improved outcomes for individuals with COPD. The evidence for this is well-established as reported in the review by Overington and colleagues (6), and centres mainly on strong engagement with clinicians about guidelines, effective dissemination and integrated systems for their implementation. Hence it is reasonable to expect that enhanced uptake of guideline recommendations into everyday practice would improve clinical outcomes for COPD, through more successful prevention, earlier detection, and better management to slow disease progression and reduce complications.

New developments in self-management of COPD

Self-management is an important element of the chronic disease management of patients with COPD. It is now increasing recognised that the patient's multi-morbidities also impact significantly on self-management strategies. Effing and co-workers (7) describe their efforts to improve on traditional self-management programs, by including action plans for common comorbidities (e.g., heart failure, ischaemic heart disease, metabolic disease, and psychological factors). They outline practical approaches to behavioural change in patients, and highlight safety features such as access to case managers. Ultimately, the goal is a fully integrated, holistic approach that is patient-focused, yet supported by health care professionals in primary and tertiary care.

Improving access to pulmonary rehabilitation

Pulmonary rehabilitation is of proven benefit for symptomatic patients with COPD, with reductions in symptoms, improvements in exercise capacity and quality of life, and decreased rate of hospital admissions. However, access to pulmonary rehabilitation programs is difficult, due to limited resourcing. In their systematic review, Jennifer A. Alison and Zoe J. McKeough (8) provide evidence for the efficacy of exercise training using minimal equipment. Although the number of clinical trials in this specific field was relatively small, the pooled differences showed benefit in terms of improved six minute walk distance and improved St. George's Respiratory Questionnaire for health-related quality of life. This timely systematic review sets the scene for further, large-scale studies of minimal equipment pulmonary rehabilitation programs.

Managing anxiety and depression as comorbidities of COPD

As described in the review by Pumar and co-authors (9), the presence of anxiety and depression in COPD patients has been shown to be associated with increased mortality, exacerbation rates, length of hospital stay, and decreased quality of life and functional status. It is not yet known, however, whether anxiety and depression are independent predictors of outcome. The authors highlight that there is currently no consensus on the most appropriate approach to screening for anxiety and depression. Furthermore, the most effective treatment modalities have not yet been ascertained by rigorous studies. However, it is likely that patients will certainly benefit symptomatically from early recognition and appropriate intervention. Whether COPD-specific outcomes can be enhanced by treating anxiety and depression is still to be determined.

State-of-the-art use of oxygen therapy for COPD

The use of long-term oxygen therapy in COPD patients with resting hypoxaemia is well-established. Nevertheless, the evidence for its use in milder severities of hypoxaemia is not as certain. In her wide-ranging review, Christine F. McDonald (10) re-examines the landmark studies of long-term oxygen therapy in COPD, with critical appraisal of study design and in the context of other advances in management of COPD. The evidence for use of supplemental oxygen in nocturnal or exertional hypoxaemia is not as clear. Other situations for potential use of oxygen therapy in COPD are evaluated, including palliative care, acute exacerbations and during pulmonary rehabilitation. This helpful review ends with a call to action for multicentre data registries and larger prospective trials of oxygen therapy (including placebo arms) for specific subgroups of COPD patients.

Lung transplant and novel bronchoscopic therapies for COPD

Treatment of advanced lung disease has long been a focus of clinicians, clinical researchers and policy-makers. Trotter and co-authors (11) provide an interesting discussion of ‘what’s on the horizon’ for lung volume reduction and lung transplantation for patients with COPD. They provide an insight into emerging bronchoscopic lung volume reduction techniques that have been recently implemented or are emerging. These include endobronchial valve therapy, bronchial thermal vapour ablation and lung volume reduction coils. Advances in lung transplantation selection, surgery and medical management are outlined, including successful reconditioning of marginal donor organs using *ex vivo* lung perfusion. Fortunately, these established and emerging therapies are now increasing the management options for patients living with advanced COPD.

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