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Journal club

Supportive care of patients with fibrosing interstitial lung disease: answering a great clinical need

Commentary on:

Wijsenbeek MS, *et al*. Comprehensive supportive care for patients with fibrosing interstitial lung disease. *Am J Respir Crit Care Med* 2019; 200: 152–159.

Context

The fibrosing interstitial lung diseases (F-ILDs) are a heterogeneous group, including idiopathic pulmonary fibrosis (IPF), connective tissue disease-associated interstitial lung disease, hypersensitivity pneumonitis and asbestosis, among others. The common feature of all F-ILDs is the irreversible replacement of normal lung parenchyma with scar tissue, resulting in impaired gas exchange and culminating in respiratory failure.

The commonest F-ILD, IPF, has a poor prognosis and an increasing incidence, and thus F-ILD is associated with increasing mortality and disease burden worldwide [1, 2]. F-ILDs are frequently progressive with a plethora of symptoms, causing an increasing impact on patients' quality of life. While a significant proportion of research has focussed on the development of disease-modifying therapies to halt disease progression, many of these drugs were not beneficial in clinical trials [3]. Furthermore, while nintedanib and pirfenidone have revolutionised the field by slowing the progression of IPF [4, 5] and possibly other forms of F-ILD [6–9], these antifibrotics are associated with significant side-effects and have proven efficacy in certain patient groups only. Therefore, a shift in focus from life-extending treatment to improving quality of life is essential in the real-world management of F-ILD.

Methods

In this perspective article, the authors summarise the care needs of patients with F-ILD [10], and describe an ideal supportive care programme to meet these needs. Wijsenbeek *et al*. give a detailed analysis of the barriers that impede the successful implementation of comprehensive supportive care in F-ILD. Given the relative paucity of controlled interventional studies in this area, the authors draw upon their experiences as well as the published literature, and define several priority areas for further research.

Main results

In qualitative studies, patients with F-ILD and their caregivers identified their primary needs as including a timely diagnosis, ILD-specific education and support programmes, good symptom control, access to pulmonary rehabilitation, and end-of-life care (EOLC) [11]. Wijsenbeek *et al*. used this as the

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Fibrosing interstitial lung disease (F-ILD) significantly reduces quality of life. F-ILD care includes symptom management, end-of-life planning and supportive measures, as well as antifibrotics. Patients and carers should be central to all care decisions. https://bit.ly/2ZAE2Ks

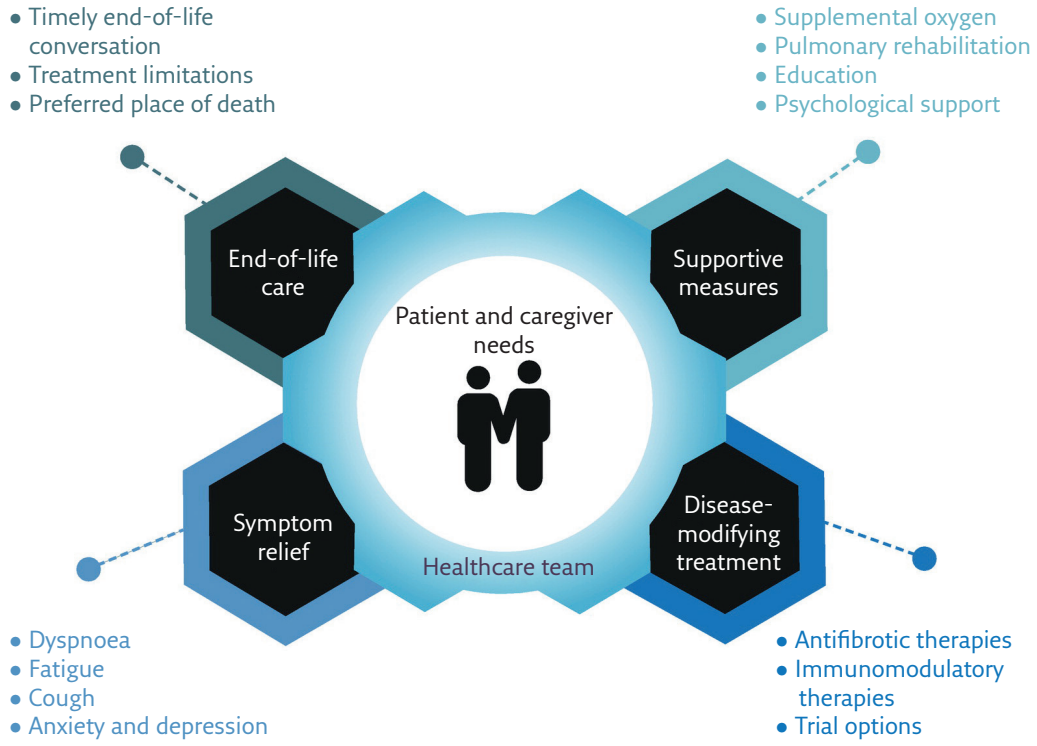

Figure 1 *A multifaceted approach to the comprehensive supportive care of F-ILD. Comprehensive supportive care of F-ILD comprises four categories of clinical approaches: end-of-life care, supportive measures, disease-modifying treatment and symptom relief. These approaches should be taken with close collaboration between patients, caregivers, and the healthcare team. Reproduced from [10] with permission of the American Thoracic Society. Copyright © 2020 American Thoracic Society. The* American Journal of Respiratory and Critical Care Medicine *is an official journal of the American Thoracic Society.*

basis for their optimal F-ILD care model, where antifibrotics, symptom management, supportive measures and EOLC take equal importance in the management of F-ILD (figure 1). In the centre of this multifaceted care model is the partnership between the patient, their caregivers and the healthcare team in making treatment decisions. The authors propose that individualised care plans should be formulated using this model treatment framework, in order to meet the complex needs of F-ILD patients.

While describing their idealised F-ILD supportive care model, Wijsenbeek *et al.* also candidly acknowledge the many barriers to achieving such a system in practice, including poor awareness of interstitial lung disease among the public and healthcare professionals, inequality of access to services such as oxygen and pulmonary rehabilitation, the refractory nature of F-ILD symptoms, and discomfort around EOLC discussions. The authors suggest several solutions to overcome these barriers, the common themes of which consist of disease-related education of patients and healthcare workers, increased research efforts, improved and equitable access to F-ILD services, and standardised treatment and referral pathways. Collaboration is a key theme underlying comprehensive supportive care of F-ILD, including a multidisciplinary team care approach to patient care, and multicentre research collaborations to improve the evidence base to guide treatment decisions.

Commentary

Wijsenbeek *et al.*'s proposal for an idealised supportive care system for F-ILD patients is comprised of simple components that are well-established in the interstitial lung disease clinic. However, the literature emphasises that many F-ILD patients and their caregivers feel that their needs are not always met, and it is likely that access to many aspects of care varies between healthcare systems. There are several examples of healthcare system-specific factors that may influence patient access to supportive care, including the availability of resources such as home oxygen delivery equipment and pulmonary rehabilitation, as well as local skills and knowledge. The authors suggest methods to improve access to supportive care for F-ILD patients; however, it is impossible to cover all potential situations, and it is for the reader to integrate the features of the optimal care model into their own practice.

Timely diagnosis was emphasised as an important unmet need of F-ILD patients [11]. Most ILD patients experience delays in diagnosis (43% delayed over 1 year and 19% over 3 years in one cohort [12]), often with early misdiagnosis and thus mismanagement. These data emphasise the need for education of primary and secondary care providers on F-ILD to improve the patient experience.

In addition to education for healthcare professionals, patients and their caregivers

are keen to have access to information on their condition, including the management plan and likely prognosis [10, 13]. Peer- and professional-led F-ILD education and support programmes, where patients and caregivers gain information about their condition, are key components of Wijsenbeek *et al.*'s care model. These programmes are valued by patients and their caregivers; however, the evidence for them is currently lacking [10]. Conversely, pulmonary rehabilitation programmes, which often include an educational component alongside physical exercise, have been shown to improve exercise tolerance and quality of life in IPF [14, 15]. Furthermore, pulmonary rehabilitation is beneficial even in advanced IPF [14] and, therefore, should be considered at every stage of the disease. The combination of physical exercise and comprehensive patient education is likely to represent a cost-effective way to meet multiple F-ILD patient needs and work is ongoing to assess effectiveness [16].

The progressive nature of many F-ILDs means that planning for patient deterioration should occur early in the disease course. The authors propose a compassionate and pragmatic approach, with close involvement of patients and their caregivers in decision making. This should involve discussions about treatment, both antifibrotic therapies and supportive measures, and must include risk–benefit discussions. EOLC planning should be integral to the management of F-ILD throughout the patient journey and should include decisions about place of death. While these discussions are uncomfortable and challenging for patients, carers and healthcare professionals, EOLC planning is an essential element of F-ILD care that can reduce patient anxiety [10].

Symptoms such as dyspnoea, fatigue and cough cause a significant impact on psychological health and quality of life in F-ILD [17]. Adequate symptom management is therefore essential, however the evidence base is lacking for many symptom-based therapies. Wijsenbeek *et al.* reviewed the limited literature in this area (summarised in table 1) and emphasised the need for individualised treatment plans formulated according to a patient's circumstances. The authors do not provide a prescriptive symptom management protocol but do identify potential components that could be used in different combinations to formulate a unique care plan for each patient.

A lack of clinical trial evidence was a common problem identified by Wijsenbeek *et al.* when describing their idealised supportive care programme for F-ILD. While research in the field of interstitial lung disease has increased exponentially in the last two decades, studies of more supportive measures are often small, underpowered and uncontrolled, explaining the lack of a standardised approach to F-ILD. However, randomised controlled trials are feasible. For example, there are few controlled studies to support the use of supplemental oxygen, a common treatment in F-ILD, but recent work demonstrated that a randomised controlled trial of ambulatory oxygen in F-ILD is feasible [19]. Therefore, large-scale real-world studies of supportive care in F-ILD are not only necessary to improve the patient experience, they are entirely achievable, and should be a primary focus for the F-ILD research community.

Throughout, Wijsenbeek *et al.* emphasise the importance of the partnership between patients, their caregivers and the healthcare team in an effective comprehensive supportive care system for F-ILD, in all aspects of management. Nonetheless, it is likely that the nature of these relationships will be dependent upon patients' individual circumstances and preferences, as well as societal norms, and all these aspects must be considered when managing patients with F-ILD.

Table 1 *Potential management approaches for common symptoms in F-ILD*

Symptom	Approximate frequency in F-ILD	Management approaches
Dyspnoea	54–98% [18]	Supplemental oxygen Benzodiazepines Opiates Pulmonary rehabilitation Multidisciplinary breathlessness service intervention
Fatigue	8–29% [18]	Pulmonary rehabilitation Supplemental oxygen
Anxiety and depression	14–50% [17, 18]	Antidepressants Cognitive behavioural therapy
Cough	59–100% [18]	Treat exacerbating factors, *e.g.* proton pump inhibitors for gastro-oesophageal reflux Pirfenidone Thalidomide (significant toxicity) Target cough reflex with gabapentin or amitriptyline Inhaled sodium cromoglycate (trial currently ongoing; clinicaltrials.gov, NCT03864328)

Implications for practice

Wijsenbeek *et al.*'s comprehensive supportive care model for F-ILD provides a useful basis for the real-world management of F-ILD. This paper acts as a firm reminder to consider all aspects of patient care, in addition to potential disease-modifying approaches, in order to maximise quality of life. Patients and their caregivers should remain central to all forms of care planning in F-ILD, and individualised care plans should be formulated according to each patient's circumstances and preferences.

Clinicians working in the interstitial lung disease clinic should actively engage with clinical research and this work should include the supportive care measures discussed in this article, in addition to the novel antifibrotics that are frequently the focus of research trials. It is only *via* this engagement in research that we will gain sufficient evidence to improve the quality of life of patients with F-ILD.

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Conflict of interest

A.T. Goodwin has nothing to disclose. G. Saini has nothing to disclose.

References

1. Hutchinson JP, McKeever TM, Fogarty AW, *et al.* Increasing global mortality from idiopathic pulmonary fibrosis in the twenty-first century. *Ann Am Thorac Soc* 2014; 11: 1176–1185.
2. Navaratnam V, Hubbard RB. The mortality burden of idiopathic pulmonary fibrosis in the United Kingdom. *Am J Respir Crit Care Med* 2019; 200: 256–258.
3. Raghu G. Idiopathic pulmonary fibrosis: lessons from clinical trials over the past 25 years. *Eur Respir J* 2017; 50: 1701209.
4. Richeldi L, du Bois RM, Raghu G, *et al.* Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370: 2071–2082.
5. King TE Jr, Bradford WZ, Castro-Bernardini S, *et al.* A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370: 2083–2092.
6. Maher TM, Corte TJ, Fischer A, *et al.* Pirfenidone in patients with unclassifiable progressive fibrosing interstitial lung disease: a double-blind, randomised, placebo-controlled, phase 2 trial. *Lancet Respir Med* 2020; 8: 147–157.
7. Behr J, Neuser P, Prasse A, *et al.* Exploring efficacy and safety of oral Pirfenidone for progressive, non-IPF lung fibrosis (RELIEF) - a randomized, double-blind, placebo-controlled, parallel group, multi-center, phase II trial. *BMC Pulm Med* 2017; 17: 122.
8. Flaherty KR, Wells AU, Cottin V, *et al.* Nintedanib in progressive fibrosing interstitial lung diseases. *N Engl J Med* 2019; 381: 1718–1727.
9. Wells AU, Flaherty KR, Brown KK, *et al.* Nintedanib in patients with progressive fibrosing interstitial lung diseases – subgroup analyses by interstitial lung disease diagnosis in the INBUILD trial: a randomised, double-blind, placebo-controlled, parallel-group trial. *Lancet Respir Med* 2020; 8: 453–460.
10. Wijsenbeek MS, Holland AE, Swigris JJ, *et al.* Comprehensive supportive care for patients with fibrosing interstitial lung disease. *Am J Respir Crit Care Med* 2019; 200: 152–159.
11. Bonella F, Wijsenbeek M, Molina-Molina M, *et al.* European IPF Patient Charter: unmet needs and a call to action for healthcare policymakers. *Eur Respir J* 2016; 47: 597–606.
12. Cosgrove GP, Bianchi P, Danese S, *et al.* Barriers to timely diagnosis of interstitial lung disease in the real world: the INTENSITY survey. *BMC Pulm Med* 2018; 18: 9.
13. Ramadurai D, Corder S, Churney T, *et al.* Understanding the informational needs of patients with IPF and their caregivers: 'You get diagnosed, and you ask this question right away, what does this mean?'. *BMJ Open Qual* 2018; 7: e000207.
14. da Fontoura FF, Berton DC, Watte G, *et al.* Pulmonary rehabilitation in patients with advanced idiopathic pulmonary fibrosis referred for lung transplantation. *J Cardiopulm Rehabil Prev* 2018; 38: 131–134.
15. Dowman L, Hill CJ, Holland AE. Pulmonary rehabilitation for interstitial lung disease. *Cochrane Database Syst Rev* 2014; CD006322.
16. Lindell KO, Nouraie M, Klesen MJ, *et al.* Randomised clinical trial of an early palliative care intervention (SUPPORT) for patients with idiopathic pulmonary fibrosis (IPF) and their caregivers: protocol and key design considerations. *BMJ Open Respir Res* 2018; 5: e000272.
17. Glaspole IN, Watson AL, Allan H, *et al.* Determinants and outcomes of prolonged anxiety and depression in idiopathic pulmonary fibrosis. *Eur Respir J* 2017; 50: 1700168.
18. Carvajalino S, Reigada C, Johnson MJ, *et al.* Symptom prevalence of patients with fibrotic interstitial lung disease: a systematic literature review. *BMC Pulm Med* 2018; 18: 78.
19. Khor YH, Holland AE, Goh NS, *et al.* Ambulatory oxygen in fibrotic ILD: a pilot, randomised, triple-blinded, sham-controlled trial. *Chest* 2020; 158: 234–244.