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CTS GUIDELINES AND POSITION PAPERS

Comprehensive management of fibrotic interstitial lung diseases: A Canadian Thoracic Society position statement

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ABSTRACT

The comprehensive management of patients with fibrotic interstitial lung disease (ILD) is multi-faceted and may include pharmacological and non-pharmacological therapies. There are no current recommendations and few resources to guide the management of patients with fibrotic ILD in Canada. This position statement provides recommendations for the management of patients with fibrotic ILD based on review of the scientific literature and consensus from a panel of ILD experts. These recommendations relate to important clinically relevant questions, and key messages are provided to guide clinical practice.

RÉSUMÉ

La prise en charge intégrée des patients souffrant de fibrose pulmonaire interstitielle est multidimensionnelle et peut comprendre des traitements pharmacologiques et non pharmacologiques. Les ressources sont peu nombreuses et il n'existe pas de recommandations pour orienter la prise en charge des patients souffrant de fibrose pulmonaire interstitielle au Canada. Cet énoncé de position présente des recommandations pour la prise en charge des patients souffrant de fibrose pulmonaire interstitielles fondées sur l'examen de la littérature scientifique et sur le consensus issu d'un panel d'experts dans ce domaine. Ces recommandations portent sur d'importantes questions pertinentes sur le plan clinique. Des messages-clés sont aussi présentés pour orienter la pratique clinique.

KEYWORDS

Interstitial lung diseases; guideline; management; medication; non-pharmacologic interventions

Introduction

Interstitial lung disease (ILD) is a group of pulmonary diseases characterized by inflammation and fibrosis of the lung parenchyma.[1] The diagnosis of fibrotic ILD is challenging, with key diagnostic considerations described and recommendations provided in a recent Canadian Thoracic Society (CTS) Position Statement.[2] The management of patients with ILD is also complex and must be multi-faceted, including pharmacological and non-pharmacological therapies.

Current international guidelines focus on pharmacologic management of idiopathic pulmonary fibrosis (IPF).[3] There have been few published therapeutic recommendations pertaining to non-IPF fibrotic ILD. The goal of this position paper is to address these gaps by providing specific recommendations for the comprehensive management of fibrotic ILD, with an emphasis on the Canadian context.

Objectives

1. To summarize the current scientific literature on the comprehensive management of fibrotic interstitial lung diseases with a focus on the Canadian health care setting.
2. To provide evidence-based recommendations for the comprehensive management of fibrotic interstitial lung diseases, and where evidence is lacking, to provide expert opinions

Methods

Working group composition

A working group was created within the CTS Interstitial Lung Disease Clinical Assembly. The group was co-chaired by two authors, and included 10 adult respirologists with expertise in the fields of ILD, lung transplantation and pulmonary rehabilitation, one palliative medicine specialist and one doctor of physical therapy. The primary target audiences for this position statement are Canadian respirologists, internists, primary care physicians, and allied health care practitioners who care for patients with fibrotic ILD. This document should also be useful to patients and patient

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advocates. Finally, health care decision makers may also use this in policy processes to inform coverage decisions.

Evidence search, appraisal and recommendation

The document was developed in accordance with the CTS requirements for a position statement (https://cts-sct.ca/guideline-library), which is derived from the CTS guideline production methodology.[4] Authors used the AGREE II checklist to guide the development of this position statement.[5] The working group identified 9 clinically important questions pertaining to the management of fibrotic ILD. The expert group based those relevant questions on their own knowledge of the literature, existing guidelines and gaps to be addressed. The PICO (problem/population, intervention, comparison, outcome) format was used when applicable to develop the questions by the co-chairs, then input from all coauthors was obtained through group discussion, and consensus was reached on the final key questions and topics. Pairs of coauthors were assigned specific sections of the paper and corresponding PICO questions based on their expertise, and conducted a search and review of the scientific literature using key word searches, supplemented by their own knowledge of relevant articles to be included. The literature was summarized and agreed upon by each pair of reviewers. Consensus was reached through emails and teleconferences, and all coauthors were in agreement with the final published key messages in this manuscript.

Review

In accordance with the CTS Guideline Production Methodology, this position statement underwent both internal and external review. External review was conducted by two international ILD experts who were independently invited by the CTS to review this position statement. Each expert provided a detailed review and suggestions, and authors responded to these reviews in detail. Internal review was conducted by two members of the CTS Canadian Respiratory Guidelines Committee, who provided further feedback for consideration by authors. A member of the CTS Canadian Respiratory Guidelines Committee also assessed the statement with the AGREE II assessment tool, highlighting areas for improvement, which were then considered by authors. Original reviews and responses to reviews are posted along with the position statement and all authors' conflicts of interest at https://cts-sct.ca/guideline-library. The CTS Executive approved the final document for publication.

Updating this statement

This position statement will be reviewed every three years or sooner by members of the CTS Interstitial Lung Disease Clinical Assembly, to determine the need for guideline updates, in accordance with the CTS Living Guideline Model (details available at https://cts-sct/guideline-library/methodology).

Summary of evidence and key messages

ILD-targeted pharmacotherapy

Q1. What pharmacotherapies should be considered for the management of fibrotic ILD?

Deciding on the most appropriate pharmacotherapy for fibrotic ILD requires an accurate diagnosis.[2] Pirfenidone and nintedanib are approved in Canada for the treatment of IPF and both anti-fibrotic medications have been recommended for the management of IPF in recent international guidelines.[3] Pirfenidone is a nonspecific anti-fibrotic agent thought to act on multiple targets along the fibrotic cascade. Pirfenidone at a dose of 2403 mg per day slows the decline in lung function compared to placebo, and pooled analyses of 3 randomized placebo-controlled trials also suggests a survival benefit and a reduced risk of respiratory-related hospitalizations.[6–8] Nintedanib is a nonspecific tyrosine kinase inhibitor acting on different targets. Treatment at a dose of 300 mg daily slows decline in lung function compared to placebo.[9] Nintedanib significantly increased time to first exacerbation in one randomized controlled trial, but this finding was not replicated in a second trial. Pooled analysis showed a trend toward a reduction in mortality for patients treated with nintedanib compared to placebo, but this did not reach statistical significance. While no direct comparison between the two drugs exists so far, multiple *post hoc* analyses have suggested similar overall efficacy of pirfenidone and nintedanib. Anti-fibrotic medications were not tolerated in approximately 15–20% of the prospective clinical trial cohorts, indicating the need for close monitoring of potential toxicity.[6,7,9] Given their similar overall benefit, these medications are often prescribed based on their side effect profile and patient preference.

Anti-fibrotic medications are not currently recommended for other types of fibrotic ILD; however, several clinical trials are evaluating their potential role in non-IPF ILD. Other medications (eg, immunosuppressive agents such as mycophenolate mofetil, azathioprine, cyclophosphamide and rituximab, among others) are often used in non-IPF fibrotic ILDs based on longstanding practice patterns, observational studies, and randomized controlled trials that exist for some ILD subtypes. These studies collectively demonstrate a trend to disease slowing without reversal of existing fibrosis, but side effects are important and specific to each immunosuppressive agent.[10–12] Review articles summarizing the evidence for immunosuppressive agents have been published elsewhere.[13] There are several unanswered questions including choice of agent and duration of therapy, and further work in the field is needed. Importantly,

immunosuppressive medications have potential to cause harm in patients with IPF,[14] emphasizing the importance of establishing the correct diagnosis in patients with fibrotic ILD.[2] Referral to a tertiary care center for enrollment in clinical trials can be considered in selected cases of fibrotic ILD.

Box 1. ILD-targeted pharmacotherapy

- *What pharmacotherapies should be considered for the management of fibrotic ILD?*

- Key Messages:

1. Accurate diagnosis is essential prior to initiation of pharmacotherapy for fibrotic ILD
2. Anti-fibrotic agents (pirfenidone or nintedanib) should be considered in patients with IPF to slow decline of lung function.
3. Immunosuppressive medications have been shown to be harmful in patients with IPF and should be avoided.
4. Immunosuppressive medications may be considered in non-IPF fibrotic ILDs based on limited evidence.

Pulmonary rehabilitation

Q2. Should patients with fibrotic ILD be referred to pulmonary rehabilitation?

Pulmonary rehabilitation (PR) is defined as a comprehensive structured exercise and education program for patients with chronic lung disease.[15] PR is weakly recommended in patients with IPF given the small number of well-controlled studies.[16] Despite this weak recommendation, 71% of PR programs in Canada accept patients with ILD.[17]

Randomized controlled trials show that PR improves functional capacity (6-minute walk distance), dyspnea and quality of life in patients with ILD,[18,19] and may also improve depression, fatigue, anxiety, and muscle strength.[20–24] In patients with chronic obstructive pulmonary disease (COPD), PR may also reduce the frequency and duration of hospitalization, improve social isolation and prolong survival;[25] however, it is unknown whether these additional benefits occur in patients with ILD. The impact of PR diminishes over time and patients with ILD may have less initial benefit and greater attenuation of this benefit compared to patients with COPD.[18,20,26] It is unknown whether ILD-specific programs would provide greater or longer-lasting benefits compared to conventional PR that is predominantly designed for patients with COPD.

Several studies have evaluated which ILD patients achieve the most benefit from PR. Two non-randomized cohort studies suggested greater and more sustained improvement in patients with milder ILD and in those who did not require oxygen at baseline.[22,27] Other cohort studies have suggested that patients with worse baseline functional capacity achieve the greatest benefits, with these studies unable to identify a specific population in which PR was ineffective.[20,23,28] The decision on when patients should be referred for PR is also impacted by the limited access to PR programs in most regions.[17]

Box 2. Pulmonary rehabilitation

- *Should patients with fibrotic ILD be referred to pulmonary rehabilitation?*

- Key Messages:

1. Patients with ILD should undergo pulmonary rehabilitation, as it improves walking distance, dyspnea, and quality of life.
2. In resource-limited settings, selected patients with advanced ILD, reduced functional capacity or pre-lung transplantation could be prioritized for pulmonary rehabilitation, as they may derive more benefits.
3. Educational and exercise components of pulmonary rehabilitation should be adapted for patients with ILD.

There are limited data on ILD-specific approaches to PR. Exercise-training protocols for ILD patients are generally similar to those for COPD: 30-60 minutes of aerobic and resistance training 2-3 times per week. Several studies have used initial exercise intensity settings similar to the approach taken for patients with COPD (eg, 60% of peak workload or 80% of 6-minute walk test speed). Despite the high prevalence of severe hypoxemia and cardiopulmonary comorbidities in fibrotic ILD,[29] a recent Cochrane review reported no adverse events in PR trials for these patients;[30] however, it may be necessary to provide supplemental oxygen more frequently to patients with ILD compared to other populations during exercise. Interval training or one-legged cycling may be appropriate for patients with severe dyspnea and/or hypoxemia, but these have not been adequately explored in ILD. There are also limited data on the magnitude of benefit from alternatives to standard PR programs (eg, home-based exercise programs);[21,31,32] however, these options may be appropriate in some patients. Two recent studies showed that the typical PR educational curriculum does not meet the needs of ILD patients, recommending additional information on ILD prognosis, medications, diagnostic tests, oxygen, management of dyspnea and advance care planning.[33,34]

Oxygen supplementation

Q3. When should the need for oxygen supplementation be evaluated and when should oxygen be initiated in patients with fibrotic ILD?

Patients with fibrotic ILD frequently develop hypoxemia in the later stages of disease due to multifactorial physiologic derangements including diffusion limitation, ventilation-perfusion mismatch, and abnormalities of the pulmonary vasculature.[35–37] The diffusion capacity of the lung for carbon monoxide (DLCO) is the most important predictor of hypoxemia in fibrotic ILD,[29] and this is the primary objective measure that indicates the need to screen for both resting and exertional desaturation. Measurement of resting oxygen saturation is widely available and should be performed at each clinical visit using

pulse oximetry, while measurement of ambulatory oxygenation is more resource-intensive and should be considered in selected patients. Common parameters that indicate the need for assessment of oxygenation include disease progression, exercise limitation, significant exertional dyspnea, reduced DLCO, polycythemia or pulmonary hypertension.

There are sparse and inconsistent data regarding the efficacy of supplemental oxygen in patients with fibrotic ILD.[38] Data supporting oxygen use in ILD patients with resting hypoxemia are mainly extrapolated from studies of non-ILD pulmonary disease that showed improved cardiac output, exercise endurance, dyspnea and survival;[39–44] however, the only study assessing mortality in patients with IPF found no survival benefit.[45] There are similarly no high quality studies evaluating the role of supplemental ambulatory oxygen in patients with fibrotic ILD; however, several small studies suggest potential benefits on endurance time, walk distance and maximal workload.[46–48] The potential adverse effects of unnecessary supplemental oxygen also remain poorly characterized.[49]

Access to oxygen supplementation varies across Canada, in part because funding criteria are defined within provincial jurisdictions.[50,51] Given the weak and predominantly indirect data, the decision to initiate supplemental oxygen for patients with fibrotic ILD should be made on an individual basis, considering mobility level, patient preference, quality of life, and the likelihood of symptomatic and/or functional benefit. International guidelines recommend continuous oxygen supplementation for patients with IPF and resting oxygen saturation below 88%, a partial pressure of oxygen (PaO_2) < 55 mmHg, or a PaO_2<60 mmHg combined with evidence of *cor pulmonale*.[16] Ambulatory oxygen supplementation is typically recommended for patients with exertional hypoxemia (oxygen saturation <88%) and an improvement in dyspnea or functional capacity on 6-minute walk test with the use of oxygen during exertion.[52,53]

Box 3. Oxygen supplementation

- *When should the need for oxygen supplementation be evaluated and when should oxygen be initiated in patients with fibrotic ILD?*

- Key Messages:

1. Patients with fibrotic ILD should be screened for resting hypoxemia at each clinical visit using pulse oximetry.
2. Continuous oxygen supplementation is recommended for all patients with resting hypoxemia (oxygen saturation <88%, PaO_2<55mmHg, or PaO_2<60mmHg with cor pulmonale), despite lack of supportive data in ILD specifically.
3. Selected patients with advanced fibrotic ILD and/or significant dyspnea (MMRC ≥3) should be assessed for exertional hypoxemia (oxygen saturation <88%) using oximetry during exercise (walk test, ambulation or exercise test).
4. Ambulatory oxygen supplementation should be considered for patients with fibrotic ILD and exertional hypoxemia (oxygen saturation <88%), who demonstrate clinical improvement on oxygen with the understanding that this will change based on regional reimbursement criteria.

Lung transplantation

Q4. Which patients with fibrotic ILD should be referred to a lung transplant program?

Fibrotic ILD is the most common indication for lung transplant in Canada.[54] Currently, there are 4 surgical lung transplant programs in Canada, located in Vancouver, Edmonton, Toronto, and Montreal, with follow-up care available in additional satellite clinics. In 2015, a total of 279 lung transplantations were performed in Canada and this number has been steadily increasing over the past decade.[55] A detailed review of patient selection, timing of referral, and other transplant-related considerations are provided in recent guidelines from the International Society for Heart and Lung Transplantation.[56]

Referral to a lung transplant center should be considered in patients with fibrotic ILD based on significant benefits on quality of life and survival;[57,58] however, there are important considerations (eg, age, comorbidities) related to specific ILD subtypes that preclude lung transplantation in many patients.[59,60] Preliminary screening for significant coronary disease and malignancy should be undertaken before referral to transplant centers. In patients with connective tissue disease (CTD)-associated ILD, extra-pulmonary disease manifestations (joint involvement, esophageal dysmotility, myopathy, renal impairment and skin involvement leading to restriction) may impact suitability for transplantation and can influence long-term outcomes. However, recent observational studies suggest that overall post-transplant outcomes may be similar to that of other lung diseases in appropriately selected patients.[61,62] Although there is a theoretical concern that anti-fibrotic medications might increase the risk of peri-operative bleeding, the limited available data do not suggest clinically significant risks associated with these agents and they are not contraindicated in patients on transplantation waitlists.[63,64] Disease recurrence in the allograft lung has been described in some fibrotic ILDs, most frequently sarcoidosis, although survival after transplant does not appear to be impacted.[65]

Box 4. Lung transplantation

- *Which patients with fibrotic ILD should be referred to a lung transplant program?*

- Key Messages:

1. Lung transplantation should be considered in all patients with fibrotic ILD; however, many patients will not be eligible for lung transplant on the basis of significant comorbidities.
2. CTD is not a contraindication to transplant, although the presence of significant extra-pulmonary disease may impact eligibility.

Q5. When should patients with fibrotic ILD be referred for lung transplantation evaluation?

Given the poor prognosis of IPF and the variable and unpredictable course of the disease, international guidelines have advocated that potentially eligible patients be

Table 1. Elements of advance care planning process.

	Item	Description
1.	Think	Encourage patients to think about their wishes and values
2.	Learn	Enable patients to learn about their own health; share prognosis and potential treatment outcomes
3.	Choose	Help patients choose someone to make decisions and speak on their behalf. Give advice about choosing a good surrogate
4.	Communicate	Encourage patients to communicate wishes and values about healthcare to a substitute decision maker, family and Health Care Providers
5.	Document	Document in an Advance Directive and/or other advance care planning documentation as per jurisdiction

Modified from (www.advancecareplanning.ca).

referred for lung transplantation evaluation at or shortly after the time of diagnosis.[16,56,66,67] Less data are available to guide optimal timing for lung transplantation referral in non-IPF fibrotic ILD. Guidelines suggest referral at the time of diagnosis regardless of lung function for idiopathic fibrotic nonspecific interstitial pneumonia (NSIP), similarly to IPF.[56] In other non-IPF ILDs, referral should be made in the setting of a forced vital capacity below 80%, DLCO below 40%, any oxygen requirement, or failure to respond to pharmacotherapy,[56,68] recognizing that the ideal timing of referral will vary between institutions based on the expected time from initial referral to transplantation. Direct communication between referring physicians and the transplant program is frequently helpful to optimize the timing and convey the urgency of referral. This is particularly important given the high waitlist mortality in Canada, with 45 deaths on the waiting list in 2016.[54]

Median unadjusted survival after lung transplant for ILD in the ISHLT registry is 4.9 years compared to 9.2 and 5.8 years for cystic fibrosis and chronic obstructive pulmonary disease, respectively.[69] However, survival may vary across programs. Given the poor prognosis of many fibrotic ILDs, especially IPF, lung transplant likely conveys a survival benefit in the appropriately selected fibrotic ILD patient.[57] Lung transplant also confers very substantial health-related quality of life benefits for patients with ILD, although this is also somewhat lower than the benefits seen for other lung diseases.[58]

Box 5. Lung transplantation

- *When should patients with fibrotic ILD be referred for lung transplantation evaluation?*
- Key messages:

1. Referral for lung transplant evaluation should be made at, or shortly after time of diagnosis for patients with IPF and fibrotic NSIP, given the poor prognosis and unpredictable disease course.
2. For non-IPF fibrotic ILD, referral should be made in the setting of a forced vital capacity below 80%, DLCO below 40%, any oxygen requirement or failure to respond to pharmacotherapy.
3. Optimal timing of lung transplant referral will vary in individual programs based on the expected time from initial referral to transplantation.

Advance care planning

Q6. When should advance care planning be discussed with patients with fibrotic ILD and their caregivers?

Advance care planning is the process of thinking about a patient's wishes for future health and personal care, with the goal to ensure that patients receive medical care that is consistent with their values, goals, and preferences during serious and chronic illness.[70] It involves sharing prognosis, exploring wishes for care and involving family and caregivers in the discussion.[71] Advance care planning can help ease decision-making by patients or by surrogate decision makers when a patient loses capacity (eg, during acute episodes).[72] The process is iterative and what is discussed often changes over the course of living with ILD. Elements of the advance care planning process are summarized in Table 1. It results in lower medical resource utilization at the end of life, improved patient quality of life near death, and improved quality of life for caregivers.[71,73] It may also reduce moral distress among health care providers with a recent study identifying lack of end-of-life conversations, inconsistent care plans and poor communication as causes of moral distress among providers in the intensive care unit.[74]

Establishing "goals of care" is important after a diagnosis of fibrotic ILD is established and, particularly, in the presence of disease progression. Resuscitation preferences, other specific treatment-related decisions and the focus or aims of care (eg, seeking to prolong life, focusing on symptom relief) should be documented and are made in relation to the patient's own personal and individualized goals for his or her care. Clinicians should consider using the "surprise question" to assist with transitioning to Goals of Care discussions:[75] "*Would I be surprised if this patient were to die within the next 12 months?*" If the clinician's answer is "*no,*" then it may be an appropriate time to review the patient's prognosis and re-elicit personal priorities in relation to his or her healthcare.

Clinicians can use information on patient preferences, goals of care, and values to make recommendations about interventions such as referral to palliative care. Palliative care should be integrated with disease-centered management early in the disease course of any severe and life limiting disease.[76] A recent retrospective study of 404 patients with IPF found that only 13.7% had a referral to palliative care, with 71% of these occurring within 30 days of death.[77] This suggests that palliative care involvement occurs late in the disease course for a large majority of patients with fibrotic ILD, if at all, despite the high palliative care needs in this population.[78] Palliative care may also be appropriate to ease symptom burden

for patients with ILD who are actively listed for lung transplantation.[79]

Box 6. Advance care planning

- *When should advance care planning be discussed with patients with fibrotic ILD and their caregivers?*
- Key messages:

1. Advance care planning (see Table 1) should be initiated with all patients with fibrotic ILD during the course of their disease.
2. Prognosis and outcomes should be shared with patients and caregivers to assist with end-of-life decision-making and establishing goals of care.

Symptom management

Q7. How should severe dyspnea be managed in patients with fibrotic ILD?

Exertional dyspnea is present in virtually all patients with advanced ILD, and dyspnea can eventually occur at rest as well. Dyspnea reduces quality of life, increases depression and anxiety,[80] can result in loss of independence and social isolation and is an important predictor of prognosis in patients with ILD.[80,81] Although dyspnea is primarily determined by the severity of ILD, it is important to identify, investigate for and treat any potentially reversible causes of dyspnea (eg, concomitant infection, pulmonary embolism, heart failure, anemia).[82]

There are many non-pharmacologic interventions that can improve dyspnea, including pacing, energy conservation, breathing retraining, body positioning, relaxation techniques, fans (external airflow) and cognitive behavioral therapy.[83,84] Randomized controlled trials have shown that pulmonary rehabilitation reduces dyspnea in patients with ILD and is, thus, an important symptom management strategy that is recommended in clinical practice guidelines.[16,18,30]

There is less evidence for the role of pharmacotherapies for the palliation of dyspnea in fibrotic ILD. Opioids are the preferred choice in advanced disease, although the only study in an ILD population is an open-label case series of 11 elderly patients with advanced IPF in which a single, low dose of subcutaneous diamorphine resulted in a significant reduction in dyspnea compared to baseline without reducing respiratory rate.[85] There are higher-quality data showing the benefit of opioids to relieve dyspnea in other advanced lung diseases such as cancer and COPD, and recent guidelines thus recommend carefully titrated low dose oral opioids for palliation of severe dyspnea in patients with chronic respiratory disease.[77] There is currently no clear role for nebulized opioids in ILD or other advanced lung diseases.[86,87] Short-acting opioids with rapid onset of action (e.g., subcutaneous, sublingual, or nasal fentanyl) have theoretical appeal for exertional breathlessness; however, studies have also not shown consistent benefit, and larger trials are underway.[88] A starting dose of immediate release morphine 1.0–2.5 mg or hydromorphone 0.1 mg orally every 4–6 hours can be used as a starting dose. Escalation of dose and conversion to long acting formulations can be done in consultation with local Palliative Care experts. Benzodiazepines are not recommended for palliation of dyspnea based on a previous systematic review that did not identify a clear benefit in a variety of advanced lung diseases.[89]

Box 7. Symptom management

- *How should severe dyspnea be managed in patients with fibrotic ILD?*
- Key messages:

1. Dyspnea is a complex and multidimensional symptom, and management should include non-pharmacologic interventions such as pacing, energy conservation, breathing retraining, body positioning, relaxation techniques, fans and cognitive behavioral therapy.
2. Low dose opioids (morphine 1.0 to 2.5 mg or hydromorphone 0.1 mg orally every 4 to 6 hours), carefully titrated to effect, may be considered in patients with fibrotic ILD and refractory dyspnea.

Q8. How should intractable chronic cough be managed in patients with fibrotic ILD?

Cough is reported in up to 85% of patients with fibrotic ILD,[90,91] can lead to reduced health-related quality of life and social isolation and is an independent predictor of mortality.[90] Although the pathogenesis of cough has not been clearly established in patients with fibrotic ILD, increased sensitivity of sensory fibers to stretch and damage in the lungs is thought to play a role in IPF.[92] Cough is frequently attributed to ILD, but other factors may contribute to cough, with one study reporting that cough was related to a process other than the underlying ILD in up to 54% of patients.[93]

Treating cough in patients with ILD is challenging and there are no high-quality studies that suggest a highly effective treatment for cough in ILD. In a small study of 43 patients, pirfenidone reduced cough frequency by 34% after 12 weeks of therapy.[94] A post-hoc analysis of recent pirfenidone clinical trials also suggested improvement in the prevalence of cough compared to placebo.[95] Opioids are frequently used to palliate cough in a variety of settings, but there are no randomized trials and only anecdotal reports of effectiveness in ILD.[85] An open-label trial of oral prednisolone at 40-60 mg daily for one month showed decreased cough severity in 6 IPF patients who had severe cough.[92] A phase II double blind crossover trial of low-dose thalidomide at 50-100 mg daily reported a significant improvement in cough-specific quality of life and in respiratory-related quality of life;[96] however, additional studies are needed to verify the efficacy and safety of this given the frequent contraindications and significant risk of adverse effects. The central-acting neuromodulator gabapentin, at doses up to 1800 mg per day, reduced cough severity in refractory chronic idiopathic cough in a blinded randomized controlled trial,[97] but has never been studied in ILD. Future trials are needed for these and other potential therapies of cough given the absence of any high quality data and the frequent toxicity of currently available options.

Box 8. Symptom management

- *How should intractable chronic cough be managed in patients with fibrotic ILD?*

- Key messages:

1. Treatment of intractable cough in patients with fibrotic ILD should be approached on an individual basis, considering the severity of cough and common adverse effects of potential pharmacotherapy.
2. Opioids may be considered for refractory cough in fibrotic ILD as a first-line pharmacotherapy.

Patient education, support, and advocacy

Q9. What are the benefits of structured patient education and advocacy programs in fibrotic ILD?

IPF and other fibrotic ILDs have a significant impact on patients' quality of life, family life, emotional and physical well-being. In many ILD centers, patient-centered management includes a large multidisciplinary team of physicians, nurses and other allied health professionals.[98] Patients rely on ILD nurses and physicians for support and information, but express the need for more accessible information on disease.[99] Patient advocacy groups can play an important role in supporting patients with chronic diseases, filling gaps in information and advocating for better care through different measures. A recent collaborative between physicians and advocacy group members identified several unmet needs in patients with IPF that could be filled by patient advocacy groups, including the need for improved access to reliable information, knowledgeable health care providers, access to treatment and holistic and palliative care.[100]

Internet-based resources are easily and widely accessible tools that can facilitate patient-centered education and management; however, many IPF-related websites contain incorrect or outdated information and there is no way for patients to reliably identify which websites provide accurate information.[101] Self-management has been shown to be of benefit in COPD[102] and may similarly be of benefit in ILD despite the absence of supportive data. Patients should actively review websites for information such as when they were last updated, who sponsored the page and where the information originates. Patients should also be encouraged to discuss with their physician if the information they read conflicts with what they have learned in clinic. Physicians should also direct their patients to trustworthy medical information websites.

Box 9. Patient education, support, and advocacy

- *What are the benefits of structured patient education and advocacy programs in fibrotic ILD?*

- Key messages:

1. Patient advocacy groups have a role in disseminating information and improving patient-centered care.
2. Internet-based resources may be useful for patient education, but their quality can be variable and patients should use these resources with caution. We suggest the following Canadian sites which have information on IPF specifically: https://cpff.ca and https://www.lung.ca/search/node/pulmonary%20fibrosis; and on ILD: http://www.livingwellwithpulmonaryfibrosis.com

Conclusion

Fibrotic ILDs are complex and heterogeneous diseases that have serious consequences on quality of life and survival. This position paper from the CTS Interstitial Lung Disease Clinical Assembly summarizes important issues and provides key messages relevant to the management of patients with fibrotic ILD. This work is limited by the lack of patient perspective, and ILD clinicians should remember that a patient-centered approach is of fundamental importance. Available evidence indicates the importance of a comprehensive approach to management that includes both pharmacologic and non-pharmacologic interventions that are ideally provided in a collaborative multidisciplinary setting.

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Editorial independence

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Members of the CTS Interstitial Lung Disease Clinical Assembly declared potential conflicts of interest at the time of appointment and these were updated throughout the process in accordance with the CTS Conflict of Interest Disclosure Policy. Individual member conflict of interest statements are posted at https://cts-sct.ca/guideline-library/.

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