Multidisciplinary Care and Prognosis in Patients With COPD and Interstitial Lung Disease Prescribed Long-Term Oxygen Therapy

Amelia CA Harrison, Julien F Robinson, Laura Tu, Christine F McDonald, and Yet Hong Khor

BACKGROUND: Home oxygen therapy is prescribed for patients with advanced lung disease based on the criteria established in landmark trials in subjects with COPD. In clinical practice, its use has been extrapolated to other diseases, including interstitial lung disease (ILD). Patients with COPD and ILD experience a high symptom burden and require access to specialized multidisciplinary care. We aimed to evaluate the health-related outcomes and supportive care needs of patients with COPD and ILD receiving home oxygen therapy. METHODS: This was a retrospective cohort study using the oxygen database of a quaternary metropolitan teaching hospital. Patients with a diagnosis of COPD or ILD who were prescribed home oxygen therapy between January 2012–December 2018 were identified. Demographic information, results of physiologic testing, comorbidities, hospitalizations, and mortality data were collected. RESULTS: Three hundred and eighty-four subjects were included for analysis, of whom 56% were male. The median age was 75 y. The majority (59%) had a diagnosis of COPD. Long-term oxygen therapy (LTOT) was prescribed for 187 (48.7%), with no significant demographic differences between those with COPD or ILD. Another 187 were prescribed ambulatory oxygen alone, with 55 transitioning to LTOT during the study period. Most subjects (65.4%) were referred for pulmonary rehabilitation; however, palliative care referrals were generally low (22.9%). Referrals to other medical specialties and allied health were common (82%). Transplant-free survival after commencement of LTOT was poor, with 38% of subjects surviving at 5 y. The 5-y survival of subjects with ILD after commencing on LTOT was 10% compared to 52% for those with COPD. Multivariable Cox regression analyses showed that the only predictor of survival after commencing LTOT was the principal respiratory diagnosis. CONCLUSIONS: This study found that subjects prescribed LTOT had poor transplant-free survival after initiation, which was significantly worse for those with ILD compared to those with COPD. Despite their poor overall survival, worse than many cancers, only a minority were referred for palliative care input. Referrals to pulmonary rehabilitation were also suboptimal. This patient population had complex care needs requiring multidisciplinary management. Appropriate and early referrals to palliative care and improved care coordination for this complex group of patients are key areas for improvement in clinical practice. *Key words: ambulatory oxygen therapy; long-term oxygen therapy; interstitial lung disease; COPD.* [Respir Care 2022;67(6):667–675. © 2022 Daedalus Enterprises]

Introduction

Home oxygen therapy is prescribed for patients with advanced lung disease, most commonly COPD and interstitial lung disease (ILD).[1,2] Long-term oxygen therapy (LTOT) is prescribed for resting hypoxemia, which is defined as resting daytime P_{aO_2} of < 55 mm Hg or 56–59 mm Hg if there is evidence of end-organ damage such as right heart failure, pulmonary hypertension, or polycythemia. This practice is based on survival benefits associated with the use of LTOT in patients with COPD and resting hypoxemia, which has been extrapolated in clinical practice to other disease populations, including ILD.[3,4,5] Ambulatory oxygen therapy is prescribed for patients who desaturate significantly on exertion, which is commonly defined as exertional desaturation to $< 88\%$ during a 6-min walk test (6MWT), with the aim of improving exercise capacity and alleviating exertional dyspnea.[6,7] The Thoracic Society of Australia and New Zealand guideline recommends nocturnal oxygen therapy for patients who experience desaturation to $\leq 88\%$ for more than one third of the night, particularly if they suffer sequelae such as pulmonary hypertension or polycythemia.[6] Previous studies have

identified reduced life expectancy in patients with COPD and ILD requiring home oxygen therapy for chronic hypoxemic respiratory failure[8,9,10]; however, few studies have compared the survival of these populations directly.

Patients with COPD and ILD experience high symptom burden, including dyspnea, cough, reflux, fatigue, and sleep disturbance along with profound psychosocial impacts.[11] The symptom burden in advanced COPD and ILD is comparable to that in advanced cancer.[12,13] Hence, symptomatic management and access to specialist palliative care services are important for patients with COPD and ILD, particularly those with advanced disease. Given the significant burden of comorbidities in this patient population, careful and considered management in line with the patient's priorities and wishes is necessary to maximize patient well-being and provide holistic care.[14,15]

We aimed to evaluate health-related outcomes and supportive care needs of patients with COPD and ILD receiving home oxygen therapy. Predictors of transplant-free survival after the initiation of home oxygen therapy in subjects with COPD and ILD were also determined and compared. We hypothesized that subjects with ILD would have poorer survival than those with COPD after commencing LTOT, and that subjects on home oxygen therapy would have high morbidity burden requiring multidisciplinary management.

QUICK LOOK

Current knowledge

Long-term oxygen therapy (LTOT) is prescribed for patients with advanced lung disease complicated by respiratory failure. Current guidelines for prescription of continuous oxygen therapy are based on criteria initially established in landmark trials in subjects with COPD and resting hypoxemia and have been extrapolated to other patient populations, including interstitial lung disease (ILD).

What this paper contributes to our knowledge

Subjects with ILD had significantly higher mortality following commencement of LTOT than those with COPD, with poor overall 5-y survival. Subjects required complex multidisciplinary management, and referrals to pulmonary rehabilitation and initiation of appropriate palliative care input were identified as key areas for improvement.

Methods

This was a retrospective cohort study using the oxygen database of a quaternary metropolitan teaching hospital. Consecutive patients with a diagnosis of COPD or ILD who were prescribed home oxygen therapy based on the Thoracic Society of Australia and New Zealand guideline between January 2012–December 2018 were identified.[6] Where a patient was prescribed oxygen on more than one occasion, the most recent oxygen prescription was used. Data extracted included demographics, 6MWTs, arterial blood gases, lung function measurements, echocardiographic data, comorbidities, key disease-related management, oxygen prescription details, hospitalizations, and mortality and lung transplantation status. 6MWTs were conducted according to current field test guidelines.[16] For subjects with resting hypoxemia on the arterial blood gas during initial assessment, 6MWTs on room air were not performed. Comorbidities were evaluated using the Charlson comorbidity index, which is a validated tool for mortality prediction based on a weighted score for 19 comorbidity categories.[17] Ethical approval was granted by the Austin Health Human Research Ethics Committee (LNR/19/Austin/45).

Statistical Analysis

The data were analyzed using GraphPad Prism version 5 (GraphPad Software, San Diego, California), Stata version 16 (StataCorp, College Station, Texas), and Microsoft Excel (Microsoft, Redmond, Washington). Testing for normality of data distribution was performed using the Kolmogorov-Smirnov test. Categorical variables were presented in absolute number (%) and compared using the Fisher exact test. Continuous variables were given in mean and SD for parametric data and median for nonparametric data. Continuous variables were compared using *t* tests or Mann-Whitney tests. Time to death or lung transplantation following the

Drs Harrison and Robinson are affiliated with Department of Respiratory and Sleep Medicine, Austin Health, Victoria, Australia; and Institute for Breathing and Sleep, Victoria, Australia. Dr Tu is affiliated with Department of Respiratory and Sleep Medicine, Austin Health, Victoria, Australia. Drs McDonald and Khor are affiliated with Department of Respiratory and Sleep Medicine, Austin Health, Victoria, Australia; Institute for Breathing and Sleep, Victoria, Australia; and Faculty of Medicine, University of Melbourne, Victoria, Australia.

Dr Khor discloses relationships with Air Liquide Healthcare, Boehringer Ingelheim, and Roche. Dr McDonald discloses relationships with Air Liquide Healthcare and Menarini. The remaining authors have disclosed no conflicts of interest.

Portions of this work were presented at the Thoracic Society of Australia and New Zealand Annual Scientific Meeting 2021, held virtually May 2021.

This study was performed at the Department of Respiratory and Sleep Medicine, Austin Health, Victoria, Australia.

Correspondence: Dr Yet H Khor MBBS (Hons) BMedSci FRACP PhD, Department of Respiratory and Sleep Medicine, Austin Health, 145 Studley Road, Heidelberg 3084 VIC. E-mail: yethong.khor@austin.org.au.

DOI: 10.4187/respcare.09446

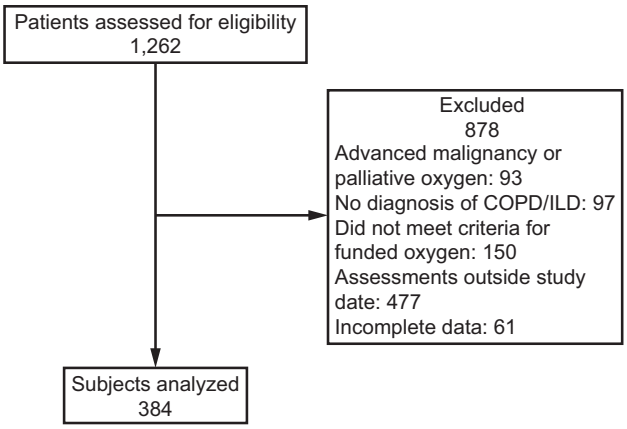


Fig. 1. Flow chart. ILD = interstitial lung disease.

initiation of LTOT was evaluated using the Kaplan-Meier method, adjusting for age and sex. The date of censoring for the survival analysis was the date of death or December 31, 2019.

Results

Subject Characteristics

Of the 1,262 patients identified, 384 were included (Fig. 1). The study cohort was male predominant (56%), with a median age of 75 (70–82) y and body mass index (BMI) of 27.4 (22.6–31.3) kg/m^2 (Table 1). Eighty-five percent ($n = 328$) were never smokers, with mean pack-year exposure of 47 among those with a history of smoking. Most subjects ($n = 231$) had COPD, whereas 121 were diagnosed with ILD, and 32 had co-existing COPD and ILD. Subjects with COPD had severe obstructive ventilatory defects with a mean $FEV_1 >$ 1 s of 43.3 ± 20.1% predicted, whereas those with ILD had moderate restriction with mean FVC of 68.6 ± 19.0% predicted. Carbon monoxide diffusing capacity (D_{LCO}) was moderate to severely reduced at 39.8 ± 13.6% predicted and 40.7 ± 13.0% predicted for subjects with COPD and ILD, respectively. The median Charlson comorbidity index was 6.0 (4.0–8.0), with heart disease (58%) and pulmonary hypertension (52%) being the most common comorbidities.

Home Oxygen Therapy

One hundred eighty-seven subjects (49%) were prescribed LTOT at the initial assessment. An additional 187 subjects were prescribed ambulatory oxygen alone, of which 55 transitioned to LTOT during the study period (ILD: 26, COPD: 26, co-existing COPD and ILD: 3). The mean time to transition from ambulatory oxygen to LTOT was 612 d. Ten subjects were prescribed nocturnal oxygen therapy only, and none of these transitioned to LTOT. The small sample of nocturnal oxygen treatment precluded further analysis. There were no significant differences in sex, age, or BMI between subjects with COPD and ILD who were prescribed LTOT on their initial assessment (Table 2). The proportion of never smokers was higher in subjects with ILD than in those with COPD (ILD: 43%, COPD: 4.1%; $P < .001$). Both groups had moderate-to-severe disease, as reflected by their spirometry and gas transfer measurements. The baseline 6MWTs on room air revealed lower nadir oxyhemoglobin saturation ($P < .001$) and worse post-exertion Borg dyspnea score ($P < .001$) in the ILD group than in the COPD group, with comparable 6-min walk distance and oxygen requirements. Subjects with COPD had a lower pH ($P < .001$) and higher P_{aO_2} ($P < .001$) on resting arterial blood gas on room air compared to those with ILD.

Subjects who were prescribed ambulatory oxygen at the initial assessment were predominantly male, with the highest proportion in those with ILD who later transitioned to LTOT (Table 3). Overall, smoking exposure was lower in those with ILD compared to those with COPD. There were statistically significant differences in spirometry and D_{LCO}, reflecting the underlying chronic lung disease. However, there were no differences in lung function measurements between those who remained on ambulatory oxygen when compared to those who transitioned to LTOT. The mean nadir oxyhemoglobin saturation was lowest for subjects with ILD who were subsequently transitioned to LTOT, with the highest oxygen requirements during 6MWTs.

Care Needs for Patients on Home Oxygen Therapy

Of the 384 subjects who required home oxygen therapy, most (65%) were referred for pulmonary rehabilitation, which was consistent across both groups (Table 4). Palliative care referrals were generally low (23%), although higher in those with ILD. Referrals to other medical specialties and allied health were common in this study population ($n = 316$, 82%), with the median number of referrals being 2 (1–4) and the maximum number of 14. The median number of hospital admissions prior to and post commencement of home oxygen therapy was comparable (prior to: 1 (0–2), post: 1 (0–2); $P = .08$).

Survival Following the Initiation of Long-Term Oxygen Therapy

Transplant-free survival after commencement of LTOT either at initial assessment or following transition from ambulatory oxygen was generally poor, with 38% of subjects surviving at 5 y (Fig. 2). The 5-y transplant-free survival of subjects with ILD after commencing on LTOT was 10% compared to 52% for those with COPD. In a separate analysis of subjects who progressed to LTOT after an initial

Table 1. Baseline Characteristics of All Subjects

	Overall (*N* = 384)	COPD (*n* = 231)	ILD (*n* = 121)
Male	215 (56)	121 (53.3)	76 (63.3)
Age, y	76 (70–82)	75 (70–81)	76 (69–82)
BMI, kg/m^2	26.7 (22.6–31.3)	26.2 (20.9–30.7)	27.5 (23.7–31.5)
Smoking status			
Ever smoker	327 (85.2)	218 (96.1)	76 (63.3)
Pack-year	47.3 ± 33.0	55.0 ± 34.3	30.2 ± 25.5
Diagnosis			
COPD	227 (59.1)		
ILD	120 (31.2)		
COPD/ILD	32 (8.3)		
Respiratory function tests			
FER		41.6 ± 15.0	79.0 ± 9.6
FEV_1, % predicted		43.3 ± 20.1	74.0 ± 21.4
FVC, % predicted		76.1 ± 21.6	68.6 ± 19.0
D_{LCO}, % predicted		39.8 ± 13.6	40.7 ± 13.0
Medications			
LAMA	247 (64.3)	201 (88.6)	14 (11.7)
LABA	235 (61.2)	199 (87.7)	13 (10.8)
Inhaled corticosteroid	232 (60.4)	199 (87.7)	12 (10.0)
Triple inhaler therapy	200 (52.1)	175 (77.1)	6 (5.0)
SABA	202 (52.6)	170 (74.9)	10 (8.3)
Antifibrotics	7 (1.8)	0	7 (5.8)
Immunosuppressants	68 (17.7)	4 (1.8)	64 (53.3)
Other*	17 (4.4)	15 (6.6)	2 (1.7)
Charlson comorbidity index	6 (4–8)	6 (5–8)	5 (4–7)
Comorbidities			
Heart disease	221 (57.5)	129 (56.8)	68 (56.7)
Pulmonary hypertension	201 (52.3)	118 (52.0)	65 (54.2)
Sleep-disordered breathing	86 (22.4)	51 (22.5)	23 (19.2)
Asthma	39 (10.1)	32 (14.1)	5 (4.7)
Bronchiectasis	35 (9.1)	21 (9.3)	7 (5.8)
Liver disease	10 (2.6)	5 (2.2)	3 (2.5)

Data are expressed as mean ± SD, median (interquartile range), or *n* (%).
* Other medical therapies included short-acting muscarinic antagonist, oral morphine, oral corticosteroid, and mast cell stabilizer.
ILD = interstitial lung disease
BMI = body mass index
FER = forced expiratory ratio
D_{LCO} = diffusing capacity of the lung for carbon monoxide
LAMA = long-acting muscarinic antagonist
LABA = long-acting β agonist
SABA = short-acting β agonist

prescription of ambulatory oxygen, only 14.5% survived 2 y after the transition, with none surviving to 5 y. Multivariable Cox regression analyses showed that principal respiratory diagnosis was the only predictor of survival after commencing LTOT either at initial assessment or following transition from ambulatory oxygen (Table 5). There were no significant predictors of survival for the COPD and ILD cohorts after adjusted analyses.

Of 207 subjects who died during the follow-up period, location of death data was not available for 126 (61%). Of those with records available, 61 subjects with COPD (26.8%) died in hospital compared with 46 (38.3%) of subjects with ILD. There was no information available on the proportion of subjects who transitioned to hospice care outside of the hospital system. Four subjects (1%) underwent lung transplantation, 3 with ILD and one with COPD.

Discussion

The 5-y transplant-free survival after the commencement of LTOT was low and was significantly worse in the ILD group than the COPD group. This finding is in keeping with previous studies that have shown that a diagnosis of ILD is a significant predictor of mortality in

Table 2. Baseline Characteristics of Subjects Prescribed Initial Long-Term Oxygen Therapy

	COPD Only	ILD Only	*P*
Characteristic			
Male	60 (49.1)	23 (50.0)	> .99
Age, y	74 (69–81)	73 (68–82)	.73
BMI, kg/m^2	28.0 (20.9–34.1)	28.3 (24.6–31.1)	.43
Smoking status			
Ever smoker	117 (95.9)	26 (56.5)	< .001
Pack-year	58.5 ± 37.6	28.3 ± 16.7	< .001
Respiratory function tests			
FER	42.9 ± 15.3	76.7 ± 11.2	< .001
FEV_1, % predicted	45.0 ± 22.0	68.3 ± 22.4	< .001
FVC, % predicted	76.3 ± 23.1	64.3 ± 20.6	.003
D_{LCO}, % predicted	40.6 ± 13.7	37.1 ± 11.3	.20
6-min walk test*			
Distance, m	164.7 ± 122.7	159.0 ± 108.2	.79
Baseline S_{pO_2} %	89.5 ± 5.4	90.2 ± 4.7	.46
Nadir S_{pO_2}, %	80.8 ± 6.6	77.8 ± 6.7	.01
Borg dyspnea score pre-walk	1.2 ± 1.2	1.4 ± 1.3	.59
Borg dyspnea score post-walk	4.3 ± 1.6	5.2 ± 2.25	.02
Oxygen use, L/min	3.8 ± 1.8	4.3 ± 1.7	.32
ABG,† on room air			
pH	7.42 ± 0.03	7.44 ± 0.03	.009
P_{aO_2} mm Hg	51.9 ± 5.9	52.6 ± 6.0	.52
P_{aCO_2}, mm Hg	46.5 ± 8.5	40.0 ± 6.8	< .001
Charlson comorbidity index	6 (5–8)	5 (4–6.75)	< .001
Comorbidities			
Heart disease	73 (59.8)	31 (67.4)	.48
Pulmonary hypertension	73 (59.8)	34 (73.9)	.11
Sleep-disordered breathing	36 (29.5)	5 (10.9)	.01
Asthma	17 (13.9)	3 (6.5)	.28
Bronchiectasis	12 (9.8)	2 (4.3)	.35
Liver disease	4 (3.2)	0	.58

Data are expressed as mean ± SD, median (interquartile range), or *n* (%).
*6-min walk tests were available for 170 of the 187 (90.9%) subjects prescribed long-term oxygen therapy. Eighty-three of those 170 (38.8%) were performed on supplemental oxygen.
†Data were available for 158 of 187 (84.5%) subjects prescribed long-term oxygen therapy.
ABG = arterial blood gas
ILD = interstitial lung disease
BMI = body mass index
FER = forced expiratory ratio
D_{LCO} = diffusing capacity of the lung for carbon monoxide

patients receiving LTOT.[18] Our study provides additional insights into the prognosis of subjects who progressed from ambulatory oxygen to LTOT, with none surviving to 5 y post transition. In addition to worse prognosis, subjects with ILD had worse exertional desaturation and dyspnea scores than those with COPD. Subjects with COPD were moderately hypercapnic, as compared to the ILD group that had a mean P_{aCO_2} within the normal range. These findings are supportive of the known differences in pathophysiology between the 2 disease types and raise questions about their potential differential therapeutic responses to supplemental oxygen.

This cohort had numerous comorbidities, with a mean Charlson comorbidity index of 6.0, indicating a predicted overall 10-y survival of only 2%. More than 50% of subjects had pulmonary hypertension, which is of prognostic importance.[18,19] Furthermore, this cohort exhibited significant symptom burden with high dyspnea scores and impaired exercise capacity as measured by 6MWT. Previous studies have shown that subjects with both COPD and ILD have similar symptom burden to subjects with advanced malignancy.[13,20,21] This highlights the importance of considering the palliative care needs of this patient population, including symptom management, advanced care planning, and appropriate referrals concurrently at the time of workup for LTOT. The oxygen assessment represents a critical opportunity for holistic management and to broach conversations regarding patients' attitudes and wishes regarding their disease management. Integrated respiratory and palliative care models are associated with reduced emergency department presentations, improved completion of advanced care planning, and achievement of preferred location of death.[22]

Significant health care utilization was observed in this patient population, with a median of 3 referrals per subject and up to 14 for one subject. This is consistent with population-based studies that found increased health care utilization and associated costs in a population with COPD, with higher likelihood of admission and longer stay than matched controls.[23] Similarly, patients with systemic sclerosis-associated ILD have increased utilization of health care resources compared to those without ILD, with the severity of disease correlating with increasing costs.[24] This raises the importance of effective care coordination and patient-focused education for these patients involving primary care physicians and allied health. Furthermore, the utilization of a multidisciplinary care team that addresses care needs and educates regarding self-management may be beneficial for patients' health outcomes. This model has been implemented in many hospitals with the Hospital Admissions Risk Program in Australia, which provides short-term case management to elderly patients with complex care needs, providing early community intervention to improve care coordination and prevent hospital readmission.[25]

Referrals for pulmonary rehabilitation, either prior or subsequent to the oxygen assessment, were suboptimal at 65% for the whole cohort, with similar proportions in the COPD and ILD groups. Pulmonary rehabilitation has well-defined benefits in advanced lung disease. A recent Cochrane review found that subjects with ILD who underwent pulmonary rehabilitation had improved functional exercise capacity,

Table 3. Baseline Characteristics of Subjects Prescribed Initial Ambulatory Oxygen Therapy

	Remained on Ambulatory Oxygen			Transitioned to LTOT			Abulatory Oxygen vs Transition	
	COPD Only	ILD Only	*P*	COPD Only	ILD Only	*P*	COPD *P*	ILD *P*
Characteristic								
Male	47 (62.7)	30 (66.7)	.70	12 (46.2)	20 (76.9)	.04	.17	.43
Age, y	77 (72–83)	77 (70–84)	.72	74 (72.3–78.8)	76.5 (70.3–82.0)	.58	.19	.63
BMI, kg/m^2	25.3 (20.5–27.2)	27.8 (23.6–32.7)	.02	26.8 (22.2–29.7)	27.0 (23.7–28.9)	.66	.09	.81
Smoking status								
Ever smoker	72 (96)	33 (73.3)	< .001	24 (92.3)	16 (61.5)	.02	.60	.42
Pack-year	47.1 ± 25.9	27.1 ± 24.8	< .001	58.5 ± 38.7	46.8 ± 36.7	.12	.11	.19
Respiratory function tests								
FER	40.8 ± 15.4	81.4 ± 6.4	< .001	36.0 ± 10.8	79.0 ± 8.3	< .001	.46	.62
FEV_1, % predicted	42.8 ± 21.0	79.9 ± 17.4	< .001	39.0 ± 11.3	72.0 ± 21.7	< .001	.43	.67
FVC, % predicted	75.7 ± 20.9	72.4 ± 15.2	.40	77.0 ± 18.2	70.0 ± 19.9	.31	.69	.92
D_{LCO}, % predicted	38.4 ± 13.7	44.5 ± 12.0	.034	40.0 ± 13.2	39.5 ± 15.6	.90	.43	.30
6-min walk test,*on room air								
Distance	206.6 ± 113.8	239.3 ± 134.1	.16	233.3.6 ± 96.2	268.4 ± 134.5	.31	.31	.39
Baseline S_{pO_2}, %	93.7 ± 2.0	94.8 ± 1.9	.003	92.6 ± 2.2	93.3 ± 2.9	.35	.03	.01
Nadir S_{pO_2}, %	83.9 ± 4.1	82.4 ± 4.2	.07	81.4 ± 4.8	79.6 ± 5.6	.24	.02	.02
Borg dyspnea score pre-walk	0.9 ± 1.0	1.4 ± 1.4	.058	0.8 ± 0.8	1.5 ± 2.1	.21	.74	.84
Borg dyspnea score post-walk	4.2 ± 1.5	4.6 ± 1.9	.24	4.7 ± 2.1	5.1 ± 1.8	.49	.28	.33
6-min walk test, on oxygen								
Distance	246.8 ± 100.7	299.4 ± 129.1	.01	273.8 ± 102.1	315.3 ± 101.7	.15	.25	.59
Baseline S_{pO_2}, %	96.5 ± 1.7	97.0 ± 1.6	.12	96.2 ± 1.6	96.4 ± 2.2	.63	.46	.24
Nadir S_{pO_2}, %	89.2 ± 4.7	87.8 ± 4.0	.08	88.0 ± 3.6	84.2 ± 5.2	< .001	.26	.01
Borg dyspnea score pre-walk	1.2 ± 1.2	1.2 ± 1.1	.90	0.8 ± 0.9	1.0 ± 1.0	.48	.20	.52
Borg dyspnea score post-walk	3.6 ± 1.6	4.0 ± 1.8	.24	3.3 ± 1.4	4.3 ± 1.5	.49	.52	.46
Oxygen use L/min	2.9 ± 1.4	3.4 ± 1.3	.053	3.8 ± 1.6	4.5 ± 1.5	.14	.01	< .001
Arterial blood gas,† on room air								
pH	7.43 ± 0.04	7.43 ± 0.02	.64	7.43 ± 0.03	7.43 ± 0.03	.90	.95	.72
P_{aO_2}, mm Hg	63.8 ± 6.1	69.4 ± 8.5	.004	60.3 ± 7.9	65.2 ± 17.7	.25	.06	.36
P_{aCO_2}, mm Hg	40.9 ± 7.1	36.9 ± 3.6	.03	42.4 ± 7.1	35.5 ± 4.7	< .001	.36	.31
Charlson comorbidity index	6 (4.5–9)	5 (4–7)	.09	5 (4–7)	5 (4–6)	.42	.10	.40
Comorbidities								
Heart disease	44 (58.7)	22 (48.9)	.35	13 (50)	13 (50)	> .99	.50	> .99
Pulmonary hypertension	29 (38.7)	15 (33.3)	.70	12 (46.2)	14 (53.8)	.78	.64	.13
Sleep-disordered breathing	9 (12.0)	12 (26.7)	.05	5 (19.2)	4 (15.4)	> .99	.34	.38
Asthma	12 (16.0)	2 (4.4)	.08	3 (11.5)	0	.23	.75	.53
Bronchiectasis	9 (12.0)	4 (8.9)	.76	1 (3.8)	1 (3.8)	> .99	.45	.45
Liver disease	1 (1.3)	3 (6.7)	.15	0	0	.99	.15	.29

Data are expressed as mean ± SD, median (interquartile range), or *n* (%).
*6-min walk test (6MWT) data were available for 130 of the 132 subjects prescribed ambulatory oxygen (98.5%). One hundred twenty-eight of 132 subjects (97.0%) performed two 6MWT.
†Arterial blood gas data were available for 69 of 132 subjects (52.3%).
LTOT = long term oxygen therapy
ILD = interstitial lung disease
BMI = body mass index
FER = forced expiratory ratio
D_{LCO} = diffusing capacity of the lung for carbon monoxide

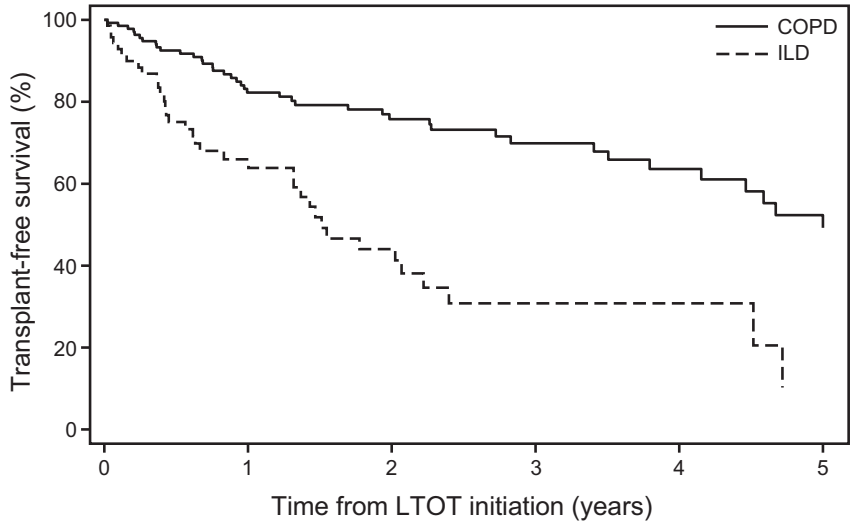
dyspnea, and health-related quality of life.[26] Similarly, benefits of pulmonary rehabilitation in COPD include improved exercise capacity, dyspnea scores, quality of life, and reduced hospital utilization.[27] Considering the known benefits of pulmonary rehabilitation in patients with COPD and ILD, it is important that they are offered this potent intervention.

This study was a single-center study with a retrospective design at a quaternary metropolitan center with a dedicated oxygen service, which may limit the generalizability of the

Table 4. Referrals to Other Services

	All Subjects	COPD	ILD	*P*
Service				
Pulmonary rehabilitation	251 (65.4)	143 (63.0)	84 (70.0)	.52
Palliative care	88 (22.9)	42 (18.5)	37 (30.8)	.05
Other services	316 (82.3)	190 (83.7)	96 (80.0)	.76
Medical Specialties				
Cardiology	105 (27.3)	60 (26.4)	35 (29.2)	.67
Surgical	105 (27.3)	66 (29.1)	27 (22.5)	.32
General medicine/geriatrics	89 (23.2)	61 (26.9)	19 (15.8)	.08
Gastroenterology	58 (15.1)	37 (16.3)	14 (11.7)	.35
Endocrinology	55 (14.3)	32 (14.1)	16 (13.3)	.78
Other[1]	282 (73.4)	164 (72.2)	82 (68.3)	.54
Nursing and allied health				
Aged care assessment service	79 (20.6)	49 (21.6)	23 (19.2)	.70
Physiotherapy (outside PR referrals)	73 (19.0)	42 (18.5)	23 (19.2)	.90
Hospital Admissions Risk Program	69 (18.0)	50 (22.0)	13 (10.8)	.05
Other[2]	186 (48.4)	114 (50.2)	59 (49.2)	.77

Data are expressed as *n* (%).
[1]Other medical specialties included ophthalmology, medical and radiation oncology, renal, rheumatology, neurology, hematology, ear nose and throat surgery, infectious diseases, lung transplant, dermatology, psychiatry/psychology, pain medicine, and genetics.
[2]Other nursing and allied health referrals included dietetics, occupational therapy, speech pathology, community nursing, social work, and podiatry.
ILD = interstitial lung disease
PR = pulmonary rehabilitation



Combined	77%	65%	56%	52%	38%
COPD	84%	78%	70%	64%	52%
ILD	66%	44%	31%	31%	10%

Fig. 2. Kaplan-Meier survival curve following the initiation of long-term oxygen therapy. ILD = interstitial lung disease; LTOT = long-term oxygen therapy.

findings. Managing these complex patients in a lower resource setting would provide additional challenges. A dedicated oxygen service with multidisciplinary assessment of patients and institution of oxygen therapy is undoubtedly beneficial to this complex population. Our study did not include data on subjects who were admitted directly from

Table 5. Predictors for Prognosis After the Initiation of Long-Term Oxygen Therapy

Variable	Hazard Ratio	95% CI	*P*
Combined cohort			
Unadjusted analysis			
Age	1.01	0.99–1.03	.45
Male sex	1.29	0.84–1.99	.24
Charlson comorbidity index	1.08	0.98–1.19	.14
D_{LCO}, % predicted	1.00	0.98–1.02	.82
6MWD, m	1.00	0.99–1.00	.02
Diagnosis (ILD vs COPD)	3.01	1.91–4.75	< .001
Adjusted analysis			
Diagnosis (ILD vs COPD)	4.22	2.27–7.83	< .001
COPD cohort			
Unadjusted analysis			
Age	1.00	0.97–1.04	.99
Male sex	0.74	0.40–1.38	.35
Charlson comorbidity index	1.15	0.99–1.32	.059
FEV_1, % predicted	1.00	0.99–1.02	.75
D_{LCO}, % predicted	0.99	0.97–1.02	.65
6MWD	1.00	0.99–1.00	.007
No significant predictors identified after adjusted analyses.			
ILD cohort			
Unadjusted analysis			
Age	1.01	0.98–1.05	.39
Male sex	1.95	0.96–3.99	.07
Charlson comorbidity index	1.02	0.87–1.20	.78
FVC, % predicted	1.01	0.99–1.03	.26
D_{LCO}, % predicted	1.03	1.00–1.05	.049
6MWD, m	1.00	0.99–1.00	.55
No significant predictors identified after adjusted analyses.			

D_{LCO} = diffusing capacity of the lung for carbon monoxide
6MWD = 6-min walk distance
ILD = interstitial lung disease

the community into hospice care; however, at our institution, referrals to hospice care are predominantly through palliative care teams, and these referrals were examined.

It is important to acknowledge geographical variability in the accessibility and eligibility criteria for home oxygen therapy.[28] Nevertheless, our prescribing criteria for LTOT are consistent with the national and other international guidelines, with the criteria for ambulatory oxygen being applicable to most countries.[6,7,29,30]

Conclusions

This study found that subjects receiving LTOT through a quaternary health service oxygen clinic had poor overall transplant-free survival after the initiation of LTOT. As hypothesized, the cohort of subjects with ILD had significantly worse transplant-free survival than those with COPD. Despite the poor survival of the overall cohort, which was worse than many advanced malignancies, only a minority were referred for palliative care input. Referrals to pulmonary rehabilitation, a potent intervention in patients with chronic respiratory failure, were also suboptimal. This patient population had complex care needs that required multidisciplinary management. Appropriate and early referrals to palliative care and improved care coordination for this complex group of patients are key areas for improvement.

REFERENCES

1. Serginson JG, Yang IA, Armstrong JG, Cooper DM, Matthiesson AM, Morrison SC, et al. Variability in the rate of prescription and cost of domiciliary oxygen therapy in Australia. Med J Aust 2009;191(10):549-553.
2. McDonald CF, Crockett AJ. Optimizing the therapeutic use of oxygen in Australia. Med J Aust 2009;191(10):526-527.
3. Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. Ann Intern Med 1980;93(3):391-398.
4. Report of the Medical Research Council Working Party. Long-term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. Lancet 1981;1(8222):681-686.
5. Cranston JM, Crockett AJ, Moss JR, Alpers JH. Domiciliary oxygen for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2005;2005(4):Cd001744.
6. McDonald CF, Whyte K, Jenkins S, Serginson J, Frith P. Clinical practice guideline on adult domiciliary oxygen therapy: executive summary from the Thoracic Society of Australia and New Zealand. Respirology 2016;21(1):76-78.
7. Hardinge M, Suntharalingam J, Wilkinson T, British Thoracic Society. Guideline update: the British Thoracic Society guidelines on home oxygen use in adults. Thorax 2015;70(6):589-591.
8. Cranston JM, Nguyen A-M, Crockett AJ. The relative survival of COPD patients on long-term oxygen therapy in Australia: a comparative study. Respirology 2004;9(2):237-242.
9. Crockett AJ, Alpers JH, Moss JR. Home oxygen therapy: an audit of survival. Aust N Z J Med 1991;21(2):217-221.
10. Crockett AJ, Cranston JM, Antic N; Cochrane Airways Group. Domiciliary oxygen for interstitial lung disease. Cochrane Database Syst 2001;2010(12).
11. Carvajalino S, Reigada C, Johnson MJ, Dzingina M, Bajwah S. Symptom prevalence of patients with fibrotic interstitial lung disease: a systematic literature review. BMC Pulm Med 2018;18(1):78.
12. Joshi M, Joshi A, Bartter T. Symptom burden in chronic obstructive pulmonary disease and cancer. Curr Opin Pulm Med 2012;18(2):97-103.
13. Ahmadi Z, Wysham NG, Lundström S, Janson C, Currow DC, Ekström M. End-of-life care in oxygen-dependent ILD compared with lung cancer: a national population-based study. Thorax 2016;71(6):510-516.
14. Crawford GB, Burgess TA, Young M, Brooksbank MA, Brown MA. Patient-centered model of care incorporating a palliative approach: a framework to meet the needs of people with advanced COPD? Progress in Palliative Care 2013;21(5):286-294.
15. Kreuter M, Bendstrup E, Russell A-M, Bajwah S, Lindell K, Adir Y, et al. Palliative care in interstitial lung disease: living well. Lancet Respir Med 2017;5(12):968-980.
16. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur Respir J 2014;44(6):1428-1446.

17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373-383.
18. Chaouat A, Naeije R, Weitzenblum E. Pulmonary hypertension in COPD. Eur Respir J 2008;32(5):1371-1385.
19. Caminati A, Cassandro R, Harari S. Pulmonary hypertension in chronic interstitial lung diseases. Eur Respir Rev 2013;22(129):292-301.
20. Maddocks M, Lovell N, Booth S, Man WD, Higginson IJ. Palliative care and management of troublesome symptoms for people with chronic obstructive pulmonary disease. The Lancet 2017;390 (10098):988-1002.
21. Wysham NG, Cox CE, Wolf SP, Kamal AH. Symptom burden of chronic lung disease compared with lung cancer at time of referral for palliative care consultation. Ann Am Thorac Soc 2015;12 (9):1294-1301.
22. Smallwood N, Thompson M, Warrender-Sparkes M, Eastman P, Le B, Irving L, et al. Integrated respiratory and palliative care may improve outcomes in advanced lung disease. ERJ Open Res 2018;4(1):00102-2017.
23. Mapel DW, Hurley JS, Frost FJ, Petersen HV, Picchi MA, Coultas DB. Health care utilization in chronic obstructive pulmonary disease: a case-control study in a health maintenance organization. Arch Intern Med 2000;160(17):2653-2658.
24. Morrisroe K, Stevens W, Sahhar J, Ngian G-S, Ferdowsi N, Hansen D, et al. The clinical and economic burden of systemic sclerosis–related interstitial lung disease. Rheumatology 2020;59(8):1878-1888.
25. Roberts RM, Dalton KL, Evans JV, Wilson CL. A service model of short-term case management for elderly people at risk of hospital admission. Aust Health Rev 2007;31(2):173-183.
26. Dowman L, Hill CJ, May A, Holland AE; Cochrane Airways Group. Pulmonary rehabilitation for interstitial lung disease. Cochrane Database of Systematic Reviews 2021;2021(2)
27. Hui KP, Hewitt AB. A simple pulmonary rehabilitation program improves health outcomes and reduces hospital utilization in patients with COPD. Chest 2003;124(1):94-97.
28. Khor YH, Renzoni EA, Visca D, McDonald CF, Goh NS. Oxygen therapy in COPD and interstitial lung disease: navigating the knowns and unknowns. ERJ Open Res 2019;5(3):00118-2019.
29. Jacobs SS, Krishnan JA, Lederer DJ, Ghazipura M, Hossain T, Tan A-YM, et al. Home oxygen therapy for adults with chronic lung disease. An official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med 2020;202(10): e121-e141.
30. Lim RK, Humphreys C, Morisset J, Holland AE, Johannson KA. Oxygen in patients with fibrotic interstitial lung disease: an international Delphi survey. Eur Respir J 2019;54(2):1900421.