

Real World Profile, Management and Outcomes of Patients Seen at a Joint Interstitial Lung Clinic

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Introduction: Interstitial lung disease (ILD) is associated with significant morbidity and mortality. Effective therapeutic intervention to halt or reverse its progression is needed. Systemic autoimmune rheumatic diseases (SARDs) are associated with ILD, and it has been shown that therapies developed initially for SARDs may also impact favourably on ILD. This has led to the growth of joint ILD clinics, frequently run by chest physicians in tandem with rheumatologists. However, little data are available on the profile, treatment and outcome of patients treated in these clinics across the UK. **Methods:** We established a clinic for patients with ILD and a diagnosis of proven or suspected SARDs in 2023. We collected data from each patient comprising age, sex, SARD diagnosis, ILD subtype on high-resolution computed tomography (HRCT), baseline pulmonary function tests (PFTs), autoantibody profile, smoking history, therapeutic intervention, changes in both HRCT and PFTs over time and survival. We analysed these for the first 130 patients attending our clinic to produce information on source and appropriateness of referral, demographics, therapeutic approaches used, outcomes and predictors of death or deterioration across the whole cohort. **Results:** Of the 130 patients referred to the clinic in the first 18 months, only 110 had definite ILD on HRCT. Their mean (standard deviation [SD]) age was 68.4 (11.7) years at referral, and 56 (50.9%) patients were female. Seventy-one patients met the criteria for a definite SARD, of which 41 were patients with rheumatoid arthritis (RA). Twelve additional patients had biopsy-proven sarcoidosis. Of the remaining 27 patients, 12 had autoantibodies associated with SARDs. In the study, 12 (11%) patients died during a median follow-up period of 12 months, with five of them from respiratory causes. Across the 110 patients with ILD, the most prescribed therapeutic agents included mycophenolate (53%), rituximab (35%) and methotrexate (17%), usually with bridging steroids. Fewer patients were treated with cyclophosphamide (10%), anti-tumour necrosis factor (TNF) therapy (10%) or azathioprine (4%), and these were often later switched to another therapy. Anti-fibrotics were given to just 11%. Death or deterioration in both lung function and HRCT appearances occurred in 21 patients who had a male:female ratio of 2:1 and a mean (SD) age of 71.3 (11.4) years. Predictors for death or deterioration included male sex (relative risk [RR] 1.89), the absence of autoantibodies (1.60), a usual interstitial pneumonia (UIP) pattern on HRCT (1.59), baseline reduction in gas transfer (1.43) and a non-SARD-ILD or sarcoid diagnosis (RR 1.31). **Discussion:** We describe a real-world experience of a joint ILD clinic. Our results suggest that therapeutic intervention can be effective in patients with SARD-ILD, but that a meaningful response can be achieved in patients with a similar autoantibody profile, even in the absence of clinical evidence of SARD. Patients with sarcoidosis also responded well to intervention. Sex, antibody status, HRCT pattern, baseline gas transfer and diagnosis influenced the outcome of the study. Longer follow-up and a larger database are essential to clarify and confirm these findings.

Keywords

Biologics, connective tissue disease, immunosuppression therapy, interstitial lung disease (ILD), mortality, outcomes, prognosis, survival, systemic autoimmune rheumatic disease

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Compliance with ethics: This study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments. Patients consented to the use of their anonymized amalgamated clinical data to allow sharing of the outcomes of the clinic and related therapeutic intervention. As this was an observational clinical service with no external influence, approval of the process and protocol by the hospital ethics committee was deemed sufficient.

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The importance of multi-disciplinary clinics for the assessment of patients with interstitial lung disease (ILD) is well established, and these are usually led by chest physicians.¹ The role of rheumatologists in such a setting has evolved more recently.² The main factor responsible for this is the recognition that several immunosuppressive and biologic agents initially used to treat systemic autoimmune rheumatic diseases (SARDs) can also impact favourably on the associated ILD, which has been recently acknowledged in therapeutic guidelines.³

There is little publicly available data on the number of SARD-ILD services in the UK, but there are a variety of different models in common use. We are aware of at least 12 such clinics nationwide, although this is likely to be an underestimate. In many cases, the service for SARD-ILD is embedded within a larger ILD service structure, with SARD-ILD clinics run anywhere from weekly to every 3 months, depending on the population size and the availability of appropriate specialist input. In some centres, such as ours, the SARD-ILD clinic is a stand-alone service, independent of the rest of the ILD clinic structure (more details are provided in the Methods section).

For many years, the treatment of ILD was empiric with a very limited evidence base. High-dose steroids, combined with azathioprine, were eventually shown to be ineffective.⁴ The recognition that ILD was a common feature across most SARDs encouraged greater efforts to explore more effective therapy.⁵ In systemic sclerosis-related (SSc) ILD, both cyclophosphamide and mycophenolate were shown to improve high-resolution computed tomography (HRCT) appearances, while the British Rheumatic Interstitial Lung (BRILL) consortium reported that both mycophenolate and rituximab were associated with improved survival in rheumatoid arthritis (RA) ILD.^{6,7} A study of patients with mixed SARD-ILD confirmed benefits from mycophenolate, while another study demonstrated equivalent efficacy in SARD-ILD between rituximab and cyclophosphamide, albeit with less toxicity with rituximab.^{8,9}

A small study demonstrated greater benefit from rituximab among patients with SARD-ILD when compared with controls with hypersensitivity pneumonitis (HSP) and idiopathic interstitial pneumonia (IIP), while a larger French study demonstrated a better response to the combination of rituximab with mycophenolate than with mycophenolate alone. This study included patients with non-specific interstitial pneumonia (NSIP) associated with SARD-ILD, IIP and interstitial pneumonia with autoimmune features (IPAF).^{10,11} Patients with IPAF have often been excluded from studies because of their variable clinical, radiological and serological patterns.¹²

In clinical practice, fewer filters are usually applied to referrals of patients to a joint ILD clinic. These often encompass each of HSP, IIP, IPAF and sarcoidosis in addition to SARD-ILD. We report on our experience of jointly running a clinic for real-world patients with ILD by chest physicians and rheumatologists, describing the profile of new referrals over the first 18 months, along with the treatment offered and the outcomes observed. We compare profiles and outcomes between patients with SARD-ILD, sarcoidosis, HSP, IIP and IPAF.

Methods

We established a face-to-face clinic for patients with ILD and a diagnosis of proven or suspected SARDs in August 2023. The clinic is held once a month and is attended by at least one chest physician and one rheumatologist, along with a respiratory nurse, trainees from both specialities and occasional medical students. Pulmonary function is undertaken on each patient by a technician immediately

prior to consultation. A radiologist is not physically present but is in virtual attendance to advise on individual cases. The clinic is located in Redcar Primary Care Hospital and serves a catchment population of 376,000 people across much of Teesside and parts of North Yorkshire. It is funded by the South Tees NHS Trust and costs an estimated £40,000 annually. The referral criteria are the presence of an established diagnosis of ILD proven by HRCT and a suspected or proven diagnosis of SARD or IPAF. Patients with sarcoidosis are also accepted. All patients gave informed consent to their data being used in anonymised form. All data was collected and analysed according to the Declaration of Helsinki.

Typically, six new referrals are seen in each clinic, with each consultation lasting a minimum of 30 min. Follow-up is usually conducted by the referring consultant, although not infrequently one of the team (Dr Clive Kelly) is requested to assume subsequent patient management. Here, we report on the data collected from the first 130 patients referred to the clinic, along with details on the source and appropriateness of referrals. A careful history and full physical examination is performed and recorded for each patient, along with their previous drug exposure history. We collect information from each patient comprising age, sex, SARD diagnosis, ILD subtype on HRCT, autoantibody profile and smoking history in pack years. Pulmonary function tests (PFTs) for each patient comprise forced expiratory volume in 1 s (FEV1), forced vital capacity, gas transfer factor (TLco) and flow volume loop, and, where appropriate, pulse oximetry is assessed before and immediately after exertion.

A diagnosis is made for each patient specifically with regard to the presence and pattern of ILD on HRCT. Similarly, the clinical and serological features of each patient are reviewed, and the presence or absence of a confirmed SARD is recorded. All therapeutic recommendations are recorded, along with the outcomes of all further investigations. Data on sequential changes in PFTs and HRCT scans are assessed and documented where these have been performed.

These data have been analysed to produce information on the source and appropriateness of referrals, their age and sex distribution, smoking status, SARD and pulmonary diagnoses, serological profile, HRCT patterns, PFTs and therapeutic intervention. We considered an increase in vital capacity (VC) or TLco of 10% or more to represent improvement, a reduction of 10% or more to represent deterioration, and any result between these to represent stability. We defined our primary endpoint as death and secondary outcomes as deterioration in VC or TLco. From these data, we calculated factors that were associated with both outcomes and with therapeutic response.

Statistical analysis

We used Student's unpaired t-test to compare results between groups and Student's paired t-test to calculate within-group changes over time. Relative risk (RR) and its significance were calculated using the chi-squared test.

Results

From the first 18 months to March 2025, there were 130 referrals to the clinic. Of these, 68 were referred by the respiratory team, and 62 from the rheumatology department. Only 110 had definite ILD on HRCT, with 10 from each referral source having another diagnosis apparent on careful review. Most patients with ILD complained of breathlessness on exertion (95), while eight were breathless at rest. The remaining seven denied breathlessness.

Table 1: Patient demographics for overall sample, IPAF, IIP, HSP, sarcoid and SARD-ILD groups

Characteristic	Overall sample (n=110)	IPAF, IIP, HSP (n=27)	Sarcoid (n=12)	SARD-ILD (n=71)
Age in years (mean, SD)	68.4 (11.7)	71.8 (9.8)	54.8 (13.2)	69.4 (10.5)
<60 years	24 (21.8%)	3 (11.1%)	5 (41.7%)	16 (22.5%)
≥60 years	86 (78.2%)	24 (88.9%)	7 (58.3%)	55 (77.5%)
Sex at birth				
Male	54 (49.1%)	14 (51.9%)	7 (58.3%)	33 (46.5%)
Female	56 (50.9%)	13 (48.1%)	5 (41.7%)	38 (53.5%)
Smoking status				
Never	59 (53.6%)	14 (51.9%)	7 (58.3%)	38 (53.5%)
Past	44 (40.0%)	12 (44.4%)	3 (25.0%)	29 (40.8%)
Current	7 (6.4%)	1 (3.7%)	2 (16.7%)	4 (5.6%)
Smoking pack years – median (IQR)	0 (0, 20)	0 (0, 22.5)	0 (0, 21.3)	0 (0, 20)

HSP = hypersensitivity pneumonitis ; IIP = idiopathic interstitial pneumonia ; IPAF = interstitial pneumonia with autoimmune features ; IQR = interquartile range ; SARD-ILD = systemic autoimmune rheumatic disease–interstitial lung disease ; SD = standard deviation.

Symptom duration

At the time of assessment in the clinic, the mean (SD) duration of breathlessness among the 103 symptomatic patients with ILD was 33 (13) months.

Demographics

Among the 110 patients with ILD, the mean (SD) age was 68.4 (11.7) years at referral, and 56 (50.9%) patients were female. Seventy-one (64.5%) patients met the criteria for a definite SARD, while 12 additional patients had biopsy-proven sarcoidosis (10.9%). Of the remaining 27 patients (24.6%) with another ILD diagnosis (controls), 12 had autoantibodies associated with SARs and met the criteria for IPAF. The majority of patients with ILD (53.6%) had never smoked, and this was independent of their diagnostic category. Median pack-year consumption did not differ between groups. Overall, there were no significant differences between patients with SARD-ILD and other patients with ILD with regard to age, sex or smoking status, although patients with sarcoidosis were younger (mean age 58.4 years) and more likely to have never smoked (58.3%). Further details are shown in *Table 1*.

Diagnoses

Diagnosis was made or altered as a result of clinic attendance in 28 patients (25.4%). This most often applies to patients with SARD-ILD or IPAF. Among 71 patients with SARD-ILD, 41 had RA (37.3% of total patients with ILD). There were significant numbers with mixed connective tissue disease (MCTD=7), SSC (5), myositis (MYO=6), Sjogren's syndrome (SJO=6) and vasculitis (VAS=5). Eight patients with SARD-ILD (11.3%) had no autoantibodies detected. Details are shown in *Table 2* along with the corresponding data for the non-SARD non-sarcoid group, where the predominant diagnoses were IIP (7), HSP (8) and IPAF (12). All patients in the IPAF group (44.4%) had autoantibodies, while those with IIP and HSP (55.6%) did not.

High-resolution computed tomography findings

HRCT results were available for all patients. The most common overall pattern on HRCT among the 71 patients with SARD-ILD was NSIP in 39

Table 2: Underlying diagnoses and autoantibody profiles

Diagnosis	Number	Number (%) with antibodies
Rheumatoid arthritis	41	36 (88%)
Mixed connective tissue disease	7	7 (100%)
Myositis	6	5 (83%)
Sjogren's syndrome	6	6 (100%)
Systemic sclerosis	5	4 (80%)
Vasculitis	5	4 (80%)
Systemic lupus	1	1 (100%)
Interstitial pneumonia with autoimmune features	12	12 (100%)
Hypersensitivity pneumonitis	8	0
Idiopathic pneumonitis	7	0

patients, while IIP was evident in 26 patients. However, this varied with the SARD, with patients with RA showing predominant IIP, while every other SARD had more NSIP. Six patients exhibited a mixed or different pattern. Patients with sarcoidosis showed upper- and middle-zone predominance with variable fibrosis. Those with HSP also showed upper lobe predominance, while patients with IPAF and IIP demonstrated a variable pattern with basal fibrosis predominant. The full results are shown in *Table 3*.

Pulmonary function

Lung function at baseline was available for all patients. Among the 71 patients with SARD-ILD, the mean per cent predicted (SD) VC was 79.2 (15.7), and the mean per cent predicted (SD) TLC₀ was 59.5 (14.9). This related to the underlying diagnosis as patients with RA-ILD had significantly higher values than patients with other SARD-ILDs. Among the 27 patients with IPAF, HSP and IIP, gas transfer was significantly lower than among patients with SARD-ILD. Baseline values were the highest among patients with sarcoidosis. Further details are shown in *Table 4*.

Changes over time in high-resolution computed tomography and pulmonary function tests

Sequential dynamic lung volume tests were available for 95 patients over a mean interval of 10 months. This showed an improvement in VC in 48 (50.5%), stability in 22 (23.2%) and deterioration in 25 (26.3%). Sequential gas transfer estimations were available for 92 patients and showed improvement in 42 (45.7%), stability in 21 (22.8%) and deterioration in 29 (31.5%). Deterioration in VC and TLC₀ was more likely to occur in patients with HSP and IIP (54.5% and 57.1%) than among patients with SARD-ILD (20.3% and 27.4%) or sarcoidosis (0% and 0%).

Table 3: Pattern of high-resolution computed tomography results within each diagnostic group

Diagnosis	NSIP	IIP	Mixed	Other
Rheumatoid arthritis	18	21	2	0
Other SARs	21	5	2	2
Sarcoid	0	0	0	12
IPAF	5	5	1	1
HSP	0	0	0	8
IIP	2	3	0	2

HSP = hypersensitivity pneumonitis ; IIP = idiopathic interstitial pneumonia ; IPAF = interstitial pneumonia with autoimmune features ; NSIP = non-specific interstitial pneumonia ; SARs = systemic autoimmune rheumatic diseases ; IIP = usual interstitial pneumonia.

Table 4: Baseline lung function for each diagnostic group

Diagnosis	Mean % predicted VC at baseline (SD)	Mean % predicted TLco at baseline (SD)
Rheumatoid arthritis	83.2% (19.5)	61.3% (20.5)
Other SARDs	74.7% (21.4)	57.3% (16.5)
Sarcoid	82.8% (15.0)	72.2 (16.4)
IAPAF, HSP, IIP	73.8 (19.8)	51.0 (17.9)

HSP = hypersensitivity pneumonitis; IIP = idiopathic interstitial pneumonia; IAPAF = interstitial pneumonia with autoimmune features; SARDs = systemic autoimmune rheumatic diseases; SD = standard deviation; TLco = gas transfer factor; VC = vital capacity.

Sequential HRCT was available for 83 patients over a mean interval of 11 months. This showed an improvement in 18 (21.7%), stability in 43 (51.8%) and deterioration in 22 (26.5%). However, deterioration in HRCT appearances occurred no more often in patients with IAPAF, HSP and IIP (22.7%) than among other patients with ILD (27.9%) (not significant [NS]).

Therapeutics

Within the ILD cohort, relatively few patients had commenced therapy for ILD prior to assessment in our clinic. The main exceptions to this included oral/intravenous steroids (n=98), methotrexate (n=13), anti-tumour necrosis factor (TNF) therapy (n=11), cyclophosphamide (n=9) and anti-fibrotic therapy (n =7). Treatment was altered in 77/110 (70%) patients following clinic attendance. The therapeutic agents most frequently prescribed included mycophenolate (53%) and rituximab (34%). Some patients previously treated with cyclophosphamide (10%), anti-TNF agents (10%) or azathioprine (4.5%) were switched to another therapy due to side effects or inefficacy. Compared with the overall cohort, patients with SARD-ILD were more likely to receive rituximab (45%), while patients with sarcoidosis were more likely to receive methotrexate (75%). Most patients treated initially with cyclophosphamide or azathioprine were switched to mycophenolate, while many patients who commenced on anti-TNF were switched to rituximab. Anti-fibrotics were prescribed in 11% of the total ILD cohort. Combination therapies were used in 57 patients (52%), the most frequent combination being rituximab and mycophenolate. Therapeutic decisions were informed by best available published evidence and guided by patient preference following discussion in clinic. Further details of relevant therapeutic interventions are shown in Table 5 and Table 6.

Table 5: Therapeutic agents employed in clinic across all diagnostic categories

Treatment	Number (percentage)
Mycophenolate	58 (52.7%)
Rituximab	37 (35.4%)
Methotrexate	19 (17.2%)
TNF inhibitor	11 (10%)
Cyclophosphamide	11 (10%)
Azathioprine	5 (4.5%)
Abatacept	4 (3.6%)
Tocilizumab	2 (1.8%)
Leflunomide	2 (1.8%)
JAK inhibitor	1 (0.9%)
Antifibrotic	12 (10.9%)

JAK = Janus kinase; TNF = tumour necrosis factor.

Table 6: Therapeutic agents employed specifically in the SARD-ILD patient cohort

Treatment	Number (percentage)
Mycophenolate	40 (56.3%)
Rituximab	32 (45.1%)
Methotrexate	10 (14.1%)
Cyclophosphamide	8 (11.3%)
TNF inhibitor	6 (8.5%)
Azathioprine	5 (7.0%)
Abatacept	4 (5.6%)
Tocilizumab	2 (2.8%)
Leflunomide	2 (2.8%)
JAK inhibitor	1 (1.4%)
Antifibrotic	7 (9.8%)

JAK = Janus kinase; SARD-ILD = systemic autoimmune rheumatic disease-idiopathic interstitial lung disease; TNF = tumour necrosis factor.

Outcomes and endpoints

Twelve (10.9%) patients died during a median follow-up period of 11 months, with five of these from respiratory causes. Death occurred in four patients with IIP/HSP (14.8%) and eight patients with SARD-ILD (11.3%), but in none with sarcoid. Death or deterioration in lung function occurred in 16/27 (59.3%) of patients with IAPAF/HSP/IIP as compared with 21/71 (32.4%) of patients with SARD-ILD, p=0.005. However, death or deterioration in HRCT occurred in 9/27 (33.3%) of patients with IAPAF/HSP/IIP and 24/71 (33.8%) of patients with SARD-ILD, p=0.98. Death or deterioration in both lung function and HRCT appearances occurred in 21 patients who had a male:female ratio of 2:1 and a mean (SD) age of 71.3 (11.4) years.

Statistically significant predictors for respiratory death or deterioration included male sex (RR 1.89), the absence of autoantibodies (RR 1.60), a UIP pattern on HRCT (RR 1.59), baseline reduction in gas transfer (RR 1.43) and a non-SARD-ILD or sarcoid diagnosis (RR 1.31), but not older age (RR 1.04) or smoking (RR 1.09).

Discussion

There has been considerable growth of interest in SARD-ILD over the last few years to address the challenges and opportunities associated with scientific developments in this area.¹³ This has spawned rapidly expanding literature assessing many aspects of its presentation and natural history and exploring the potential effect of new therapies on outcome.¹⁴ As part of this process, prediction scores for the presence and progression of ILD in SARDs have been developed.^{15,16} A five-factor score to predict deterioration in lung function among patients with RA-ILD has just been published.¹⁷

Recognition of the importance of patient-related outcomes has informed the development of recent guidelines for the diagnosis and management of ILD, reflected in a more patient-focused approach for the management of SARD-ILD, especially among older people.^{18,19} It has been proven that patients with SARD-ILD assessed in a multidisciplinary team (MDT) are significantly more likely to have their diagnosis and/or treatment altered, while the central role of the MDT in decision-making for patients with SARD-ILD has been recently emphasized.^{20,21}

Our data are likely to be representative of those patients referred to a large UK hospital but may be less selective than those seen in a specialized regional unit, where patients with specific disorders may be more concentrated. In addition, all our patients were assessed face-to-face, with lung function performed on the same day. Patients attending national or regional units may be more likely to be assessed virtually. Hence, although we report data across a wide range of ILD types, this should represent a real-world experience for many UK-based clinicians in rheumatology and chest medicine. At present, there are few published data available on the number of clinics for patients with SARD-ILD in the UK. A nationwide audit has been proposed to address this, which would be timed to coincide with the production of joint British Society of Rheumatology (BSR)/British Thoracic Society (BTS) management guidelines.²² The opportunity costs of the clinic appear justified on the basis of the data presented, which suggests that it offers a cost-effective and time-efficient means of identifying and treating those patients most likely to benefit from newer therapeutic options, whilst also offering teaching and training to non-consultant healthcare providers. It would be of considerable relevance to compare and contrast our model of service delivery with that of larger regional centres. In particular, it would be useful to assess the effect of devolving decision-making around more expensive therapeutic agents to local services.

The standardization of PFTs is an essential aspect of ensuring reliability when comparing changes in values of spirometric measurements and gas transfer within and between patient groups, and a similar approach has been adopted with regard to HRCT scoring systems.^{23,24} Death from progressive respiratory failure from ILD is common in systemic sclerosis, and recently, risk factors for progression have been proposed.^{25,26} PFTs are a valid means of monitoring both the natural history of ILD and the potential influence of therapy.^{27,28} They are both sensitive to early disease and predictive of subsequent mortality.^{29,30} Staging ILD with HRCT has also been standardized and validated in this regard, and the combination of PFTs and HRCT has been shown to provide effective monitoring with good correlation between functional and structural assessments, as well as with clinical assessment.^{31–35} Using these criteria, cyclophosphamide was shown to have some efficacy in SSC-ILD, and a decade later, mycophenolate demonstrated comparable benefits with less toxicity.^{36,37} Rituximab was later found to be effective in patients with SSC-ILD, even among those resistant to mycophenolate.^{38,39} Combination of mycophenolate with rituximab has been shown to be effective in such patients.⁴⁰

Mortality is increased in patients with RA-ILD, which causes nearly as many deaths as cardiovascular disease in RA.^{41,42} The role of progressive preclinical ILD in RA has been recognized, and the prevalence of clinical disease has also been established.^{43,44} Risk factors for the development of ILD in patients with RA include older age, male sex, smoking, active disease and seropositivity.⁴⁵ The clinical characteristics of RA-ILD have been described and compared to physiological and radiological features and prognostic factors in a multicentre study of 230 UK patients.^{46,47} The importance of early intervention to alter the natural history of RA-ILD has been emphasized.⁴⁸ Rituximab was associated with a slower rate of progression when measured by decline in lung function.⁴⁹ This was later confirmed, while other therapeutic agents, including abatacept and Janus kinase (JAK) inhibitors, have shown promise.^{50,51}

Sjogren's syndrome (Sjo) is also associated with the development of ILD, and risk factors have also been identified for Sjo-ILD.^{52,53} Although

Sjo-ILD appears to have a better natural history than RA-ILD, it also appears to be responsive to immunosuppressive therapy.^{54,55} MYO-associated ILD carries a variable prognosis, partly determined by the HRCT pattern and the specific antibody profile.^{56,57} Immunosuppression offers the potential for prolonging life expectancy in all SARD-ILDs and appears most effective among those with a predominantly inflammatory pattern (e.g. NSIP). Recently, evidence has accumulated to suggest that even patients who do not meet the criteria for SARD-ILD may still benefit from immunosuppressive therapy. These include those with HSP, IIP and IPAF.^{58,59}

In all patients with progressive pulmonary fibrosis, whether or not they have proved responsive to immunosuppression, anti-fibrotic therapy should be considered.⁶⁰ Evidence for a reduction in the rate of decline in lung function with anti-fibrotic therapy has been shown in SSC-ILD, RA-ILD and in a group with mixed SARD-ILDs.^{61–63} Our study indicated a relatively low usage of anti-fibrotic therapy, which might relate to the need for such patients to be discussed with the regional centre and the time delay that resulted from this process.

The 12 patients with sarcoidosis generally responded well to treatment with most receiving steroids and methotrexate. Three patients also required anti-TNF, and responses were very good. Given their small numbers and better outcomes, we have focused most of our analyses and discussion on the remaining 98 patients with either SARD-ILD or a mixture of HSP, IIP and IPF (control patients with ILD). Baseline PFTs were worse in control patients with ILD than in patients with SARD-ILD and deteriorated more rapidly during follow-up, correlating with our observation of worse outcomes in this group. By contrast, changes in HRCT appearances showed no overall differences between the two groups. However, a UIP pattern on HRCT was an independent predictor of death or deterioration in both lung function and HRCT appearances. This was more common in patients with RA-ILD than in the other patients with SARD-ILD, who were more likely to have an NSIP pattern on HRCT.

Other statistically significant predictors for death or deterioration included male sex, which has been previously reported across a range of ILD subtypes, including SSC-ILD.⁶⁴ Perhaps, a more novel but not entirely unexpected finding was that those patients with positive antibody results demonstrated better outcomes than those without antibodies across all diagnostic categories, although small numbers limited their statistical interpretation. Nonetheless, it appears logical that patients with active auto-immune responses are more likely to respond to therapeutic strategies aimed at suppressing such responses, which may, in part, explain the beneficial effects observed with rituximab in a variety of SARD-ILDs.^{8–11,37–40,49,50}

Nearly half of the patients with SARD-ILD were treated with rituximab, while over half of the whole cohort received mycophenolate. The combination of these agents has been shown to be both efficacious and well tolerated across many SARD-ILDs, and our experience reflected this.^{7,11,39,40,50,59} Patients with IPAF also often responded to one or both agents, emphasizing the potential relevance of their positive autoantibody status. Overall mortality was in line with that reported by other UK and European centres.⁶⁵ Less than 20% of our patients died or demonstrated deterioration in both lung function and structure at a median follow-up of 12 months, which might have contributed to relatively low rates of anti-fibrotic use in just 11% of our total ILD cohort.

Our data relate to a single centre's experience with limited numbers and relatively short follow-up. These combined limitations, albeit offset by excellent data collection and completion rates, emphasize the need for larger, longer collaborative studies which might be most effectively

facilitated via a combined respiratory and rheumatological database for patients with SARD-ILD. We are working towards attaining this ambition. ▣

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