ERS International Congress 2022: highlights from the Thoracic Surgery and Lung Transplantation Assembly

Dimitrios E. Magouliotis [1], Saskia Bos [2], Dorina Esendagli [3], Marco Nardini[4], Marcello Migliore [5], Michael Perch[6,7], Giuseppe Cardillo[8,9], Federica Meloni [10], Sara Ricciardi [11,12] and Merel Hellemons [13,14]

[1]Department of Cardiothoracic Surgery, University of Thessaly, Larissa, Greece. [2]Translational and Clinical Research Institute, Newcastle University, and Institute of Transplantation, Newcastle upon Tyne, Hospitals NHS Trust, Newcastle upon Tyne, UK. [3]Faculty of Medicine, Chest Diseases Department, Baskent University, Ankara, Turkey. [4]Thoracic Surgery, St James's University Hospital, Leeds, UK. [5]Program of Minimally Invasive Thoracic Surgery and New Technologies, University Hospital of Catania, and Department of Surgery and Medical Specialties, University of Catania, Catania, Italy. [6]Department of Cardiology, Section for Lung Transplantation and Respiratory Medicine, Heart Center, Rigshospitalet, Copenhagen, Denmark. [7]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark. [8]Unit of Thoracic Surgery, San Camillo Forlanini Hospital, Rome, Italy. [9]Unicamillus – Saint Camillus International University of Health Sciences, Rome, Italy. [10]Transplant Center, IRCCS Policlinico San Matteo Foundation, Pavia, Italy. [11]Unit of Thoracic Surgery, San Camillo Forlanini Hospital, Rome, Italy. [12]Alma Mater Studiorum, University of Bologna, Bologna, Italy. [13]Dept of Respiratory Diseases, Erasmus University Medical Center, Rotterdam, The Netherlands. [14]Erasmus Transplant Institute, Erasmus University Medical Center, Rotterdam, The Netherlands.

Corresponding author: Dimitrios E. Magouliotis (dimitrios.magouliotis.18@ucl.ac.uk)

Shareable abstract (@ERSpublications)
The Thoracic Surgery and Lung Transplantation Assembly (Assembly 8) of the @EuroRespSoc is delighted to present an enhanced insight into the highlights from the 2022 #ERSCongress (Spain) https://bit.ly/3HED6Jj

Cite this article as: Magouliotis DE, Bos S, Esendagli D, *et al*. ERS International Congress 2022: highlights from the Thoracic Surgery and Lung Transplantation Assembly. *ERJ Open Res* 2023; 9: 00671-2022 [DOI: 10.1183/23120541.00671-2022].

Received: 3 Dec 2022
Accepted: 1 Feb 2023

Abstract

The thoracic surgery and lung transplantation assembly (Assembly 8) of the European Respiratory Society (ERS) is delighted to present the highlights from the 2022 ERS International Congress that took place in a hybrid version in Barcelona, Spain. We have selected the four main sessions that discussed recent advances across a wide range of topics including the effects of coronavirus disease 2019 on thoracic surgery and the challenges regarding lung transplantation in connective tissue diseases and common variable immunodeficiency. The sessions are summarised by early career members in close collaboration with the assembly faculty. We aim to provide the reader with an update and enhanced insight into the highlights of the conference in the fields of thoracic surgery and lung transplantation.

Introduction

Assembly 8 includes physicians and surgeons with tremendous clinical expertise and a broad spectrum of research activities in state-of-the-art concepts regarding thoracic surgery (Group 8.1) and lung transplantation (Group 8.2). Group 8.1 includes surgeons with a special interest in an interdisciplinary approach toward various thoracic pathologies that may require surgical intervention as a part of the treatment strategy for either diagnostic/staging or therapeutic purposes. Furthermore, group 8.1 focuses on the possibilities of interactive sessions during the European Respiratory Society (ERS) International Congress to foster a culture of interdisciplinary collaboration between surgical and non-surgical members of the ERS. On the other hand, group 8.2 mainly consists of pulmonologists/respiratory and specialists/thoracic surgeons who have a special interest in lung transplantation. It is a group strongly engaged in working together to improve patient and donor selection and further enhance post-transplant morbidity, quality of life, and post-transplant survival outcomes. In the following paragraphs, we will explore the highlights and key concepts that were presented by members of Assembly 8 during the 2022 ERS Congress.

Group 8.1

The positive downside of the COVID-19 pandemic on advances in thoracic surgery

René Petersen presented the important advances in thoracic surgery that occurred in 2022 despite the coronavirus disease 2019 (COVID-19) pandemic. The aims of his talk were the following: 1) to demonstrate the superiority of video-assisted thoracoscopic surgery (VATS) when performing lobectomy over the open approach, 2) to show the impact of implementing enhanced recovery after surgery (ERAS) strategies after performing VATS, 3) to demonstrate the evidence for superiority of segmentectomy over lobectomy in selected cases, and 4) to highlight the future potential of combining immunotherapy with salvage surgery.

R. Petersen began his presentation with a recent study on VATS *versus* open lobectomy for early-stage lung cancer by Lim *et al*. [1]. This was a multicentre superiority randomised controlled trial (RCT) that compared patients (1:1 VATS *versus* open lobectomy) in early-stage lung cancer (T1-T3, N0-N1) [1]. The primary endpoint was physical functioning at 5 weeks using the EORTC QLQ-C30 questionnaire. The patients treated with VATS had superior physical functioning at 5 weeks after the procedure when compared to open lobectomy, but this difference was not seen at 12 months. Other endpoints like pain, length of stay, number of lymph nodes, and R0 resection did not differ between groups. Although the number of severe adverse events was similar between groups there were significantly fewer adverse events in the VATS-treated group. Consequently, VATS was associated with an enhanced physical function at 5 weeks after the procedure, but overall outcomes needs further follow-up to be fully unveiled.

The next topic discussed was the impact of enhanced recovery on clinical outcomes following VATS surgery. According to a single-centre observational cohort study conducted by Huang *et al*. [2], age and low lung function were significant risk factors for an extended length of in-hospital stay. In addition, another study by the same team [3] highlighted the significant role of "days alive out of hospital" as a new metric of clinical outcomes following VATS in the context of an ERAS pathway. They also showed that air leaks, pneumonia, and recurrence represent the most common reasons for readmission and extended hospitalisation following VATS [3].

A novel concept was the comparison between segmentectomy and lobectomy for small-sized peripheral non-small cell lung cancer (NSCLC). In this context, R. Petersen presented the outcomes from the RCT JCOG0802, a multicentre, non-inferiority trial that incorporated patients from 70 Japanese institutions [4]. There was a median follow-up of 7.3 years, and segmentectomy was associated with a significantly higher median survival than lobectomy (94.3% *versus* 91.1%, respectively; p=0.0082). Although the recurrence-free survival was similar between the two groups, the JCOG0802 trial showed the incidence of local relapse to be significantly higher after segmentectomy (10.5%) than after lobectomy (5.4%) (p=0.0018).

Finally, R. Petersen presented data on the role of minimally invasive surgery following immuno-chemotherapy in 51 patients with initially unresectable stage III NSCLC [5]. Following immuno-chemotherapy, 31 patients (61%) were considered operable and all of them underwent VATS [5]. According to their findings, the addition of surgery after immuno-chemotherapy in initially unresectable cIIIB NSCLC is safe and is associated with significantly higher disease-free survival compared to those without (27.5 *versus* 16.7 months).

Take-home messages

- Patients undergoing VATS lobectomy had enhanced early physical function compared to thoracotomy, but similar surgical and oncological outcomes.
- Segmentectomy was superior to lobectomy in terms of median survival for patients with small peripheral NSCLC, but with a significantly higher incidence of local recurrence.
- Radical surgery following immuno-chemotherapy is associated with higher disease-free survival for patients with initially unresectable cIIIB NSCLC.

Thoracic surgery and the COVID-19 pandemic: an unexpected intimate relationship

In this session, experts debated the impact of COVID-19 on the field of thoracic surgery.

In the first part of her talk, Isabelle Opitz described the most common COVID-19-related complications that required surgical intervention, namely persistent pneumothorax, pneumatocele with persistent air leak, empyema, haemothorax and acute respiratory distress syndrome (ARDS) that required extracorporeal membrane oxygenation and in some cases progressing into lung fibrosis with the occasional use of lung transplantation.

A monocentre observational study from the USA showed that 13 (0.7%) out of 1954 patients admitted to hospital for COVID-19 (March–July 2020) required surgery, mostly due to pneumothorax and pneumatocele, with a survival rate of 77% [6].

Another retrospective multicentre study including 83 patients with similar surgical complications (March–May 2021) had an overall 72% survival, with the most common cause of death being ARDS. Going into detail, survival after surgical intervention for pneumothorax was reasonable (64%), surgical intervention of empyema had the best survival (76%), while haemothorax (46%) and haemoptysis (62%) had the worst prognosis. Multivariate analysis of morbidities related to postoperative complications showed an increased risk for older patients (HR 1.05, 95% CI 1.01–1.10, p=0.023) [7].

In the second part of her talk, I. Opitz described the relationship between COVID-19 and thoracic malignancies. Data from the University Hospital of Zurich between 2019 and 2020 showed that despite the ongoing pandemic prompt surgical treatment of patients with thoracic malignancies was guaranteed, without any increased incidence of advanced-stage thoracic malignancies. Moreover, among 50 patients hospitalised for thoracic surgery during the pandemic, only six experienced COVID-19 symptoms [8].

The TERAVOLT analysis, a multicentre (28 institutions from Europe, North America, South America and Asia) collaborative study on 346 patients with chest malignancies (86% NSCLC) and COVID-19 reported different results. In this cohort a delayed cancer treatment was found in 57% of patients. Furthermore, patients with NSCLC showed an increased risk of contracting COVID-19 infection, with a worse course of the disease. This could be explained by the wide range of centres from many countries with different exposure to the pandemic. COVID-19 vaccination showed a protective effect on hospitalisation and death (OR 0.30, 95% CI 0.15–0.57, p=0.0003) [9].

This was also seen in a nationwide analysis from Asia, where a considerable number of cancer patients experienced complications due to COVID-19 infection (HR 3.56, 95% CI 1.65–7.69) [10].

Exploring the possible transmission of COVID-19 to healthcare providers while performing minimally invasive surgery through the CO_2 or the plume created by electrocautery was not shown [11].

Marco Lucchi discussed tracheal complications related to COVID-19. He reported a cohort of 98 patients with COVID-19 who developed severe respiratory failure, and of whom 30 underwent prolonged invasive ventilation (⩾14 days). Severe tracheal complications occurred in 47% of cases: full-thickness tracheal lesions (10/30, 33%) or tracheo-oesophageal fistulas (4/30, 13%), The clinical manifestations were subcutaneous emphysema (43%), pneumomediastinum (33%) and pneumothorax (20%) with a high mortality rate (27%). Factors that might be related to the incidence of tracheal complications are pronation manoeuvres (increasing the cuff pressure on the tracheal wall), high doses of systemic steroids, microvascular injury related to COVID-19 and high viral replication of the virus within the tracheal epithelium [12].

M. Lucchi further reported a single-centre experience from the University Hospital of Pisa, regarding tracheal laceration related to intubation or tracheotomy. Out of 10 tracheal lacerations, eight patients were treated conservatively, while two cases required surgical intervention, according to their previously reported technique [13]. Four cases with tracheo-oesophageal fistula were treated either conservatively or with the standard Grillo's technique, where the oesophageal wall is sutured directly and the sternocleidomastoid muscle interposed between the oesophagus and trachea, followed by tracheal resection and reconstruction. The two patients who were treated conservatively died while the two who underwent surgery were successfully discharged.

Lastly, one of the most important late complications of tracheotomy or prolonged intubation is tracheal stenosis [14]. M. Lucchi presented a case of laryngotracheal resection after post-tracheotomy stenosis in a patient with COVID-19, showing that both macroscopically and microscopically, the mucosa and tracheal tissues were characterised by inflammatory infiltrate and necrosis that may delay healing of the anastomosis [15].

Take-home messages

- Pneumothorax, pneumatocele, empyema and haemothorax were the most common indications for thoracic surgical interventions in patients with COVID-19.
- Patients with thoracic malignancies were at increased risk of a severe course of COVID-19 disease.
- Tracheal complications are common complications in mechanically ventilated COVID-19 patients, which require a tailored approach.

Group 8.2

Lung involvement in common variable immunodeficiency: from diagnosis to lung transplantation

Pere Soler discussed the pathogenesis and diagnosis of common variable immunodeficiency (CVID) in both paediatric and adult patients. CVID is characterised by genetic, immunological and clinical heterogeneity, which makes the process of reaching this diagnosis challenging. Currently over 40 genetic defects have been identified in patients with a CVID phenotype, which is not considered CVID. Excluding other primary antibody deficiencies or secondary causes of hypogammaglobulinaemia is important when establishing the CVID diagnosis [16–19]. The common immune defects in CVID patients are loss of B-cell function, a relative loss of T-cell function and defects in thymus maturation, monocyte/dendritic cell defects, and impaired innate immune responses including loss of natural killer cells [16–19]. For the diagnosis, it is important to use age-adapted reference values for immunoglobulins and T- and B-cell subsets, and also to perform a differential diagnosis of hypogammaglobulinaemia [20, 21]. CVID patients present with recurrent upper and lower respiratory tract infections, bronchiectasis, lung function decline, gastrointestinal infections, autoimmune enteropathy and lymphadenopathies, thus requiring a multidisciplinary approach. P. Soler emphasised the importance of genetics in CVID and recommended testing all patients, and especially those with early age onset of disease (younger than 5 years of age), those with infection-plus phenotype (presence of infection), and those with increased number of transitional B-cells.

David M. Lowe pointed out that the respiratory tract (both upper and lower) is abnormal in CVID patients. Sputum analysis of these patients showed an increase in pro-inflammatory cytokines like interleukin (IL)-1, IL-6, IL-8, tumour necrosis factor-α, IL-5 and IL-13, even in patients with radiologically normal airways, thus suggesting the presence of chronic inflammation. In contrast to normal, patients with CVID do not excrete IgA in their airways but do have increased IgG as a consequence of treatment with immunoglobulin replacement, which is considered standard. Nonetheless, this is insufficient to completely prevent pulmonary inflammation and infections [22]. Moreover, CVID patients have an altered microbiome. The more diverse the microbiome, the more inflammation and airway damage occurs [22]. Another problem with the recurrent usage of antibiotics for this group of patients, including macrolide prophylaxis, is the increased incidence of antimicrobial resistance.

Antibiotic use is frequent in this group: on average 0.36 courses of antibiotics per patient month [23]. Because viruses are especially dominant in acute respiratory infections, antibiotics are often not required, and should be selected for established bacterial infection, where treatment should be extended and be given for 2 weeks.

Antibiotic prophylaxis to prevent infections has been shown to delay the time to antibiotic usage and reduce hospitalisation, but had no effect on forced expiratory volume in 1 s [24]. Other measures to prevent infections, apart from intravenous immunoglobulin (IVIG) treatment and antibiotic prophylaxis, are advice on nutritional intake, occupation, travel, smoking, sputum clearance, physiotherapy and vaccines for patients and their household members.

Additional challenges that can be encountered in patients with CVID are colonisation with *Haemophilus influenzae* or *Pseudomonas aeruginosa*, chronic sinusitis, mycobacterial infections, and atypical extrapulmonary infections. Presentations may be atypical, and diagnosis and treatment are challenging.

Elisabetta Renzoni discussed the non-infectious lung involvement in CVID patients with a focus on CVID-associated interstitial lung disease (granulomatous–lymphocytic interstitial lung disease (GLILD)), which is a lung manifestation of systemic immune dysregulation. According to the British Lung Foundation (BLF)/United Kingdom Primary Immunodeficiency Network (UKPIN) consensus statement, GLILD is a distinct clinic-radiopathological interstitial lung disease (ILD) occurring in patients with CVID, associated with a lymphocytic infiltrate and/or granulomata in the lung, and in whom other conditions have been considered and excluded [25]. GLILD occurs in approximately 10–30% of CVID patients and consists of a multi-system immune dysregulation often associated with splenomegaly, adenopathy, autoimmune diseases and gastrointestinal/hepatic disease [26, 27]. GLILD can be misdiagnosed as sarcoidosis and patients should be tested for serum (pan) hypogammaglobulinaemia and lack of antibody production following immunisation (especially used in patients with sarcoidosis) [28]. Recurrent infections, autoimmune disease, splenomegaly, hepatomegaly and diffuse adenopathies are findings that are more common in GLILD [28]. There is a wide range of histopathological findings that often include a combination of granulomatous and lymphocytic infiltrates and a variety of patterns like follicular bronchiolitis, lymphocytic interstitial pneumonia, diffuse or nodular lymphoid hyperplasia together with areas of organising pneumonia [29]. Management of the disease according to the BLF/UKPIN consensus includes IVIG and GLILD-specific treatment in case of deteriorating lung function. This consists of

corticosteroids as the first-line treatment and azathioprine, rituximab or mycophenolate as a second-line therapy [25]. The treatment should be individualised according to comorbidities and patient preferences. Management is highly complex due to limited experience and further studies are needed.

Lastly, Michael Perch pointed out that the primary goal of lung transplantation is to provide a survival benefit. The mean survival of lung transplant patients, even though it has improved over the years, is still on average 7 years [30]. According to the latest version of the consensus document for the selection of lung transplant candidates, patients are classified according to risk factors [31]. Candidates with conditions classified as absolute contraindications are at too high a risk for achieving a successful outcome post lung transplantation and should not undergo transplantation except in very exceptional circumstances [31]. Candidates who have risk factors with high or substantially increased risk should only be considered in centres with expertise for these specific conditions as these risk factors are associated with unfavourable short- and/or long-term outcomes. Some of these risk factors are high age and body mass index, heart or kidney disease, difficult to treat chronic infections *etc*. [31]. The presence of more than one risk factor is thought to be multiplicative in terms of increasing the risk of adverse outcomes post-transplant [31].

Lung transplantation should be considered for adults with chronic, end-stage lung disease who meet the following criteria: 1) high risk of death from lung disease within 2 years if transplantation is not performed; and 2) high likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function [31, 32]. Listing for transplantation should occur when life expectancy is greatly reduced but nonetheless greater than the expected waiting time. Modifiable conditions should be optimised if possible.

Regarding lung transplantation for end-stage lung disease in CVID there is a limited experience, mostly obtained from cases. In several cases it was found that patients can mount sufficient T-cell responses to cause acute cellular rejection and at the same time had signs of both infection and inflammation, resulting in early mortality and limited survival benefit [33].

Nathan *et al*. [34] reported a median survival of 4 years after lung transplantation for bronchiectasis related to immunodeficiency, despite receiving IVIG after transplantation. In this series, survival was similar to patients transplanted for other indications, but overall this survival was rather limited and not in line with current aims after transplantation.

Taking in consideration the present data, CVID is not simply the absence of IgG. Lung transplantation for CVID is highly complicated and needs a multidisciplinary approach in an experienced transplant centre. After transplantation, continuation of IVIG treatment and antimicrobial prophylaxis should be tailored carefully and further studies regarding complications and outcome are needed regarding this complex group of patients.

Take-home messages

- CVID is characterised by genetic, immunological and clinical heterogeneity. Common features of CVID are: 1) immunological (*e.g*. loss of B-cell function, a relative loss of T-cell function and natural killer cells, defects in thymus maturation, and monocyte/dendritic cell defects); 2) clinical (*e.g*. recurrent upper and lower respiratory tract infections, bronchiectasis, lung function decline, gastrointestinal infections, autoimmune enteropathy, and lymphadenopathies); 3) genetic, thus making genetic testing recommended especially in those patients with early age onset of the disease.
- CVID patients have chronic inflammation and altered microbiome in the lungs and frequent usage of antibiotics can lead to resistance; thus, multiple measures to prevent infections should be taken.
- CVID is associated with systemic immune dysregulation that may lead to GLILD.
- Lung transplantation for CVID is highly complex given the potential co-occurrence of acute rejection and infection episodes and long-term outcomes are uncertain.

Interstitial lung diseases in connective tissue diseases: the patient's journey from diagnosis and new treatment strategies to transplantation

Antoine Froidure started the session on ILD in connective tissue diseases (CTD) and highlighted that genetic testing has changed the way we practise medicine in recent years. From a physician's perspective, it can help understand underlying disease mechanisms, refine diagnosis, identify patients at risk, genetic counselling and prevention, and may have therapeutic implications [35]. There are also advantages from a patient's perspective, such as the ability to understand their own disease and to know whether relatives are at risk. On the other hand, genetic testing can also negatively affect the patient with fear, stress, uncertainty and socio-economic consequences [35].

With regard to ILD, we know that the risk of CTD-ILD is higher in patients with systemic sclerosis and inflammatory myositis compared to rheumatoid arthritis (RA) and Sjögren syndrome [36]. It was recently detected that variants of the MUC5B promoter are not only related to idiopathic pulmonary fibrosis, but also make patients with RA more prone to develop lung fibrosis [37, 38]. Along with other risk factors such as male and age, the risk to develop subclinical RA-ILD can be as high as 94.5% [37, 38]. However, the presence of a MUC5B variant is not a predictor for disease progression [38].

Finally, A. Froidure emphasised the importance of telomere-related gene mutations, which are not only correlated with a risk of idiopathic pulmonary fibrosis, but also lung fibrosis in CTD [39].

Secondly, Bruno Crestani focused on the diagnosis of CTD-ILD and new treatment strategies. CTD-ILD accounts for an important part of ILD and multidisciplinary discussion is essential because of heterogeneity of phenotypes [40]. High-resolution computed tomography remains the gold standard for diagnosis and is also the best screening tool, although other tools such as lung ultrasound, electronic stethoscope, exhaled air, blood biomarkers and risk scores are being investigated [41].

Treatment of CTD-ILD is evolving rapidly and ranges from corticosteroids and immunomodulators (*e.g.* rituximab [42, 43], cyclophosphamide, mycophenolate mofetil, tocilizumab [44, 45]) to antifibrotic agents (nintedanib [46–48], pirfenidone [49, 50]) based on the degree of inflammation and fibrosis. Interestingly, methotrexate may delay the onset of ILD in patients with RA [51], while withdrawal can accelerate disease progression [52]. As such, methotrexate might become the treatment of choice in RA-ILD and should not be discontinued upon ILD detection unless there is clear suspicion of methotrexate-associated ILD, although rare [53]. To determine the best therapeutic strategies, disease-specific algorithms should be pursued and an ERS/European Alliance of Associations for Rheumatology (EULAR) clinical practice guideline for CTD-ILD screening, diagnosis and treatment is underway.

Lung transplantation is a reasonable treatment option for carefully selected end-stage CTD-ILD patients and José Cifrián addressed the main challenges if a CTD-ILD patient is referred for lung transplantation. An updated consensus document on the selection of lung transplant candidates from the International Society for Heart and Lung Transplantation has recently become available [31], as is a consensus document on the evaluation of CTD candidates [54]. The latter aims to standardise the evaluation, listing and post-transplant management of CTD candidates to allow for risk stratification, as these patients often have specific risk factors that may increase the risk of unfavourable short- and long-term post-transplant outcomes [54]. On the other hand, outcomes comparable to patients with other types of ILD were observed in well-selected patients with systemic sclerosis and RA, and outcomes for systemic lupus erythematosus and polymyositis and dermatomyositis were comparable to idiopathic pulmonary fibrosis [54].

When considering a CTD-ILD patient for lung transplantation, thorough evaluation of extrapulmonary manifestations of CTD is critical. Involvement of a multidisciplinary team in pre-transplant evaluation and selection and post-transplant care is essential to optimise outcomes [55]. Detailed organ-specific evaluation recommendations can be found in the consensus document and the ones highlighted by J. Cifrián are summarised in table 1 [54]. Absolute contraindications for lung transplantation are mainly related to persistent, active extrapulmonary manifestations despite maximal therapy [54].

Because of the medical complexity of CTD patients, early referral (“the sooner the better”) to a lung transplant centre is recommended, also to identify modifiable risk factors that could improve the candidacy for lung transplantation or survival [54].

Lastly, Ingrid Lundberg concluded the session by discussing new trends in the treatment of myositis associated ILD. An increasing number of autoantibodies specific for myositis have been detected that are not found in other auto-immune diseases [56]. These 16 myositis-specific antibodies are associated with specific clinical phenotypes [56], some of which have a strong association with lung disease (*i.e.* anti-melanoma differentiation-associated protein 5 (MDA5) [57] and anti-synthetase antibodies [58]). Detection of antibodies can guide the diagnosis as patients may present with symptoms varying from myositis, ILD, concomitant myositis and ILD to polyarthritis without ILD or myositis [59]. Patients with anti-MDA5 antibodies are especially at risk for rapidly progressive ILD [57].

Currently, no RCTs regarding optimal treatment are available. Expert recommendations divide treatment of myositis-associated ILD into two groups based on disease severity (mild-moderate and severe) and treatment options are relatively similar to those for other CTD-ILD, including corticosteroids,

TABLE 1 Organ-specific risks and considerations in connective tissue disease-related interstitial lung disease candidates based on the International Society for Heart and Lung Transplantation consensus document [54] and highlighted by J. Cifrián

Gastrointestinal	• In SSc, ineffective or absent oesophageal peristalsis leading to reflux occurs in 75–80% of patients, gastroparesis in up to 50% and small intestinal bacterial overgrowth in 30–60% of patients. • A 24-h pH-metry with impedance testing and manometry is recommended. • Computed tomography can reveal oesophageal dysfunction by dilatation and/or air-fluid levels. • Input from a nutritionist is important pre- and post-transplant. • Patients with severe gastro-oesophageal reflux or oesophageal dysfunction should be evaluated for anti-reflux surgery.
Cardiac	• Myocarditis, pericarditis, congestive heart failure or conduction defects are seen in 7–39% of SSc and 50% of SLE patients. Myocarditis is also possible in PM/DM. • The incidence of myocardial infarction is five times higher in SLE than in the general population due to premature atherosclerosis. • Cardiac MRI is recommended in cases of suspected myocarditis, abnormal rhythm on Holter monitoring or restrictive cardiomyopathy on echocardiogram. • To confirm active inflammation, a myocardial biopsy is needed.
Haematological	• Cytopenia is detected in 30–60% of patients with Sjögren syndrome. • In progressive SSc, 20–50% have hypergammaglobulinemia and 10–15% MGUS. • There is an increased risk of venous thromboembolism if antiphospholipid antibodies are present (10–43% in SSc, 35% in SLE). • A hypercoagulable evaluation for the risk of thrombophilia is recommended, as is a haematological evaluation for patients with antiphospholipid antibodies. • In patients treated with rituximab or mycophenolate mofetil, immunoglobulin levels should be checked.
Oncological	• Patients with Sjögren syndrome have a 15–20-fold risk of malignant lymphoid disorders. • B-cell lymphomas are seen in 5% of progressive SSc patients. • Patients should be screened for risk factors for B-cell lymphomas and a PET scan should be performed if ESSDAI index $\geqslant$5 with three or more risk factors. • Special attention should be paid to patients with PM/DM because of the risk of cancer-associated myositis.
Renal	• Scleroderma renal crisis occurs in 5–85% of SSc patients. Risk factors include rapid progression of skin fibrosis, diffuse cutaneous scleroderma, disease duration of <4 years, presence of anti-RNA polymerase III antibodies and high-dose steroids (prednisolone >15 mg·day^{-1}). • Up to 50% of SLE patients develop lupus nephritis.
Vascular	• Risk of digital ischaemia due to Raynaud phenomenon in 95% of SSc patients, with digital ulcers in 30–50% and risk of amputation in 20%. • Rheumatological evaluation is important to assess the severity of Raynaud phenomenon, along with an arterial Doppler of upper and lower extremities.

SSc: systemic sclerosis; PM/DM: polymyositis and dermatomyositis; SLE: systemic lupus erythematosus; MRI: magnetic resonance imaging; MGUS: monoclonal gammopathy of undetermined significance; PET: positron emission tomography; ESSDAI: EULAR Sjögren syndrome disease activity index.

cyclophosphamide, rituximab, mycophenolate mofetil, calcineurin inhibitors but also Janus kinase inhibitors. For progressive disease, abatacept is being tested in clinical trials [60].

Finally, as mentioned in all CTD-ILD presentations, I. Lundberg ended by emphasising the importance of multidisciplinary management because of the complexity of cases.

Take-home messages

- Genetic testing enhances pathobiology research, diagnostic and risk-stratification work-up, and genetic counselling, along with prevention and treatment.
- Treatment of CTD-ILD ranges from corticosteroids and immunomodulators to antifibrotic agents, based on the degree of inflammation and fibrosis. Lung transplantation is a reasonable treatment option for carefully selected end-stage CTD-ILD patients.
- A multidisciplinary approach in the diagnosis and management of CTD-ILD and in the selection and care of lung transplant candidates is essential because of the heterogeneity and complexity.
- Thorough assessment and treatment of extrapulmonary manifestations of CTD are critical in the evaluation and selection of lung transplant candidates to optimise outcomes as well as early referral.

Conclusion

Owing to the ongoing COVID-19 pandemic, the 2022 ERS Congress was in a hybrid form. Once again the annual ERS Congress was a great success. Topics were very diverse and included important sessions on innovation and state-of-the-art in thoracic surgery and lung transplantation. In this article, we have summarised the highlights of the most important sessions in the field of thoracic surgery and lung transplantation of the 2022 ERS Congress, representing a wide range of topics. We look forward to the next ERS International Congress, to be held in Milan, Italy, from 9 to 13 September 2023.

Provenance: Commissioned article, peer reviewed.

Conflict of interest: M. Hellemons is an associate editor of this journal. The remaining authors declare no conflicts of interest.

References

1 Lim E, Batchelor TJP, Dunning J, *et al.* Video-assisted thoracoscopic or open lobectomy in early-stage lung cancer. *NEJM Evid* 2022; 1.
2 Huang L, Kehlet H, Petersen RH. Reasons for staying in hospital after video-assisted thoracoscopic surgery lobectomy. *BJS Open* 2022; 6: zrac050.
3 Huang L, Frandsen MN, Kehlet H, *et al.* Days alive and out of hospital after enhanced recovery video-assisted thoracoscopic surgery lobectomy. *Eur J Cardiothorac Surg* 2022; 62: ezac148.
4 Saji H, Okada M, Tsuboi M, *et al.* Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial. *Lancet* 2022; 399: 1607–1617.
5 Deng H, Liu J, Cai X, *et al.* Radical minimally invasive surgery after immuno-chemotherapy in initially-unresectable stage IIIB non-small cell lung cancer. *Ann Surg* 2022; 275: e600–e602.
6 Chang SH, Chen D, Paone D, *et al.* Thoracic surgery outcomes for patients with Coronavirus Disease 2019. *J Thorac Cardiovasc Surg* 2021; 162: 1654–1664.
7 Raveglia F, Scarci M, Rimessi A, *et al.* The role of surgery in patients with COVID-19-related thoracic complications. *Front Surg* 2022; 9: 867252.
8 Werner RS, Lörtscher A, Kirschner MB, *et al.* Surgical management of lung cancer during the COVID-19 pandemic - a narrative review and single-centre report. *Swiss Med Wkly* 2022; 152: w30109.
9 Bestvina CM, Whisenant JG, Torri V, *et al.* Coronavirus disease 2019 outcomes, patient vaccination status, and cancer-related delays during the omicron wave: a brief report from the TERAVOLT analysis. *JTO Clin Res Rep* 2022; 3: 100335.
10 Liang W, Guan W, Chen R, *et al.* Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020; 21: 335–337.
11 Porter J, Blau E, Gharagozloo F, *et al.* Society of Robotic Surgery review: recommendations regarding the risk of COVID-19 transmission during minimally invasive surgery. *BJU Int* 2020; 126: 225–234.
12 Fiacchini G, Tricò D, Ribechini A, *et al.* Evaluation of the incidence and potential mechanisms of tracheal complications in patients with COVID-19. *JAMA Otolaryngol Head Neck Surg* 2021; 147: 70–76.
13 Mussi A, Ambrogi MC, Ribechini A, *et al.* Acute major airway injuries: clinical features and management. *Eur J Cardiothorac Surg* 2001; 20: 46–51.
14 Tapias LF, Lanuti M, Wright CD, *et al.* COVID-19-related post-intubation tracheal stenosis: early experience with surgical treatment. *Ann Surg* 2022; 275: e271–e273.
15 Lucchi M, Ambrogi M, Aprile V, *et al.* Laryngotracheal resection for a post-tracheotomy stenosis in a patient with coronavirus disease 2019 (COVID-19). *JTCVS Tech* 2020; 4: 360–364.
16 Abbott JK, Gelfand EW. Common variable immunodeficiency: diagnosis, management, and treatment. *Immunol Allergy Clin* 2015; 35: 637–658.
17 Ameratunga R, Allan C, Woon ST. Defining common variable immunodeficiency disorders in 2020. *Immunol Allergy Clin* 2020; 40: 403–420.
18 Yazdani R, Habibi S, Sharifi L, *et al.* Common variable immunodeficiency: epidemiology, pathogenesis, clinical manifestations, diagnosis, classification, and management. *J Investig Allergol Clin Immunol* 2019; 30: 14–34.
19 Bogaert DJ, Dullaers M, Lambrecht BN, *et al.* Genes associated with common variable immunodeficiency: one diagnosis to rule them all? *J Med Genet* 2016; 53: 575–590.
20 Garcia-Prat M, Vila-Pijoan G, Martos Gutierrez S, *et al.* Age-specific pediatric reference ranges for immunoglobulins and complement proteins on the Optilite automated turbidimetric analyzer. *J Clin Lab Anal* 2018; 32: e22420.
21 Bonilla FA, Khan DA, Ballas ZK, *et al.* Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol* 2015; 136: 1186–1205.
22 Schnell A, Davrandi M, Saxenhofer M, *et al.* Airway inflammation and dysbiosis in antibody deficiency despite the presence of IgG. *J Allergy Clin Immunol* 2022; 149: 2105–2115.

23 Sperlich JM, Grimbacher B, Workman S, *et al.* Respiratory infections and antibiotic usage in common variable immunodeficiency. *J Allergy Clin Immunol Pract* 2018; 6: 159–168.
24 Milito C, Pulvirenti F, Cinetto F, *et al.* Double-blind, placebo-controlled, randomized trial on low-dose azithromycin prophylaxis in patients with primary antibody deficiencies. *J Allergy Clin Immunol* 2019; 144: 584–593.
25 Hurst JR, Verma N, Lowe D, *et al.* British Lung Foundation/United Kingdom Primary Immunodeficiency Network consensus statement on the definition, diagnosis, and management of granulomatous-lymphocytic interstitial lung disease in common variable immunodeficiency disorders. *J Allergy Clin Immunol Pract* 2017; 5: 938–945.
26 Baumann U, Routes JM, Soler-Palacín P, *et al.* The lung in primary immunodeficiencies: new concepts in infection and inflammation. *Front Immunol* 2018; 9: 1837.
27 Prasse A, Kayser G, Warnatz K. Common variable immunodeficiency-associated granulomatous and interstitial lung disease. *Curr Opin Pulm Med* 2013; 19: 503–509.
28 Verbsky JW, Routes JM. Sarcoidosis and common variable immunodeficiency: similarities and differences. *Semin Respir Crit Care Med* 2014; 35: 330–335.
29 Larsen BT, Smith ML, Tazelaar HD, *et al.* GLILD revisited: pulmonary pathology of common variable and selective IgA immunodeficiency. *Am J Surg Pathol* 2020; 44: 1073–1081.
30 Ali HA, Neely M, Long A, *et al.* Factors associated with prolonged survival (>15 years) after lung transplantation: analysis of the ISHLT registry. *J Heart Lung Transplant* 2019; 38: S327–S328.
31 Leard LE, Holm AM, Valapour M, *et al.* Consensus document for the selection of lung transplant candidates: an update from the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant* 2021; 40: 1349–1379.
32 Burton CM, Milman N, Andersen CB, *et al.* Common variable immune deficiency and lung transplantation. *Scand J Infect Dis* 2007; 39: 362–367.
33 Lopes JP, Ho HE, Cunningham-Rundles C. Interstitial lung disease in common variable immunodeficiency. *Front Immunol* 2021; 12: 605945.
34 Nathan JA, Sharples LD, Exley AR, *et al.* The outcomes of lung transplantation in patients with bronchiectasis and antibody deficiency. *J Heart Lung Transplant* 2005; 24: 1517–1521.
35 McGowan ML, Glinka A, Highland J, *et al.* Genetics patients' perspectives on clinical genomic testing. *Per Med* 2013; 10: 339–347.
36 Froidure A, Marchal-Duval E, Homps-Legrand M, *et al.* Chaotic activation of developmental signalling pathways drives idiopathic pulmonary fibrosis. *Eur Respir Rev* 2020; 29: 190140.
37 Palomäki A, FinnGen Rheumatology Clinical Expert Group, Palotie A, *et al.* Lifetime risk of rheumatoid arthritis-associated interstitial lung disease in MUC5B mutation carriers. *Ann Rheum Dis* 2021; 80: 1530–1536.
38 Juge PA, Granger B, Debray MP, *et al.* A risk score to detect subclinical rheumatoid arthritis-associated interstitial lung disease. *Arthritis Rheumatol* 2022; 74: 1755–1765.
39 Juge PA, Borie R, Kannengiesser C, *et al.* Shared genetic predisposition in rheumatoid arthritis-interstitial lung disease and familial pulmonary fibrosis. *Eur Respir J* 2017; 49: 1602314.
40 Ottaviani S, Khaleche S, Borie R, *et al.* Rheumatological evaluation of patients with interstitial lung disease. *Scand J Rheumatol* 2022; 51: 34–41.
41 Hoffmann-Vold AM, Maher TB, Philpot EE, *et al.* The identification and management of interstitial lung disease in systemic sclerosis: evidence-based European consensus statements. *Lancet Rheumatol* 2020; 2: E71–E83.
42 Maher TM, Tudor V, Saunders P, *et al.* Rituximab versus cyclophosphamide for the treatment of connective tissue disease associated interstitial lung disease (RECITAL): a multi-centre randomised controlled trial. *Am J Respir Crit Care Med* 2022; 205: A4779.
43 Ebata S, Yoshizaki A, Oba K, *et al.* Safety and efficacy of rituximab in systemic sclerosis (DESIRES): a double-blind, investigator-initiated, randomised, placebo-controlled trial. *Lancet Rheumatol* 2021; 3: E489–E497.
44 Khanna D, Lin CJF, Furst DE, *et al.* Tocilizumab in systemic sclerosis: a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Respir Med* 2020; 8: 963–974.
45 Khanna D, Lin CJF, Furst DE, *et al.* Long-term safety and efficacy of tocilizumab in early systemic sclerosis-interstitial lung disease: open-label extension of a phase 3 randomized controlled trial. *Am J Respir Crit Care Med* 2022; 205: 674–684.
46 Highland KB, Distler O, Kuwana M, *et al.* Efficacy and safety of nintedanib in patients with systemic sclerosis-associated interstitial lung disease treated with mycophenolate: a subgroup analysis of the SENSCIS trial. *Lancet Respir Med* 2021; 9: 96–106.
47 Assassi S, Distler O, Allanore Y, *et al.* Effect of nintedanib on progression of systemic sclerosis-associated interstitial lung disease over 100 weeks: data from a randomized controlled trial. *ACR Open Rheumatol* 2022; 4: 837–844.
48 Flaherty KR, Wells AU, Cottin V, *et al.* Nintedanib in progressive fibrosing interstitial lung diseases. *N Engl J Med* 2019; 381: 1718–1727.

49 Solomon JJ, Danoff SK, Woodhead FA, *et al.* Safety, tolerability, and efficacy of pirfenidone in patients with rheumatoid arthritis-associated interstitial lung disease: a randomised, double-blind, placebo-controlled, phase 2 study. *Lancet Respir Med* 2023; 11: 87–96.

50 Behr J, Prasse A, Kreuter M, *et al.* Pirfenidone in patients with progressive fibrotic interstitial lung diseases other than idiopathic pulmonary fibrosis (RELIEF): a double-blind, randomised, placebo-controlled, phase 2b trial. *Lancet Respir Med* 2021; 9: 476–486.

51 Juge PA, Lee JS, Lau J, *et al.* Methotrexate and rheumatoid arthritis associated interstitial lung disease. *Eur Respir J* 2021; 57: 2000337.

52 Cano-Jiménez E, Vázquez Rodríguez T, Martín-Robles I, *et al.* Diagnostic delay of associated interstitial lung disease increases mortality in rheumatoid arthritis. *Sci Rep* 2021; 11: 9184.

53 Wells AU. New insights into the treatment of CTD-ILD. *Nat Rev Rheumatol* 2021; 17: 79–80.

54 Crespo MM, Lease ED, Sole A, *et al.* ISHLT consensus document on lung transplantation in patients with connective tissue disease: Part I: Epidemiology, assessment of extrapulmonary conditions, candidate evaluation, selection criteria, and pathology statements. *J Heart Lung Transplant* 2021; 40: 1251–1266.

55 Bermudez CA, Crespo MM. Managing connective tissue disease: how to select and facilitate successful transplantation. *Curr Opin Organ Transplant* 2022; 27: 191–197.

56 Gunawardena H, Betteridge ZE, McHugh NJ. Myositis-specific autoantibodies: their clinical and pathogenic significance in disease expression. *Rheumatology (Oxford)* 2009; 48: 607–612.

57 Sato S, Hoshino K, Satoh T, *et al.* RNA helicase encoded by melanoma differentiation-associated gene 5 is a major autoantigen in patients with clinically amyopathic dermatomyositis: association with rapidly progressive interstitial lung disease. *Arthritis Rheum* 2009; 60: 2193–2200.

58 Betteridge Z, Gunawardena H, North J, *et al.* Anti-synthetase syndrome: a new autoantibody to phenylalanyl transfer RNA synthetase (anti-Zo) associated with polymyositis and interstitial pneumonia. *Rheumatology (Oxford)* 2007; 46: 1005–1008.

59 Trallero-Araguás E, Grau-Junyent JM, Labirua-Iturburu A, *et al.* Clinical manifestations and long-term outcome of anti-Jo1 antisynthetase patients in a large cohort of Spanish patients from the GEAS-IIM group. *Semin Arthritis Rheum* 2016; 46: 225–231.

60 Oddis CV, Aggarwal R. Treatment in myositis. *Nat Rev Rheumatol* 2018; 14: 279–289.