Invited review

ERS International Congress 2023: Highlights from the Thoracic Surgery and Lung Transplantation Assembly

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**Title:** ERS International Congress 2023: Highlights from the Thoracic Surgery and Lung Transplantation Assembly

**Running Head:** ERS 2023 Assembly 8 Highlights

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**Abstract:**
Five sessions presented at recent European Respiratory Society Congress 2023 were selected by Assembly 8, consisting of thoracic surgeons and lung transplant professionals. Highlights covering management of adult spontaneous pneumothorax, malignant pleural effusion, infectious and immune-mediated complications after lung transplantation, as well as pro & con debate on age limit in lung transplantation and results of ScanCLAD study were summarized by early career members, supervised by the assembly faculty.

**Keywords:**
spontaneous pneumothorax, malignant pleural effusion, mesothelioma, phage therapy, chronic lung allograft dysfunction, graft vs. host disease, antifungal prophylaxis, lung transplant candidate selection, maintenance immunosuppression

**Introduction**
Assembly 8 of European Respiratory Society (ERS) consists of 499 members, focused on state-of-the-art knowledge and both basic and translational research, encouraging interdisciplinary and multicentric interactions, as well as interconnection with the other Scientific Assemblies. Group 8.1 is formed by surgeons specialized in prevention, diagnostic and surgical interventions of a wide range of thoracic pathologies, such as trauma, infections and malignancies. Group 8.2 consists of physicians involved in lung transplantation, focusing on risk prevention, diagnostics and therapy of a spectrum of immune- and non-immune modulated
Management of Adult Spontaneous Pneumothorax

The medical management of spontaneous pneumothorax (SP)

Steven Walker from UK presented the first European guidelines on the management of SP. A literature review was conducted, followed by a meta-analysis with evaluation based on the GRADE system, followed by an “Evidence to Decision framework” process.

Spontaneous pneumothorax (therapeutic possibilities listed based on the level of their invasiveness):

1) **Conservative management** - the literature review identified 1 large randomized controlled trial (RCT) favoring the observational approach compared to chest drain: shorter duration of stay (median 4.5 days; min. 3.18; max. 5.82 days), lower recurrence rate (median 81 fewer/1000 cases, min. 5; max. 121), fewer overall repeated pleural procedures (median 152 fewer/1000 cases, min. 94; max. 182). Based on this evidence, the panel suggested the conservative management of SP in selected cases (minimally breathless, clinically and radiologically stable patients), regardless of size of pneumothorax (conditional recommendation, very low certainty of evidence).

2) **Needle aspiration (NA)** - 6 RCT showed that the NA was associated with lower length of stay (2.2 days lower, range 2.92 lower to 1.49 lower), lower symptom scores compared to chest drain management (1.21 lower, range 1.68 lower to 0.74 lower) and fewer overall repeated procedures (40 fewer/1000 cases, range from 198 fewer to 59 more). Based on these findings the panel recommends NA over the chest tube drain for the initial treatment of SP (strong recommendation, low certainty of evidence).

3) **Ambulatory devices by using a Heimlich device** - 1 RCT reviewed this topic. Ambulatory care compared to chest drain was associated with lower length of stay (3 days lower), fewer overall recurrence (39 fewer/1000, from 122 fewer to 92 more) and fewer overall pleural procedures (148 fewer/1000, from 5 fewer to 220 fewer). The panel suggested ambulatory management for the initial treatment of SP in centers with appropriate expertise and pathways to manage patients with ambulatory devices as outpatients (conditional recommendation, low certainty of evidence).

4) **Chest drain** - the current standard of care in the majority of the centers (as confirmed by a voting during the presentation over a case report).

5) **Early surgical management** - in the literature review, there were 2 studies that looked up the role of first line approach of surgery for SP. They demonstrated: tendency for a lower rate of recurrence (271 fewer/1000, from 339 fewer to 46 more) and fewer overall complications (95 fewer/1000, from 119 fewer to 13 fewer) with early surgery compared to usual care (previous guidelines reserves surgery to more than once recurring pneumothorax). The panel suggested consideration of early surgical intervention for the initial treatment of SP in patients who prioritize recurrence prevention (conditional recommendation, lower certainty of care).

The recommendations are summarized in Table 1.

Persistent air-leak (compared to the standard of care - chest tube):

1) **Autologous blood patch (ABP)** - RCT in the literature review demonstrated: shorter length of stay (2.37 days fewer, range 3.09 fewer to 1.65 fewer) and quicker resolution of the pneumothorax (222 more per 1000, from 30 more to 462 more). Based on these findings, the
panel suggests that ABP could be considered in patients with persistent air-leak who are not fit for surgery (*conditional recommendation, very low quality of evidence*).

2) **Bronchial valves** - 1 RCT in this topic demonstrated: lower air leak duration (3.18 days fewer, range 3.93 fewer to 2.43 fewer) and quicker resolution of the pneumothorax (240 more/1000, from 48 more to 486 more). However, the guideline stated no recommendation regarding bronchial valves in patients with SSP who are not fit for surgery due to lack of conclusive evidence (*no recommendation, very low quality of evidence*).

3) **Suction to chest drain** - 1 RCT did not show any significant difference in any of the outcomes, looked up in terms of duration of air leak. The guideline gave no recommendation due to lack of conclusive evidence (*no recommendation, very low quality of evidence*).

**Surgical management of Spontaneous Pneumothorax**

Marcello Migliore from Italy deliberated upon the existing literature, guidelines, as well as gaps in the current knowledge with regards to the surgical management of SP. According to BTS guidelines\(^1\), surgical evaluation is indicated only for patients with recurrent or bilateral, hydropneumothorax or clinically unstable patients. In the ERS statement\(^2\), no recommendations concerning surgical management were given for primary SP or persistent/recurrent pneumothorax due to the lack of randomized evidence. The ERS committee left a few open questions for further research:

1. Relative benefits of talc versus talc and bulllectomy in recurrence prevention.
2. Role of lung parenchyma resection in recurrence prevention

Meta-analysis by Vuong et al. including 4262 patients of 29 RCT concluded that in patients with first episode of pneumothorax, VATS ranked the highest in preventing recurrence (P-score = 0.95), followed by pleurodesis (P-score = 0.69), aspiration (P-score = 0.27) and tube drainage (P-score = 0.08). The recurrence incidences of VATS, pleurodesis, tube drainage, and aspiration were 0, 8, 13 and 30 per 100 person-year, respectively.\(^3\) Brown et al. evaluated 316 patients (154 patients in intervention group, 162 in conservative-management group) in an open-label, multicenter, non-inferiority trial, assessing whether conservative management is an acceptable alternative to interventional management for uncomplicated, moderate-to-large primary SP. There was no difference in lung re-expansion (RD −3.8%; 95% CI −8.3 to 0.7) or time to resolution (15.5 versus 14 days in the intervention and conservative management group, resp.; HR 1.11; 95% CI, 0.88-1.40). The conservative management arm had fewer invasive procedures, shorter hospital stay, faster return to work, less recurrence, and adverse events.\(^4\)

Randomized study by Marx et al. included 200 patients with NA and 202 with chest tube drainage from 31 French hospitals. The treatment failure was observed in 29% patients with NA and in 18% with chest tube drainage. Failures of NA were treated with chest drain insertion. The authors concluded that NA was better tolerated with fewer adverse events, leading to higher failure rates.\(^5\)

The discussion then moved on to the first European guidelines on adults with spontaneous pneumothorax. Of the 12 clinical questions, the two questions of surgical relevance were:

1. Should treatment with pulmonary intervention (VATS) be used for recurrence prevention in spontaneous pneumothorax (compared with VATS plus pleurodesis)?
2. Should surgical pleurecctomy be used for recurrence prevention in spontaneous pneumothorax (compared to chemical pleurodesis delivered surgically or medically)?

However, no recommendations could be made for either of the above questions given the lack of available evidence. The presentation proceeded with two clinical cases. The first case described a patient with persistent pneumothorax with a large bulla in the apex, resected with a base of normal lung tissue. The further management (no pleurodesis, pleurectomy, pleural abrasion, talc pleurodesis) is eminence-based, due to the lack of the evidence. The second case
presented a patient with Stage 1 pneumothorax, without any bulla/bleb - representing nearly 20% cases in experienced centers, with no current guidelines regarding further management (apical wedge resection, pleurodesis). Dr. Migliore shared his preference on performing a wedge resection, may not have any implication in terms of recurrence prevention, but could aid to obtain a definitive diagnosis of the cause of pneumothorax.  

The current limitations on surgical management of pneumothorax are: no consensus on the size cut off for small versus large pneumothorax, insufficient evidence for management of persistent air leak, surgical approach (uniportal/multiportal), method of pleurodesis and strategies for Stage 1 pneumothorax. Dr. Migliore highlighted the unmet need of generating good quality evidence.

**Optimizing diagnostic tools and treatment for malignant pleural effusion and mesothelioma**

Matthew Tate from Scotland presented: “The Scottish Mesothelioma Network: Impact of a national MDT on overall survival in pleural mesothelioma”. A dedicated Scottish MDT was established in 2019, collecting mesothelioma data pre- (April 2017 - March 2019) and post-network (April 2019 - April 2022) to set-up cohorts - 273 (41.4%) and 386 (58.6%) cases, respectively. Multivariable restricted mean survival time analysis proved better overall survival for post-network non-epithelioid cases in comparison to pre-network ones (+4.6 months; p=0.004) and no difference was observed for epithelioid cases between the groups. In patients receiving systemic anti-cancer therapy, overall survival in the post-network group was significantly increased in non-epithelioid cases (median 16.6 compared to 10.7 months in pre-network group; p<0.0001). The possible explanations are the use of immunotherapy as a standard of care in non-epithelioid MPM (in 15.3% post-network patients), better histologic classification, lower attrition on diagnostic pathways and better symptom management.

Dinesh Addala from UK presented: “Qualitative study of patient priorities in the malignant pleural effusion (MPE) pathway”. In the mixed methods study, 56 patients with MPE were included. Median time from first contact to diagnosis was 46 days (range 28-54) and to definitive treatment 70 days (range 45-84). The delays resulted in prolonged breathlessness (more than one month in 60% of patients), a higher number of required (≥3 in more than 70% of patients) and emergency procedures (60% of patients). In the survey, up to 70% of patients would be willing to consider an earlier indwelling pleural catheter (IPC). Dr. Addala summarized his talk addressing breathlessness and time to diagnosis being the key areas of concern, highlighting the urge to accelerate both diagnostic and treatment, suggesting earlier biopsy and IPC insertion.

Richa Gupta from India presented the study analyzing “The efficacy of the time-dependent (12h) vs. volume-dependent (<150mL/day) chest tube removal for talc pleurodesis in patients with MPE”. The results of this prospective RCT including 100 patients showed no differences in complications, mortality and pleurodesis success at day 7, 30 and 90 between time- and volume-dependent groups. Average time from pleurodesis to chest tube removal was 12 ± 0.52 hours for time- and 44 ± 56 hours for volume- dependent groups (p<0.001). Dr. Gupta concluded that comparable outcomes were achieved by both methods, with patients in the time-arm having shorter hospital stays.

Hugh Welch from UK presented: “Does a novel IPC drainage system improve patient experience?” IPCs are increasingly used to manage recurrent pleural effusions. Most systems involve vacuum bottle drainage, applying variable vacuum pressures, leading to drainage-
related pain. Electronic pump system Geyser was designed to minimize the drainage pain by a ramped drainage profile consisting of 4 minute cycles of maximum in-line pressure 50 cmH$_2$O, with maximum 250mL of fluid removal. 15 patients were included in this single-center prospective study. Geyser and standard of care ICP systems drained similar volumes of pleural fluid, with the Geyser group describing lower post-drainage pain scores. Further studies should be performed in order to avoid limitation by small-sized cohort and pro-innovation bias.

Maria Giovanna Mastromarino from Italy presented: “Pressurized Intra-Thoracic Aerosol Chemotherapy (PITAC): preliminary results in malignant pleural effusion”. Malignant pleural effusions (MPE) affect up to one third of oncological patients, lowering the quality of life and overall survival. PITAC is a novel therapy combining the advantages of surgery and loco-regional chemotherapy. Patients were divided into two groups: PITAC with tailored dose of cisplatin (10.5mg/m$^2$) + doxorubicin (2.1mg/m$^2$), selected for their cytostatic and sclerosing effect, versus talc poudrage (current standard of therapy). Cytostatics were inserted into the chest cavity via a nebuliser and left in steady state for 30 minutes, with intrathoracic pressure 12mmHg CO$_2$ to increase the drug penetration. Both groups developed effective pleurodesis at day 30 and month 5 follow-up, with no significant difference observed in pleural effusion recurrence survival ($p=0.16$). The study proved the comparability of PITAC approach to talc pleurodesis in management of pleural effusion, however its oncological role requires a further investigation.

**Infectious and non-infectious complications of immunosuppressed patients**

Mariagrazia Di Luca from Italy presented a pre-recorded session “Multidrug-resistant bacterial pulmonary infections: challenges of phage therapy”. Phages are viruses with the ability to selectively and exclusively attach harmful bacteria at the strain level, leading to their rapid lysis. Moreover, they are active as well against biofilm-embedded bacteria and might be used as adjuvant therapy to antibiotics, creating synergism, with some in vitro studies proving possible restoration of the sensitivity to antibiotics. Currently, there are two ways of obtaining the phage therapy products - a personalized approach, using selected phages from the phage bank or a standard formulation, a phage cocktail from pharmaceutical company. Dr. Di Luca presented a published case report - a patient with a chronic infection caused by Pseudomonas aeruginosa treated by a combination of meropenem and personalized phage therapy. Over a 2-year follow-up, no severe adverse events or clinical signs of infection relapse were observed.

Robin Vos from Belgium followed with the presentation: “Chronic lung allograft dysfunction (CLAD) and pulmonary chronic graft versus host disease (PcGvHD): common pathogenic mechanism and clinical features”. His talk covered the late-onset non-infectious pulmonary complications after Tx (LONIPC) - clinically manifesting as CLAD in lung transplantation (LuTx) and PcGvHD in hematopoietic stem cell transplantation (HSCT) recipients. Immunological pathways of CLAD are a consequence of allo-reactive lymphocytes of the recipient, while PcGvHD is caused by the graft-originated ones. Both CLAD and PcGvHD are driven by numerous risk factors, such as immune activation caused by HLA and non-HLA mismatch, respiratory infections, systemic inflammation, gastroesophageal reflux, exposure to toxins or ex-smoking. CLAD and PcGvHD are very similar on the cellular level, with two common endpoints - air-way centered fibrosis (bronchiolitis obliterans; OB/constrictive bronchiolitis; CB) and interstitium-affecting alveolar fibroelastosis (AFE) or fibrosis. On a molecular level, study by Vanstapel et al. showed increased expression of connective tissue growth factor in end-stage CLAD and PcGvHD, suggesting its potential role in CLAD,
especially restrictive allograft syndrome (RAS), and PcGVHD. Jonigk et al. proved that as well molecular characteristics in OB and AFE are alike in CLAD and PcGvHD. Current definition of CLAD is based on 2019 ISHLT consensus, identifying 4 different phenotypes – bronchiolitis obliterans syndrome (BOS), RAS, mixed and undefined. However, current NIH PcGvHD consensus criteria account only for BOS. Recent study by Pang et al. divided PcGvHD patients based on CLAD 2019 ISHLT consensus definition, with less than a half of the patients meeting the NIH criteria for BOS, demonstrating the potential of adapting CLAD criteria in PcGvHD population. The similarities and differences of obstructive and restrictive phenotypes of CLAD and PcGvHD are summarized in Table 2, adapted by Bos et al. NIH cGvHD working report 2020 recommended full pulmonary function tests (lung volumes and DLco included) prior to HSCT, at day 100 and year 1, followed by annual examination even in asymptomatic patients with spirometry on month 6 and 9, and in patients with cGvHD every 3 months. Threshold for referral to Specialized Transplant Team should be FEV1 decline of more than ≥10% of patient’s pre-HSCT baseline or a day 100 assessment, followed by short interval repeat testing (within 2-4 weeks).

Dr. Vos ended his presentation highlighting the necessity of earlier detection of both CLAD and PcGvHD, with randomized clinical trials being an unmet need in order to further improve outcomes after LuTx and HSCT.

Daniel Wolff from Germany followed with the presentation: “CLAD and PcGvHD: old and new therapeutic approaches”. This presentation follows the path of analogies between PcGVHD and CLAD and analyses therapeutic strategies in order to highlight common therapeutic targets. Bergeron et al. proved that the combination of inhaled fluticasone, azithromycin, and montelukast (FAM) with a brief steroid pulse may halt pulmonary decline in new-onset BOS in HSCT recipients – only 6% of the patients experienced treatment failure at month 3 (compared to 40% in historical controls). Study by Vos et al. included patients with different grades of CLAD (BOS 76.2%; RAS 24.8%) that started montelukast therapy. Montelukast was associated with attenuation of FEV1 decline at month 3 and 6 (p<0.0001 for both), as well as significantly better progression-free (p<0.0001) and overall survival (p=0.0002) in the patients with improvement or stabilization at month 3 of therapy. Li et al. proved that azithromycin prophylaxis was associated with improved survival (p=0.002), but no significant reduction in CLAD onset (p=0.0697) was observed. Still considering azithromycin effect, the study by Bergeron et al. in PcGvHD had to be pre-emptively stopped - the group with azithromycin prophylaxis had significantly higher cumulative incidence of hematological relapse within 2-year follow-up period (33.5% vs. 22.3% on placebo, p=0.002). Based on given data, Dr. Wolff summarized that in HSCT recipients, azithromycin prophylaxis and prolonged application should be avoided, with FAM being standard of care in manifest BOS or drop of FEV1 without formal diagnosis of BOS. Special attention should be paid to patients with otherwise increased risk for secondary malignancies. Randomized trial by Zeiser et al. in PcGvHD patients presented significantly better response to ruxolitinib in comparison to control group (49.7% vs. 25.6, resp.; p<0.001) at week 24, as well as longer median failure-free survival (>18.6 vs. 5.7 months, resp.; p<0.001) and higher symptom response (24.2% vs. 11.0%, resp.; p=0.001). Study by Hefazi et. al. showed results of retrospective analysis on the effect of extracorporeal-photopheresis (ECP) in BOS of HSCT recipients, where ECP was associated with a better overall survival (p=0.001). ECP is applied by 72% of German-speaking centers, with half of the centers using ECP either upfront or in 2nd line. DeFilipp et al. analyzed HSCT patients with BOS, treated by belumosudil, showing higher response rates in less advanced disease, however, no significant correlation was observed in predominantly mild or moderate disease. Several trials still in the setting of PcGvHD were assessing role of abatacept in BOS, demonstrating its effectiveness with an overall response rate 57% but subjective improvement appeared to be more sensitive compared to FEV1. Currently, there are no
organ specific trials available for treatment of BOS (except FAM), however, some agents have supportive data of its use in this clinical setting. Dr. Wolf concluded his presentation by highlighting the need for early intervention in patients affected by CLAD or PcGvHD.

Shahid Husain’s (from Canada) talk was about preventive and treatment strategies around fungal infections in solid organ and bone marrow transplant recipients. Study by Kontoyiannis et al. showed that the cumulative overall incidence of invasive fungal infections (IFI) within the first year in HSCT recipients was 3.4%. In comparison, cumulative incidence of IFI for solid organ transplant recipients (SOTRs) was 3.1% - 11.6% for small bowel, 8.6% for lung and heart-lung, 4.7% for liver, 4.0%, pancreas and kidney-pancreas, 3.4% for heart and 1.3% for kidney transplant recipients. In SOTRs, Candidiasis was the most common IFI within 12 month (71.4%), except for LuTx recipients (23.9%), where the most common was Aspergillosis (24.8% compared to other 12.6% in other SOTRs). Moreover, cumulative probability of IFI rose consistently over the first 5 years following LuTx reaching 20.1%. Different prophylactic strategies are used across the centers, however, three meta-analysis did not prove any advantage of universal prophylaxis on the incidence of invasive Aspergillosis (IA) compared to none. Meta-analysis by Phoompoung et al. showed that risk factors for IFI in LuTx include previous fungal colonization (OR 2.44; 95% CI 0.08-0.47), cytomegalovirus infection (OR 1.96; 95% CI 1.08-3.56), and single LuTx (OR 1.77; 95% CI 1.08-2.91), with preemptive antifungal therapy being a protective factor for IA (OR 0.2; 95% CI 0.08-0.47). As well statins were proved to be associated with a lower risk of IA (SHR 0.30; 95%CI 0.14-0.64; p=0.002). In terms of Aspergillus colonization, meta-analysis by Bhaskaran et al. did not prove any significant difference between groups with and without voriconazole prophylaxis (21% and 28%, resp.; p=0.48). Dr. Husain presented data of his own study from 2018 regarding pre-emptive treatment based on BAL galactomannan and cultures - pre-emptive therapy was associated with significantly lower rates of IA at 1 year post-LuTx compared to pre-emptive therapy (HR 0.23, 95%CI 0.09 to 0.58). In the multicenter RCT, no difference in 6 months of fungal-free survival was proved between patients treated with fluconazole or voriconazole, despite trends favoring voriconazole in fewer IFI (7.3% vs. 11.2% in fluconazole group, p=0.12). Study by Ullmann et al. found posaconazole to be as effective as fluconazole in preventing IFI (OR 0.56; 95%CI 0.30-1.07; p=0.07) and superior in prevention of proven or probable IA (OR 0.31, 95% CI 0.13-0.75; p=0.006). In the posaconazole group, fewer breakthrough IFI (2.4% vs. 7.6%; p=0.004%) and particularly IA (1.0 vs. 5.9%; p=0.001) were observed. Study by Bose et al. regarding isavuconazole prophylaxis demonstrated probable and proven IFI in 6% and 12% patients, respectively, with excellent tolerability. Meta-analysis including 69 RCT patients concluded that posaconazole was associated with the best probability of success against IFI and IA and voriconazole was associated with significant reduction in invasive candidiasis compared to placebo. Study By Marty et al. regarding mucormycosis management demonstrated that day 42 all-cause mortality 33% in primary-treatment isavuconazole cases was similar to 39% in amphotericin B-treated matched controls (p=0.595). Novel promising antifungals as fosmanogepix, ibrexafungerp, olorofim, opelconazole, and rezafungin are not ready to be used in clinical setting yet. Recommendations on prophylaxis are summarized in Table 3.

The Pro & Con Debate on Age Limit for Lung Transplant Candidacy

Pro: Age of 65 years is no longer a barrier for lung transplant candidacy

Konrad Hoetzenecker from Austria highlighted the differences between chronological and actual biological age. According to the 2021 ISHLT consensus on the selection of LuTx candidates, age between 65 and 70 years is considered to be a risk factor while age >70 years a
Zhou et al. observed a prominent increase in ≥70 year old LuTx recipients (from 2.2% in 2005 to 14.3% in 2020), with a 83% increase in the number of LuTx performed in patients aged ≥70 years. Candidates ≥70 years had favorable waitlist outcomes (LuTx within one year since listing) in comparison to ones 60-69 years old (81.2% and 72.7%, resp.; p=0.001). The odds for death or deterioration within one year since listing were as well in favor of ≥ 70 years old candidates, when compared to 60-69 years old ones (9.1% and 10.1%, resp. p<0.001). Moreover, elder recipients had superior perioperative outcomes in terms of acute rejection incidence (6.7% in patients aged ≥ 70 years, 7.4% in the ones 60-69 years and 9.2% in the group aged 18-59 years; p<0.001) and prolonged intubation (21.7% in ≥ 70 years, 27.4% in 60-69 years and 34.5% in the group aged 18-59 years; p<0.001). The study by Singer et al. demonstrated that age was not associated with meaningful differences in the health-related quality-of-life benefits of LuTx. However, frailty was a significant risk factor leading to a 12.2% (95% CI: 3.1%-21%) increased risk of death within the first year after LuTx . The same study proved that frailty is reversible and possesses the prognostic value in only ~ 15% of LuTx recipients remaining frail at post-LuTx month 6 frailty assessment. Novel approach combining standard frailty tests in combination with biomarkers such as IL-6, GDF-15 or apelin might allow us to improve the evaluation of these patients. Dr. Hetzenecker presented data of Vienna LuTx Program - in 2022, 23% of their donors were aged 65-69 years and 15% >70 years, rising the question why to discriminate the elder generation if there is a significant organ donor pool created by the very same age groups, with aim not to discuss the acceptability of elder LuTx candidates, but to foster the research improving their post LuTx outcomes.

Con: Age still matters in candidate selection for lung transplantation

Are Martin Holm from Norway stated that given the limited amount of donor organs available, three main questions should be asked by the clinicians:
1. Who is the most urgent? Following the rule of rescue - saving lifes.
2. Who has the best prognosis? Assessing priority by medical criteria.
3. Who has the most to lose? Addressing justice and equity.

Dr. Holm presented data from Oslo LuTx Center, comparing significantly differing survival of patients after LuTx (survival at year 5 ~ 70% year 10 ~ 55%) to non-transplanted patients (50% deceased at year 2). Data from Organ Procurement and Transplantation Network Registry 2021 demonstrated unfavorable survival outcomes in recipients >65 years. The retrospective analysis by Iyanna et. al. demonstrated that the rate of LuTx in recipients ≥ 70 increased particularly in low-volume centers (LVCs) and currently high-volume centers (HVCs) and LVCs perform similar rates of LuTx for recipients ≥ 70. Survival time was shorter for recipients ≥ 70 compared to recipients < 70 old (HR 1.36, 95%CI 1.28-1.44; p< 0.001). HVCs were associated with a survival advantage in recipients < 70 (HR 0.91, 95% CI: 0.88-0.94, p =< 0.001); but for recipients ≥ 70 survival did not differ significantly between HVCs and LVCs (HR 1.11, 95% CI:0.99-1.25; p< 0.08). Dr. Holm summarized that among many valid criteria for rationing life years, such as sarcopenia, urgency, frailty or telomere lengths, the age is the only one absolutely certain and absolutely fair.

ScanCLAD: RCT on once-daily tacrolimus versus twice-daily cyclosporine

Göran Dellgren from Sweden presented the results of the ScanCLAD study - a multi-national, multi-centric, randomized, parallel group and open-label study evaluating if once-day tacrolimus versus twice-day cyclosporine reduces the 3-year incidence of CLAD. There is low-level evidence regarding the impact of choice of calcineurin inhibitor (CNI) on CLAD incidence, and none is based on the current CLAD definition. As all programs in Scandinavia were using twice-daily cyclosporine (CyA group), 1:1 randomisation to once-daily...
tacrolimus (Tac group) was performed. Patients were enrolled over a period of 24 months and follow-up for another 36 months, respectively. Repetitive spirometric measurements were performed in all of the included patients and evaluation was performed based on current CLAD definition. Of 249 patients included in the final analysis, 125 were in CyA (50.2%) and 124 in Tac group (49.8%). 6 and 9 patients were not evaluated due to the early death in the CyA and Tac group, resp. (4.8%, resp. 7.3%). Results showed significantly higher incidence of acute rejection (p=0.011) in the CyA (56.8%) than in the Tac group (40.3%). Significant difference (p=0.002) was described also in acute rejection episodes in the affected patients with 118 and 71 episodes described in the CyA and Tac group, resp. (average 1.67 and 1.42 episodes per patient, resp.). Cumulative incidence of CLAD was 38.4% in the CyA group and 12.9% in the Tac group with death/re-LuTx as competing events (p<0.00). Composite event-free survival was significantly inferior for the CyA group (p=0.0024). No statistically significant difference was observed in overall and graft survival between the groups (p=0.25; p=0.058, resp.). In patients affected by CLAD, graft survival was statistically higher in Tac group (p=0.021). No significant difference in serious adverse effects was observed. Dr. Dellgren concluded that tacrolimus should be regarded as the first choice of CNI after LuTx.

Conclusion:
The article aimed to summarize diverse, inspiring presentations, covering a wide range of challenging topics in both thoracic surgery and LuTx, presented at ERS Congress 2023 (Table 4). We look forward to the next ERS Congress, in Vienna, Austria, from 7 to 11 September 2024!

Conflicts of Interest
The participating authors declare no conflicts of interest.

Ethical Approval
Does not apply.

Informed Consent
Does not apply.

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Table 1: Summary table comparing different clinical approaches in the management of SP

<table>
<thead>
<tr>
<th>Treatment option</th>
<th>Conservative</th>
<th>Needle aspiration</th>
<th>Ambulatory care</th>
<th>Chest drain</th>
<th>Surgery</th>
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</thead>
<tbody>
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<td>Mean initial hospital stay</td>
<td>1.0 day</td>
<td>2.6 days</td>
<td>0 days</td>
<td>4.8 days</td>
<td>4.0 days</td>
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<tr>
<td>Chance of SP recurrence within 1 year</td>
<td>9%</td>
<td>25%</td>
<td>24%</td>
<td>21%</td>
<td>6%</td>
</tr>
<tr>
<td>Required further pleural procedure</td>
<td>15%</td>
<td>22%</td>
<td>21%</td>
<td>25%</td>
<td>3%</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th></th>
<th>BOS after LuTx</th>
<th>BOS after HSCT</th>
<th>RAS after LuTx</th>
<th>Restrictive PcGvHD after HSCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>Approx. 50%</td>
<td>Approx. 5-15%</td>
<td>≤ 30%</td>
<td>Not accurately known, about 12-60% of LONIPIC</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Asymptomatic, cough, exertional dyspnea, dyspnea at rest, inability to perform activities of daily living</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>FEV1 &lt;80% of baseline and absence of CT opacities and exclusion of the other causes</td>
<td>FEV1% &lt;75% of predicted and &gt;10% decline over &lt;2 years and FEV1/FVC &lt; 0.7 and signs of air-trapping (PFT/CT) or other organ cGvHD in absence of respiratory infection</td>
<td>FEV1 &lt;80% of baseline and TLC ≤ 90% of baseline and persistent CT opacities and exclusion of the other causes</td>
<td>No definition yet</td>
</tr>
<tr>
<td>Grading</td>
<td>CLAD staging: Grade 1: FEV1 &gt; 65-80% baseline Grade 2: FEV1 &gt; 50-65% baseline Grade 3: FEV1 &gt; 35-50% baseline Grade 4: ≤ 35% baseline</td>
<td>NIH lung cGvHD grading: Grade 1: mild; FEV1 60-79% predicted Grade 2: moderate; FEV1 40-59% predicted Grade 1: severe; FEV1 ≤ 39% predicted</td>
<td>CLAD staging: Grade 1: FEV1 &gt; 65-80% baseline Grade 2: FEV1 &gt; 50-65% baseline Grade 3: FEV1 &gt; 35-50% baseline Grade 4: ≤ 35% baseline</td>
<td>NIH PcGvHD grading: Grade 1: mild; FEV1 60-79% predicted Grade 2: moderate; FEV1 40-59% predicted Grade 1: severe; FEV1 ≤ 39% predicted</td>
</tr>
<tr>
<td>CT findings</td>
<td>Air-trapping, bronchiolitis (tree-in-bud), bronchiectasis</td>
<td></td>
<td>Ground-glass opacities, consolidations, pleural or septal thickening, bronchiectasis, volume loss</td>
<td>Ground-glass opacities, consolidations and less often pleural or septal thickening, bronchiectasis, volume loss</td>
</tr>
<tr>
<td>Histology</td>
<td>Chronic bronchitis, bronchiolitis obliterans</td>
<td>Most common: DAD, AFE, PPFE, and concurrent OB/CB Other: NSIP, AFOP, (C)OP</td>
<td>More heterogeneous: NSIP, LIP, DAD, AFE, PPFE, and concurrent OB/CB Less frequent: OP, AFOP, (C)OP</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2:** The clinical similarities and differences of obstructive and restrictive phenotypes of CLAD and PcGvHD
**Prognosis**

<table>
<thead>
<tr>
<th></th>
<th>Median survival 3-5 years</th>
<th>Median 5-year survival 60%</th>
<th>Median survival 1-2 years</th>
<th>Median 2-year survival 61% (less data)</th>
</tr>
</thead>
</table>

**Table 3: Recommendations on antifungal prophylaxis in LuTx**

**Recommendations on prophylaxis**

- Prophylaxis or preemptive therapy can be employed as a strategy to prevent, depending on the availability of the diagnostic tests (*strong; moderate*)

- In case where a preemptive treatment strategy is employed, both BAL culture and galactomannan should be incorporated into the protocol (*strong; low*)

- It is recommended to initiate targeted antifungal prophylaxis if any of the risk factors (pre-LuTx or within first year after LuTx Aspergillus colonization, SLuTx or positive Aspergillus perioperative culture in CF patient) is present (*strong; moderate*)

- Duration 4-6 months in universal and targeted prophylaxis and 3-4 months in preemptive strategy (*strong; moderate*)

- Caution with voriconazole in patients with history of squamous cell carcinoma, residing in geographic areas with higher incidence of cutaneous malignancy and photo-protective measurements and enhanced skin surveillance to be put in place (*strong; high*)

- Alternatives to voriconazole may include posaconazole or isavuconazole (*weak; low*)

**Table 4: Summarized Highlights of ERS Congress 2023 and take home messages of the review.**

**Group 8.01 - Thoracic Surgery**

**Management of Adult Spontaneous Pneumothorax**
- Patients with spontaneous pneumothorax may benefit from VATS as a modality for recurrence prevention. However, more research is needed.
- Currently there is variability in practice with regards to the method of pleurodesis and RCTs are needed to choose between nothing, pleurectomy, pleural abrasion and talc pleurodesis.
- In stage 1 pneumothorax when no bulla/bleb is noted, wedge resection may be useful for diagnosis of pneumothorax.

**Optimizing diagnostic tools and treatment for malignant pleural effusion and mesothelioma**
- Patients with mesothelioma might benefit from a centralized, multidisciplinary network.
- Earlier insertion of indwelling pleural catheter should be offered to patients with malignant pleural effusion.
- Time-dependent (12h) chest tube removal for talc pleurodesis in patients with malignant pleural effusion showed comparable results as volume-dependent (<150mL/day).

**Group 8.02 - Lung Transplantation**

**Infectious and non-infectious complications of immunosuppressed patients**
Earlier detection and better diagnostics of both CLAD and PcGvHD is necessary in order to improve survival.

Multicentric RTC are necessary in development of novel, effective therapeutic options for both CLAD and PcGvHD.

Prophylaxis or preemptive antifungal therapy can be employed as a strategy to prevent, depending on the availability of the diagnostic tests.

The Pro & Con Debate on Age Limit for Lung Transplant Candidacy

- LuTx for recipients > 65 years of age leads to good short- and acceptable long-term survival with an excellent quality of life.
- Well selected patients >70 years with acceptable risk profile should not be excluded from LuTx candidacy.
- Among many valid criteria for rationing life years, such as sarcopenia, urgency, frailty or telomere lengths, the age is the only one absolutely certain and absolutely fair.

ScanCLAD: RCT on once-daily tacrolimus versus twice-daily cyclosporine
- Tacrolimus should be regarded as the first choice of calcineurin inhibitor after LuTx.

References:


34. Phoompoung P, Villalobos APC, Jain S, Foroutan F, Orchanian-Cheff A, Husain S. Risk factors of invasive fungal infections in lung transplant recipients: A systematic


46. Iyanna N, Chan EG, Ryan JP, et al. Lung Transplantation Outcomes in Recipients


Figure: Highlights from the thoracic surgery and lung transplantation assembly from ERS Congress 2023

**Assembly 8.1 - Thoracic surgery**
- Management of Spontaneous Pneumothorax
  - Medical
  - Surgical
- Diagnostics & Treatment of Malignant Pleural Effusion
- Diagnostics & Treatment of Mesothelioma

**Assembly 8.2 - Transplantation**
- Complications of Immunosuppressed Patients
  - Infectious
  - Immune-mediated
- Pro & Con Debate on Age Limit for Transplant Candidacy
- Once-daily Tacrolimus vs. Twice-daily Cyclosporine