



Early View

Invited review

ERS International Congress 2020: Highlights from the Thoracic Surgery and Transplantation Assembly

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ERS International Congress 2020: Highlights from the Thoracic Surgery and Transplantation Assembly

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ABSTRACT

The thoracic surgery and lung transplantation Assembly of the European Respiratory Society is delighted to present the highlights from the 2020 Virtual International Congress. We have selected four sessions that discussed recent advances in a wide range of topics: From use of robotic surgery in thoracic surgery and extracorporeal life support as a bridge to lung transplantation to lung transplantation in the era of new drugs. The sessions are summarized by early career members in close collaboration with the assembly leadership. We aim to give the reader an update on the highlights of the conference in the fields of thoracic surgery and lung transplantation.

INTRODUCTION

Assembly 8 Thoracic Surgery and Transplantation includes physicians and surgeons with an extraordinary knowledge of the state of the art in the field of Thoracic Surgery (Group 8.1) and Lung Transplantation (Group 8.2). Both groups are strongly engaged with the other Scientific Assemblies, focusing on surgical options for the treatment of lung diseases. The overall number of members as of August 31, 2020 is about 500 with a steady yearly increase of 10%. The rate of acceptance of abstracts at annual Congress is very high (86,5% in Vienna) thus indicating a high quality of submitted abstracts.

The members of Thoracic Surgery Group include surgeons who have a special interest in an interdisciplinary approach towards various thoracic pathologies eventually requiring surgical intervention in terms of a diagnostic or a therapeutic procedure, such as malignancies, pleuro-pulmonary or mediastinal infections, trauma or other benign diseases of the lung, pleura or mediastinum. The group focuses on the possibilities of interdisciplinary and interactive sessions during the annual Congress in order to create a culture of interdisciplinary between surgical and non-surgical members of the Society.

The members of Transplantation Group include pulmonologists/respiratory specialists who have a particular interest in lung transplantation. It is a group strongly engaged in collaborative working to better understand the risk factors, mechanisms and treatment options for lung transplant recipients who develop chronic lung allograft dysfunction affecting their post-transplant survival and causing post-transplant morbidity. This group focuses on high quality symposia during the annual congress, it is publishing monographs on Lung transplantation, it already delivered three very successful Transplant ERS school courses and it organized several meet-the-professor-sessions.

In the last congress, Assembly 8 organized/took part in 2 symposia, 2 joint sessions with European Society of Thoracic Surgeons, one pro/con debate, one expert view. The highlights of these important sessions are represented in this paper.

Group 8.1 Thoracic Surgery

Session: Pro/Con debate: *Do I need a robot in my thoracic surgery operation theater?*

This session debated the potential utility of robotic technology for thoracic surgery.

Pro: Progress in robot-assisted thoracic surgery (RATS)

In her presentation, Giulia Veronesi provided all the recent evidence on the progress and utility of robot implementation in the field of thoracic surgery. After demonstrating the evolution from

open surgery to minimally invasive, robotic, and digital surgery, she pointed to the great possibilities that big data and machine learning bring to thoracic surgery by providing increased possibilities of preoperative surgical planning and enhancing outcomes. In this context, the adoption of robotic technology was rapid in recent years, with the number of robot-assisted lobectomies reaching up to 18% in 2016, from 1% in 2010. In addition, she stressed the technical advantages that the robotic approach provides, such as intuitive movements, tremor filtration, increased degrees of freedom, motion scaling, stereoscopic vision, and eye-hand-target alignment. Due to these advantages, RATS is associated with a learning curve of 20 patients in contrast to the over 50 patients that are needed for video-assisted thoracoscopic surgery (VATS) [1,2]. All these characteristics contribute to enhanced clinical outcomes, in terms of readmissions and grade 3-4 complications. In fact, RATS is associated with lower mortality rate compared to open surgery and VATS, improved quality of life, and reduced pain compared to open surgery, improved lymph node dissection and radicality regarding either anatomic segmentectomy [3] or a more extended resection for locally advanced non-small cell lung cancer [4] compared to VATS, with similar oncological outcomes. Furthermore, RATS provides enhanced outcomes when applied in complex cases and thymectomy in myasthenic patients [5]. Finally, it was demonstrated that both VATS and RATS are associated with similar costs when complications, length of stay and readmissions are taken into consideration.

Con: VATS superiority over RATS

In his presentation, Rene Horsleben Petersen focused on three topics: 1) advantages and disadvantages of RATS, 2) advantages of VATS and 3) the potential of robotic systems evolution in the near future. Petersen listed the disadvantages of RATS as they were presented in a recent review [6]. These disadvantages included higher cost, longer operation time, the necessity of a skilled assistant on the table, the lack of tactile feedback, along with the number and size of the ports [6]. Petersen then demonstrated newly developed equipment for VATS that is not available in RATS, such as advanced staplers and energy systems. Besides, the introduction of three dimensional and uniportal VATS has increased the feasibility and ergonometic of VATS at levels equal to RATS. According to the outcomes of a meta-analysis that compared VATS and RATS, no significant difference was reported regarding conversion to open rate, number of dissected lymph nodes, length of hospital stay, mean operation time, drainage volume after surgery, and postoperative morbidity [7]. Nonetheless, that meta-analysis was associated with certain limitations, such as high heterogeneity in pooled outcomes and not clearly indicated inclusion-exclusion criteria regarding the stage of disease and the extent of surgery, thus posing biases in its conclusions [7]. For final positioning of RATS future robotic developments should be awaited. Furthermore, there is important potential of artificial intelligence, big data, image fusion and other novelties in thoracic surgery.

Highlights:

1. The number of robot-assisted lobectomies has increased tremendously.
2. It remains unclear whether the advantages of robot-assisted thoracic surgery outweigh the disadvantages, especially in the light of other innovations in the field of video-assisted thoracic surgery.

Session: *What's new with ground glass opacities?*

Increased use of chest CT in daily practice not only provides earlier detection of lung cancer but also increased detection of incidental findings such as ground glass opacities (GGOs). This has warranted the development of specific approaches regarding follow-up, diagnosis, and treatment for these lesions. In this session the management of GGOs was discussed, aiming for the optimal approach.

First, Klaus Loureiro Irion elaborated on the terminology of GGO and ground glass nodule (GGN), technical factors affecting GGN analysis, and diagnosis, follow-up and biopsy recommendations. Lesions can be subdivided in pure ground glass nodules (pGGN), including AAH (atypical adenomatous hyperplasia) and AIS (adenocarcinoma in situ) & partly solid ground glass nodule (psGGN) including MIA (minimally invasive adenocarcinoma) and invasive adenocarcinoma. The larger the size of the nodule and the shorter the volume doubling time, the higher is the prevalence of malignancy [8]. If present, the solid component of the nodule should be assessed in various settings, not alone in the mediastinal setting, as the size can be underestimated. Temporal progression should be monitored and underestimated, as some GGNs don't change over the years. It's recommended doing 6-12 monthly follow-up scan for pGGN, and 3-6 monthly follow-up scans for psGGN, with a minimum of 5 years follow-up. A change in GGN size more than 2 mm and increased density will require evaluation [9]. Even with a negative biopsy, patients cannot be reassured, and a positive lung biopsy does not eliminate the need for lymph node staging. Individual counseling regarding risks and benefits is the key, and multidisciplinary team discussion can guide diagnostic and therapeutic decisions.

Secondly, François Montagne spoke about the role of artificial intelligence methods for the pulmonary nodule classification. Deep neural networks are designed for lung cancer classification [10] as well as different deep learning models for detecting or classifying pulmonary nodules are suggested. Currently, these models are only supportive in the clinical decision-making process. These techniques hold promise for the future.

Thirdly, Jean-Marc Baste spoke about the problems and solutions in contemporary thoracic surgery for GGO. He focused on three basic goals in his presentation: minimally invasive sub-lobar resections, pre-op and peri-op visible dye marking and surgical planning using multi-images strategies. Decision making on minimally invasive surgical resection type is essential. While wedge resection is adequate for clinical stage I GGO with solid component <50%, segmentectomy with lymphadenectomy is suggested for clinical stage I GGO with solid component > 50%. If lymph nodes are suspected, peri-operative frozen sections can be performed during surgery to proceed to lobectomy if positive.

Current techniques to assist in minimally invasive surgery are pre-operative planning using 3D reconstruction, real-time per-operative CT scans on hybrid operation theatres or peri-operative aid by bronchoscopy, as is electromagnetic navigation bronchoscopy guided dye marking for resection of pulmonary nodules. An important technical consideration was described using Endo GIA Black Reload for the larger wedge and extended segmentectomy to increase the surgical margin.

A controversial issue is whether or not to perform lymphadenectomy for GGOs. The current state of the evidence is that for pure GGOs there is no need for lymphadenectomy. For semi-solid GGOs lymphadenectomy is a must. The utility of sentinel node identification and of peri-operative frozen section is still to be elucidated.

Regarding preoperative and peri-operative marking techniques for GGOs, the pleural dye marking using radial endobronchial ultrasound and virtual bronchoscopy was emphasized the most. A well-managed case was presented of wide wedge resection after pleural dye marking using radial endobronchial ultrasound. By presenting another case that underwent posterior (S2) segmentectomy, he emphasized that marking techniques are also useful in clarifying segmental plans. He concluded his presentation by emphasizing the efficacy of multi-image assistance and stating that these procedures will become routine in the future.

In the final presentation of this session, Isabelle Opitz spoke about non-surgical alternatives for the treatment of GGOs. She focused on stereotactic body radiation therapy (SBRT) and ablation methods, which include radiofrequency ablation (RFA), microwave ablation (MWA), and cryoablation (CRA).

Lung RFA of GGOs was shown to be a feasible, safe, and useful therapeutic option to control GGO-dominant lung adenocarcinoma, with overall and cancer-specific survival rates 100% and 100% at 1 year, 96.4% and 100% at 3 years, and 96.4% and 100% at 5 years respectively [11]. SBRT in patients with lung tumors composed of mainly GGO yielded cause-specific and overall survival at 3 years of 98.2 and 94.6%, respectively [12]. Despite these promising results, limitations of these non-surgical techniques are lack of long-term survival information, inability for pathological confirmation (for SBRT) and lymph node dissection, and difficulties in the follow-up.

In conclusion, while developing technology requires us to make new definitions like GGO, pGGN, and psGGN, it helps us to improve our diagnosis and treatment methods. This session has made an important contribution to the congress by sharing the most up-to-date information and experiences in approaching GGOs.

Highlights:

1. Novel techniques (such as 3D reconstruction and pleural dye techniques) have made minimally invasive sub-lobar resection for GGOs safe and feasible.
2. There are several non-surgical alternatives for the treatment of GGOs including SBRT, RFA, MWA and CRA with good outcomes but also important disadvantages.

Group 8.2: Lung transplantation

Session: *Extracorporeal life support (ECLS) in lung failure and lung transplant bridging: when and how?*

Arne Neyrick gave an overview of the technical aspects regarding ECLS and its use in severe acute respiratory failure, ARDS, and its use for bridging to lung transplantation. The use of ECLS, also named extra-corporeal membrane oxygenation (ECMO), dramatically increased in the last decade [13]. When ECMO was initially developed, it was mainly applied as a rescue

strategy. It is now increasingly used in combination with other treatment strategies, such as ultraprotective ventilation or even as a scenario in which mechanical ventilation can be avoided or weaned completely. The main aim of ECMO is to improve oxygen delivery. In case of respiratory failure usually veno-venous (VV) setup is used for this purpose. In this setup there is venous withdrawal of blood, followed by gas-exchange and then venous return [14]. The oxygenation capacity of this setup depends on blood flow through the system and the sweep gas FIO₂. Also, CO₂ can be removed by this setup if applicable, and the capacity for CO₂ removal depends on the gasflow. The purpose of ECMO is to optimize gas exchange (i.e. to minimize hypoxemia and hypercapnia). Doing this has major advantages, such as decreasing tissue hypoxemia and reduction of right ventricular afterload. It will also help to minimize lung stress and strain. These features are thought to eventually result in reduced organ failure and mortality.

Veno-arterial (VA) ECMO differs from VV ECMO in the sense that the return of oxygenated blood is into the arterial circulation instead of the venous circulation. This leads to several differences, such as that the oxygenation is more homogenous in VV ECMO, the risk of bleeding and leg ischemia is higher in VA ECMO, but the major advantage of unloading of the heart is only seen in VA ECMO. The fact that VA ECMO unloads the heart by returning the oxygenated blood into the arterial system is the main reason to use in the setting requiring hemodynamic support, apart from support of gas exchange.

ECMO can be cannulated centrally, in the chest, or peripherally. Both options have their advantages and disadvantages. Central ECMO had as most important downside that the chest has to be opened and left open. Main advantage is the bigger caliber of the vessels and decreased mixing of oxygenated and de-oxygenated blood caused by counterflow, though delivery of blood in the aortic arch instead of through the groin – which is less in line with the usual physiological situation – potentially compromises oxygen delivery in the aortic arch and centrally. The size of the cannulas that are indicated, also depend on the indication for which ECMO is applied. For patients in circulatory failure high flow is required and larger cannulas are indicated compared to patients with ‘only’ hypercapnic respiratory failure.

Complications of ECMO are frequent; circuit problems (25%), bleeding (24%), acute kidney injury (21%), infections (11%) being most frequent, and neurological (5%) being most severe [14]. Meanwhile, further respiratory complications can be prevented, by facilitating lung protective ventilation. In ARDS, driving pressure was shown to be the most important determinant of mortality [15].

Evidence for use of ECMO for severe ARDS is still scarce and largely obtained from retrospective series. In the CESAR trial patients with acute respiratory failure were referred to a specialized center and were randomized to either the conventional arm with standard treatment protocol or the intervention arm consisting of standard protocol including consideration for ECMO. Of the patients assigned to the intervention arm 75% of the patients received ECMO. In the intervention group, lung protective ventilation could more often be applied and patients more often received corticosteroids. Overall, this resulted in improved survival in the group where ECMO was considered [16].

In a large multicenter RCT patients with severe ARDS on mechanical ventilation were randomized to either the control arm with EXPRESS ventilation (high PEEP, high recruitment)

or ECMO with highly protective ventilation. Importantly, there was a possibility for cross-over to ECMO for patients failing on therapy in the control group. The primary outcome of 60 day mortality was 35% in the ECMO group compared to 46% in the control group. Although this result seems to indicate a clear benefit for ECMO, the difference was non-significant. Importantly though, rescue cross-over to ECMO occurred in 28% of patients in the control group, of whom 43% survived [17]. It was hypothesized that ECMO nonetheless has a survival benefit. In recent recommendations ECMO is incorporated for patients with ARDS with a PaO₂:FIO₂ ratio <150mmHg, after other treatment options have first been considered [18] or patients with PaO₂:FIO₂ ratio <80mmHg [19]. Currently, the The Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score is the best prediction score for survival with ECMO in ARDS [20].

A relatively new application for ECMO is bridging patients with respiratory failure to lung transplantation. Like the application of ECMO for ARDS, the practice of bridging patients to lung transplantation is increasing. Treatment decisions regarding ECMO are based on the underlying condition for which bridging will be used. Patients may suffer from pulmonary hypertension and right heart failure, necessitating choice for VA ECMO over VV ECMO. It is more likely that patients with pulmonary hypertension either group 1 or group 3 listed for lung transplantation will be bridged using VA ECMO [21]. An important aspect in bridging patients to lung transplantation – differing from application of ECMO for other forms of acute respiratory failure – is the aim to ambulate patients while on ECMO. The successful ambulation of patients is even regarded as a criterium before proceeding to transplantation by some [21]. Outcomes of patients bridged with ECMO versus those not bridged are increasingly similar [22] with improving technology and increasing experience. Early complications such as primary graft failure, bleeding and acute renal failure are more common in patients bridged with ECMO [23]. Likely, center volume is contributing to the success of bridging as experience is of key importance.

Just as important is good recipient selection, which is more strict than for non-bridged patients. Important contra-indications for bridging are irreversible extrapulmonary organ failure and heparin induced thrombocytopenia. Prolonged mechanical ventilation, increasing age and obesity are among important relative contra-indications. Pre-existing condition and the potential for ambulation play an important role whether to bridge to transplantation. Candidate selection and timing are of key importance for outcome, together with center experience and volume. Nonetheless, not all patients can be successfully bridged to lung transplantation, also difficult decisions regarding delisting and end-of life are important.

Highlights

1. ECMO can be considered in ARDS after optimal conservative management.
2. ECMO is increasingly used as a bridge to transplantation in carefully selected patients.

This session focused on the impact of new drugs on the indications and outcomes of lung transplantation regarding cystic fibrosis (CF), interstitial lung diseases (ILD) and pulmonary hypertension (PH).

First, Christian Benden pointed out that lung transplantation is still the standard of care in advanced CF ranging as third most frequent indication for LTx in adults and as most important indication in children [24]. According to the registry of the International Society for Heart and Lung Transplantation (ISHLT) median survival after LTx for CF is 9.9 years and CF is the subgroup with on average the best outcomes after LTx. Interestingly the best survival was seen in the 40+ group (median survival was 10 years) and the worst one in 0-17 age group (median survival was 5.6 years) [25]. High mortality rate in paediatric group was attributed to the poor adherence to the treatment, especially in teenagers [25].

As the underlying pathology of CF is related to the various mutations that reduce CF transmembrane conductance regulator (CFTR) proteins function, modulators that either potentiate or correct the defect have been developed [26]. Combinations of drugs from the two groups are used, and lately a triple combination of elexacaftor/tezacaftor/ivacaftor is used in patients with PheF508del homozygous and other heterozygous mutations. The majority of CF patients was shown to be eligible for CFTR modulators which could restore a significant portion of the CFTR function [27]. Randomized controlled trials and open-label studies showed that CF patients with advanced disease could also benefit from modulator therapy [27]. Thus a larger proportion of CF patients will be treated with these therapies and the age of CF patients at transplant referral will be higher in the next year as well as the drug related toxicity issues. Lung transplantation is the ultimate therapy option for progressive lung disease if there is no other available therapy, suggesting that patients should undergo a treatment trial if new drugs become available and lastly any CF patient should be evaluated for transplantation if eligible [28].

Second, Sara Tomassetti emphasized that the new antifibrotic drugs have changed dramatically the clinical practice and enabled the shift from immunosuppressives to antifibrotics [29-30]. It was shown that the new drugs not only slow down the progression of the disease, but also improve survival and reduce acute exacerbations and hospitalizations of the patients. More recently, it has also become clear that antifibrotics are effective even in other progressive fibrosing interstitial lung diseases PF-ILD [31-32].

Whereas antifibrotics for IPF are now established, several areas of uncertainty however remain for antifibrotics for PF-ILD. Long-term outcome data on survival and hospitalization are still lacking for antifibrotics in PF-ILD. Also, many questions remain regarding the positioning of antifibrotics versus immunosuppressive treatment with respect to effect, timing and need for combination of therapy. Lastly, biomarkers for identification of treatment responders are currently still lacking.

The benefit for lung transplantation in idiopathic pulmonary fibrosis (IPF) in terms of survival was demonstrated on older studies with patients with severe disease [33]. These studies showed a significant survival benefit with LTx. Whether this remains valid in the current era of antifibrotic usage needs further investigation.

Regarding IPF there are several challenges for transplantation like the presence of many comorbidities, in general advanced age and potential underlying telomerase mutations that are

associated with increased complications after LTx [34]. Also the optimal timing for LTx referral, screening and listing is not always easy to be determined. New scoring systems, novel biomarkers and deep learning with artificial intelligence in the future can be used to stratify the ILD patients according to prognosis and identify the subgroup that can benefit the most from LTx.

Nowadays two approaches are used, either referral of all suitable patients at time of diagnosis particularly individuals at age limit (>60) or identification of the patients that can progress rapidly (10% decline in FVC or 15% in DLCO over 6 months period, low diffusion capacity, desaturation in 6-MWT, pulmonary hypertension, hospitalizations for respiratory deterioration) and early referral for transplantation [34].

In scleroderma, even though 1 and 5 year post-transplant survival is similar to IPF, only a limited number of patients is referred for LTx and transplanted. LTx in these patients is yet more complicated due to extrapulmonary involvement (such as esophageal dysfunction and cardiac involvement) and the potential of relapse of the disease after LTx [35]. In the light of the current evidence it can be concluded that antifibrotics are safe drugs that should be used to attenuate the disease until transplantation and do not result in more surgical complications thus functioning as a bridge to and not a replacement of the lung transplantation [36,37]. Novel therapies are still warranted to stabilize the disease and to overcome the need for LTx.

In the third presentation of this session, Marion Delcroix discussed the place of LTx in the treatment of pulmonary arterial hypertension (PAH), tools for timely referral and the outcomes of LTx in PH. She showed that patients of PAH had 3 year survival of 73%, with annual mortality of 10% in idiopathic pulmonary arterial hypertension (IPAH) patients [38,39]. Based on the ISHLT Registry data, the 3 year survival post LTx in IPAH group is 64 % [40]. It is therefore crucial to determine adequate timing for LTx in these patients.

As per ESC/ERS 2015 guidelines, LTx should be considered if there is inadequate clinical response despite double or triple sequential combination therapies [41]. As per 6th WSPH proceedings, in non-vasoreactive and treatment-naive patients at high risk, initial combination therapy including i.v. prostacyclins (PCA) is recommended and referral for LTx should also be considered [42]. The importance of risk stratification into low, intermediate and high risk was emphasized, in order to identify which subset of patients may benefit most from LTx while minimizing overall risk and resource utilization [39, 43,44].

The utility of using REVEAL 2.0 scoring in risk stratification provides better characterisation of actual risk of mortality at 12 months than COMPERA or the French registry [45]. REVEAL 2.0 includes nonmodifiable risk factors, more variables and weighting of these variables. The frequently used Lung Allocation Score (LAS) doesn't always adequately reflect disease severity in PAH as shown by discrepancy in observed and predicted mortality by LAS. In the REVEAL Registry, observed 1-year mortality exceeded that predicted by LAS in two subgroups of patients: those with mRAP more than or equal to 14 mm Hg and those with 6-MWT less than or equal to 300 m [46], factors that are not incorporated in the LAS. A modified LAS model that includes both 6MWT and mean right atrial pressure better discriminates waitlist urgency for patients with PAH than the current LAS.

The study by Brouckaert *et al.* [47], a 24 year single centre retrospective study demonstrates that bilateral LTx remains preferred procedure for all forms of precapillary PH, except in

patients with complex congenital heart disease where heart-lung transplantation is preferred. Overall graft and CLAD-free survival were comparable and improved over time. Giant Pulmonary Artery Aneurysm (PAA) is a late complication of idiopathic pulmonary arterial hypertension (IPAH). Bilateral LTx with aneurysmal repair is possible in such cases with replacing recipient PAA with donor pulmonary artery (PA) or aorta [48-50]. Heart-Lung Transplantation (HLTx) remains an option for IPAH complicated by giant sized PAA and right heart failure.

The role of ECLS as a bridge to LTx in the form of peripheral VA ECMO and NOVALUNG (a pumpless membrane oxygenator inserted between PA-LA) was highlighted, emphasising that centres performing LTx in PAH should have an established ECLS program. In the review by Hoeper *et al* [51], it was shown that 77 out of 81 patients received ECMO as a bridge to transplant. 72 out of 77 patients (94%) were successfully bridged to transplant with 78% of them getting discharged. Intraoperative ECMO vs. cardiopulmonary bypass (CPB) was highlighted with reference to study by Dell'Amore *et al* [52], stating that intraoperative ECMO has almost completely replaced CPB as it is associated with reduced peri-operative complications including renal failure, reduced need of transfusions of blood products and better survival. In patients with PH and RHF, VA ECMO is occasionally established prior to GA to avoid hemodynamic instability. Indications for CPB remain: extreme cardiomegaly which makes the access to the left pulmonary hilum without complete heart emptying impossible, severe dilatation of the main branches of the pulmonary arteries and supra-systemic pulmonary artery pressure with reduced cardiac index.

Bilateral LTx for IPAH with intraoperative VA ECMO support seems to provide superior outcome compared with the results reported about the use of CPB. Prophylactic prolongation of VA ECMO into the early postoperative period provides stable postoperative conditions and better survival outcomes [53]. The main cause of primary graft dysfunction (PGD) in this patient group is usually not residual PH but incapability of the left ventricle to cope with the preload after LTx. It was demonstrated in this study that an important problem causing early PGD after BLTx in patients with end-stage PAH is, rather than elevated pulmonary pressures with increased shear stress or RV failure, LV dysfunction with predominantly diastolic failure, and elevated filling pressures. The above study stated that early after bilateral LTx (BLTx) for severe PH, the LV may be unable to handle normalized LV preload. This can be effectively bridged with awake VA ECMO [54]. Also at 72 hr, the PGD scores in the BLTx-ECMO and HLTx groups were significantly lower than those in the BLTx-ventilation group.

In the final presentation, the aim by Jens Gottlieb was to describe the effects of the new therapeutic strategies in patients with PH, ILD and CF on needs and indications for LTx and to evaluate outcomes of LTx for the three indications. Based on the ISHLT Registry data ILD is increasing as the primary indication for LTx, whilst CF has remained the same in last few years [40]. The ILD subgroup patients comprise a relatively elderly cohort with multiple comorbidities while the CF cohort comprises a relatively younger population. The Collaborative Transplant Study (CTS) Registry data for LTx shows that survival improved post LTx from 42.6% 5 year survival (before 2000) to 56.5 % 5 year survival (after 2000). The ISHLT Registry shows that conditional 1 year survival was best in CF subgroup (85%), followed by IPF (80%) and worst in PAH (74%) [40]. However, comparing the conditional 5 year survival data, the PAH subgroup had the best long-term survival (75%) along with CF (75%), while IPF had worst survival (64%). Above the age of 65 years the 5 year survival was only 38%.

Association of transplant centre volume and post LTx mortality was discussed [55]. Lower transplant volume centre is independently associated with higher 5 year mortality. Many retrospective studies were analysed with specific mention of studies by Vock *et al* [56] and Thabut *et al* [57], concluding that there is survival benefit post LTx, with the greatest potential benefit in patients with higher lung allocation scores or restrictive native lung disease or CF. Thabut *et al* showed a median survival of 8.9 years for CF patients, 6.7 years for chronic obstructive pulmonary disease (COPD) with alpha-1 antitrypsin deficiency (AATD), 5.6 years for COPD without AATD, 4.8 years for idiopathic interstitial pneumonia and 2.8 years for re-transplantation.

In the first year post LTx, the common causes of death were infections and graft failure while after the first year, the important causes of death are CLAD (Chronic Lung Allograft Dysfunction) followed by infections, malignancy etc. Recipient age was more important than the donor age [40]. Within 5 years post LTx, hypertension (81.7%) was the most common morbidity followed by renal dysfunction (53.9%), CLAD (41.6%) and diabetes mellitus (35.9%) [58].

The new definition of CLAD was recently published by Verleden *et al* [59], and defined as a substantial and persistent decline ($\geq 20\%$) in measured FEV1 value from the reference (baseline) value. Two important phenotypes of CLAD exist: obstructive and restrictive CLAD. The obstructive (BOS) phenotype has a better survival than restrictive (RAS) phenotype. BOS had 5 year survival of 46% while RAS phenotype had 0% 5 year survival.

In a study by Singer JP *et al* [60] it was shown that LTx improved Health Related Quality of Life (HRQL) by all five measures ($p < 0.05$) and all but SF12-Mental Health improved by three-fold or greater than the minimally clinically important difference. Visual Analogue Scale (VAS) quality of life (QoL) showed an improvement from 40 pre-transplant to 80 in post-transplant. Older subjects (≥ 65 years) had substantially smaller improvement in QoL. Smallest benefit was seen in PAH subgroup. Patients age 65 or older derived substantially less HRQL benefit than younger patients with 11% in study not improving in QoL. A second study by Singer LG *et al* [61] showed that age was not associated with meaningful differences in the HRQL benefits of transplantation. There was less HRQL benefit in ILD than in CF. Regarding return to work post LTx, according the ISHLT Registry 14% of patients returned to work at 1 year with only 18% at 5 years [40]. In another study by Suhling H *et al*, 38% of the patients were employed after LTx. Employment was associated with a better quality of life and median time from transplantation to the return to work was 11 months [62]. In a Swiss study of LTx in CF recipients by Radtke *et al*, the number of subjects employed at 3-5 years post LTx was 75% [63].

Highlights

1. The majority of CF patients is eligible for CFTR modulator therapy and a treatment trial is indicated prior to lung transplantation.
2. Novel antifibrotics are effective to slow down progression in IPF and PF-ILD and can be safely used until the time of transplantation.
3. There is a crucial role of ECMO before, during and after LTx for PAH.
4. LTx is associated with significant increase in QoL, but less so in elderly recipients.

COCLUSIONS

Due to the SARS-CoV-2 pandemic this congress was the first “virtual” congress of the European Respiratory Society and it was a great success, with very diverse and important sessions on innovation and state of the art in thoracic surgery and lung transplantation. In this article we summarized the highlights of the most important sessions of this congress representing a wide range of topics. We look forward to next year’s conference, to be held in Barcelona, Spain, from 4-8 September 2021.

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