ISHLT2022 Roving Reporters – Reports from Advanced Lung Failure and Transplantation (ALFTX)

- **Wednesday, 27 April, 2022**
  - SYMPOSIUM SESSION 10: Equity and Equality in Cardiothoracic Transplantation: Access to Care
  - SYMPOSIUM SESSION 13: Outside-of-the-Box Immunosuppression for Lung Transplantation
  - SYMPOSIUM SESSION 17: Lung Transplant Biomarkers Now
  - ORAL SESSION 03: Through the Looking Glass: Advanced Lung Assessment During EVLP
  - ORAL SESSION 20: Coming to a Bedside Near You: Translational Studies in Lung Organ Perfusion
  - MINI ORAL 02: COVID-19 Disease and Vaccination Issues Relevant to Lung Transplantation
- **Thursday, 28 April, 2022**
  - Featured Abstract 3 at Plenary 2: Evaluation of 10°C as the Optimal Storage Temperature for Injured Donor Lungs in a Large Animal Transplant Model
  - SUNRISE 02: The Path Forward in Developing Novel Therapies in Lung Transplantation
  - SUNRISE 04: Challenges in Pediatric Lung Transplant: What Learning Can We Impart to Our Adult Colleagues?
  - SYMPOSIUM SESSION 38: Vaccination in Cardiothoracic Transplant Candidates and Recipients: The Time is Now?
  - SYMPOSIUM SESSION 40: Take a Chance on Me: Updates in Lung Transplant Candidate Selection
  - ORAL SESSION 26: Rejection Revelations: Novel Insights into Lung Transplant Rejection
  - ORAL SESSION 29: Survival of the Fittest: BMI and the Frailty Construct as Risk Factors for Lung Transplantation
- **Friday, 29 April, 2022**

- SYMPOISUM SESSION 48: Cut to the Chase: Lung Transplantation from the Operating Room to the ICU
- SYMPOISUM SESSION 55: Improving Quality of Lung Transplant Care: Survival is Only the Beginning
- SYMPOISUM SESSION 62: Save the Beans: Recognition and Protection of Renal Function in Lung Transplantation
- SYMPOISUM SESSION 66: Navigating the COVID Pandemic: Clambering into the Lung Transplant Life Raft
- ORAL SESSION 45: Molecular Assessment of Lung Allograft Injury
- ORAL SESSION 59: Age, Size, Location: Studies in Survival after Lung Transplant

- **Saturday, 30 April, 2022**
  - SYMPOSIUM SESSION 78: Human Versus Beast: Advances in Translational Models of Lung Transplant
  - ORAL SESSION 72: COVID Consequences: Can We Protect the Lung?
  - ORAL SESSION 75: A Cure for CLAD? Update on CLAD Therapeutics

Thank you to all of our ISHLT2022 Roving Reporters.

ADVANCED HEART FAILURE AND TRANSPLANTATION (AHFTX)

Anju Bhardwaj, MD, University of Texas / McGovern Medical School / Memorial Hermann Hospital, Houston, TX, USA
Rachna Kataria, MD, Massachusetts General Hospital, Boston, MA, USA
Brian Wayda, MD, Stanford University School of Medicine, Stanford, CA, USA

ADVANCED LUNG FAILURE AND TRANSPLANTATION (ALFTX)

Prangthip Charoenpong, MD, MPH, LSU Health Science Center Shreveport, Shreveport, LA, USA
Grant Turner, MD, MHA, UCLA, Los Angeles, CA, USA

MECHANICAL CIRCULATORY SUPPORT (MCS)

David Bearl, MD, MA, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN, USA
Varinder Randhawa, MD, PhD, Cleveland Clinic / University of Toronto, Toronto, ON, Canada

PULMONARY VASCULAR DISEASE (PVD)

Nicholas Kolaitis, MD, MAS, UCSF, San Francisco, CA, USA

SESSION 10: Equity and Equality in Cardiothoracic Transplantation: Access to Care

One of the challenges in lung transplant comes before any surgical procedure—accomplishing the high financial barrier required to even make it to the first consult appointment with a transplant center can be daunting. In this **symposium**, the speakers discussed the difficulty of getting access to care pre- and post-transplant, and how both can widen disparities already present in transplant.

First, we heard the perspective from the Toronto program in Canada. Being the largest program in Canada, they often get referrals from across the country for patients who may not have the means to make it to an appointment. **Aman Sidhu, MD** presented their experience leveraging virtual visits to complete most of the transplant workup remotely before moving to within 4 hours for transplant listing; their center has previously published on the cost-savings measures of using virtual visits without sacrificing outcomes. They were also able to create a virtual application (as described in Marks et al. 2022 *JHLT*, https://doi.org/10.1016/j.healun.2021.01.447) which allows for asynchronous communication and biometric monitoring.

Next, we discussed gender disparities in cardiothoracic transplant presented by **Miriam Aguilar Pérez, MD**. There is a clear difference in completed heart transplants, with almost 75% of recipients being men. Changes to the allocation systems have not improved this percentage or improved women's waitlist mortality, while waitlist mortality for men has decreased. In lung transplant, men comprise 58% of recipients. Considerations for the difference in genders include allosensitization related to pregnancies and transfusions and body size, with women having overall shorter stature and a known correlation between death or removal from the waiting list based on height. A helpful review on the topic is available from Melk et al. (DOI: 10.1097/TP.0000000000002655).

“No cash, no heart” was the opening of the informative discussion, led by **Khadijah Breathe, MD, MS** on insurance-related barriers to pre- and post-transplant care in the United States. While insurance coverage of cardiothoracic transplant, especially Medicare and Medicaid, has improved since their inception, there are still significant barriers. The most important current obstacle is for states in the US that did not expand Medicaid; Medicaid expansion was correlated with a 30% increase in heart transplant listings for Black patients (Breathett et al. *JACC: Heart Failure* 2017). Private insurance was also associated with higher survival to transplant in LVAD patients (Emani et al. https://doi.org/10.1111/ctr.12875). The key to fixing this involves multiple efforts at the state and national levels to affect policy changes. The physician voice can help to affect change in these key outcomes for our socially and historically disadvantaged patients.

Access to pediatric transplant is a complex issue as well, as **Brigitte Willemse, MD, PhD** presented, with limited centers with adequate experience, limited donors and difficulty with donor sizing discrepancies, and allocation system differences between adult and pediatrics.

Finally, **Jesse Schold, PhD** presented data regarding the unintended negative consequences of

public data regarding transplant and subsequent access to care. Healthcare report cards are becoming more common within the public and private sectors. Still, the evidence on the utility of these is mixed regarding access to care, improving healthcare literacy, finances, and overall performance. These report cards may cause patients not to seek care or seek alternative care, which can cause perceived decreased access to care. Additionally, most programs are unhappy with the current metrics. They note they can result in risk-averse decisions and would like survival benefits and five-year survival data to be included.

Overall, this session was a reminder that while we continue to increase the number of individuals who receive transplants yearly, we must be conscious about ensuring all individuals have the opportunity to receive the life-saving gift of transplant. Continued research into aspects of this will be crucial to meeting our goal of saving as many patients as possible.

– Summary by Grant Turner, MD, MHA

Let's Look at Geography: Challenges in Delivering Cardiothoracic Transplant Care in Rural and Remote Settings
Aman Sidhu, MD, University Health Network, Toronto General Hospital, Toronto, ON Canada

Gender Differences: Do Women Get a Fair Shot in Cardiothoracic Transplant? Are the Rules Stacked Against Them?
Miriam Aguilar Pérez, MD, University Puerta de Hierro Majadahonda Hospital, Madrid, Spain

Effect of Health Insurance Status on Pre- and Post-Cardiothoracic Transplant Access to Care and Outcomes
Khadijah Breathett, MD, MS, University of Arizona, Tucson, AZ USA

The Unique Aspects of Pediatric Cardiothoracic Transplant Limiting Access to Care
Brigitte W. Willemse, MD, PhD, University Medical Center Groningen, Groningen, Netherlands

Show Me Your Dirty Laundry: the Unintended Negative Consequences of Public Performance Reporting and Impact on Access to Cardiothoracic Transplantation
Jesse Schold, PhD, Cleveland Clinic, Cleveland, OH USA

VIEW SESSION DETAILS

SESSION 13: Outside-of-the-Box Immunosuppression for Lung Transplantation

Immunosuppression is a key to preventing rejection, and too much of it can increase the risk of infection. This **symposium** provided new information on novel strategies to monitor immunosuppression and new evidence on potential agents that might be able to be used in lung transplant patients.

Targeting Personalized Immunosuppression via Novel Monitoring Strategies

Peter Jaksch, MD, Medical University of Vienna, Vienna, Austria

Dr. Jaksch started out this session with novel monitoring strategies for immunosuppression. He focused on three things that can be used to monitor immunosuppression:

1. QuantiFERON Monitor (QFM) - measuring interferon -y (IFNy) production in blood after incubation with innate and adaptive immune stimulants. In lung transplant patients, the quantiferon level usually declined during post-transplant period. The level is significantly impacted by steroids. Low levels after 3 months post-transplant are associated with infection. QFM could tell us how immunosuppressed patients are and may be used to guide us adjust doses of immunosuppressive agents.
2. ImmuKnow - measuring the amount of ATP synthesis in stimulated CD4 cells which reflects the T cell function. Solid organ transplant patients with infection have very low ATP values compared to values when they were stable and high levels (>700 ng/ml) were 30 times more likely to develop acute cellular rejection.
3. Torque Teno Virus (TTV) is a small non-enveloped, circular ssDNA virus, classified into genus Anellovirus that most of us had infection early in life and had lifelong persistence (high prevalence in humans > 90%). We do not know if this virus is pathological or not. However the level of TTV DNA in the blood is shown to increase with immunosuppression, thus a high level of TTV DNA correlates with infection and a low level is associated with a high risk of CLAD.

These 3 biomarkers could potentially be used to predict the level of immunosuppression and predict clinical complications in lung transplant patients. However, a prospective trial is needed to validate their efficacy.

Belatacept Use Following Lung Transplantation

Cody A. Moore, PharmD, University of Pittsburgh Medical Center, Pittsburgh, PA USA

Belatacept is a selective T-cell costimulator blocker by binding CD80 and CD86 on APC, thus blocking CD28 mediated costimulation of T lymphocytes. It has been used in kidney transplant patients to avoid Calcineurin Inhibitor (CNI) toxicities such as neurotoxicity, cardiovascular outcomes, glycemic control, and acute kidney injury though it comes with risks of ACR, infections, PTLD, and cost/coverage. Dr. Moore showed us data on lung transplants and concluded that routine de novo use in lung transplants is not recommended at this time as data from a study showed a higher incidence of death in the belatacept group, thus requiring the trial to stop early. Using belatacept combined with low-dose CNI for recovery requires more experience. Finally, there are several questions that are needed to be answered before routine use in lung transplant

patients such as optimal dosing regimen, ACR risk and infection susceptibility, and its impact on DSAs.

Non-Induction Basiliximab for a Calcineurin Inhibitor (CNI) Holiday

Georgina Waldman, PharmD, Massachusetts General Hospital, Boston, MA USA

Basiliximab is an IL-2 inhibitor, by blocking IL-2 receptor on the surface of activated T lymphocytes, thus preventing the proliferation of activated CD4 and CD8 T cells, inhibiting differentiation of regulatory T cells, and may prevent enhanced cytotoxicity of NK cells and limiting B cell proliferation. Dr. Waldman reviewed data from a case-matched cohort of CNI holiday for various reasons in lung transplant, compared between basiliximab group (received 2 doses, 2 weeks apart) and matched control. Although all patients recover from neurotoxicity from CNI, the basiliximab group had a higher incidence of rejection and 96% of this group were also treated with infection. Further information in terms of the regimen, dosing, and outcomes are still needed before routine use in Lung transplant patients.

Extracorporeal Photopheresis and Total Lymphoid Irradiation

Anna Reed, MBChB, MRCP, PhD, Royal Brompton & Harefield, Harefield, UK

Total lymphoid irradiation (TLI) has been shown to slow the rate of decline but is not associated with improvement in lung function. It also increases the risk of infection. It may benefit lung transplant patients with rapid progressive CLAD and recurrent ACR. Extracorporeal photopheresis (ECP) has been used in CLAD, catastrophic AMR, and may have a role in patients not able to tolerate standard immunosuppression such as in patients with recurrent infection, kidney failure, and malignancy. Given data in this field is scarce and from case series, we need more RCTs and need to standardize definitions of response and failure to treatment. Dr. Reed also pointed out that maybe it's time to have a consensus statement/guideline on ECP and LTI.

Is it Time to Reconsider Inhaled Immunosuppression?

Irina L. Timofte, MD, University of Maryland, Baltimore, MD USA

During the past few years, there have been studies on inhaled cyclosporine in lung transplant patients. Dr. Timofte reviewed a recent paper from Neurohr, et al. on inhaled cyclosporine that showed that it may prevent BOS when given prophylactically. However, this paper has limitation as it was terminated early, thus enrolling less than half (n=74) of the initially planned (180) and the median follow was also reduced to only 58 weeks. Currently, there are 2 ongoing trials on inhaled cyclosporine as a treatment of CLAD/BOS - BOSTON 1 (single lung transplant) and BOSTON 2 (double lung transplant). She concluded that adding inhaled cyclosporine to the standard regimen may minimize systemic exposure and side effects of CNI.

Future Frontiers in Lung Transplant Immunosuppression

Patricia Ging, PharmD, Mater Misericordiae University Hospital, Dublin, Ireland

Lastly, Dr. Ging reviewed data on potential agents that might be able to use for immunosuppression in lung transplantation including JAK inhibitor (Tofacitinib), IL-6 inhibitors (Tocilizumab, Clazakizumab, Olamkicept), and lastly, Imlifidase desensitization which was tried on highly sensitized kidney transplant candidates and was shown to eliminate HLA antibodies within 6 hours of infusion and eliminate all compliment activating antibodies within 1 hour which could

be a promising treatment for sensitized lung transplant candidate.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SESSION 17: Lung Transplant Biomarkers Now

One of the most complicated issues after a lung transplant is accurately predicting and diagnosing acute and chronic rejection. Transbronchial biopsy, the gold standard in diagnosing acute rejection, can have significant issues with inter-observer reliability and carries potential morbidity. Chronic lung allograft dysfunction (CLAD), the major limitation to long-term survival in lung transplant, is difficult to predict and diagnose outside of spirometric parameters. In this **symposium**, the presenters evaluated different biomarkers for acute and chronic rejection and how they may affect the future of lung transplant.

First, **John McDyer, MD** presented the donor-specific T Cell responses and their impact on CLAD. We know that ACR is a significant risk factor for CLAD, but does the treatment of acute cellular rejection (ACR) cause an effect on the alloreactive T Cell clones created in response? In their work evaluating CD8+ alloreactive T Cells during and after an episode of ACR, they found persistence of the cells and accumulation around airways, which was discordant with circulating T cell populations (Snyder et al. *JEM* 2022 https://doi.org/10.1084/jem.20212059). The airway transcriptome was also discussed, with small airways and the use of distal airway brushings as a potential marker for future CLAD being investigated (Iasella 2020 *AJT* https://doi.org/10.1111/ajt.16360).

Small airway rejection was also a topic presented by **John Greenland, MD, PhD**, who discussed its use to identify CLAD and infection. By using a 'meta-gene' of information obtained by large-airway brushes, researchers have found specific gene transcription in small-airway brushes correlated with CLAD. Brushings of the small airways collect epithelial cells and immune cells in equal proportions and can also be used to identify the microbiome of a patient and, through the use of diversity, can predict or help diagnose infections.

Micro RNA (MiRNA) is another potential biomarker for acute and chronic rejection. **Alessandro Palleschi, MD** presented on their use; MiRNAs are small, stable molecules in body fluids with dynamic expression and could have potential diagnostic and prognostic functions in lung transplant for ACR and CLAD.

Donor-derived cell-free DNA (ddcfDNA) has been one of the most promising new biomarkers in lung transplantation, as demonstrated in many publications (Agbor-Enoh *JHLT* 2018, Agbor-Enoh *EBioMedicine* 2019, Jang *JHLT* 2021). Briefly, cell-free DNA is purified from a recipient's plasma at various time points. Using DNA analysis, we can determine the percentage of the cfDNA derived from the donor and the recipient, expressed as a percentage. Based on several studies, the cutoff of 1% is most helpful in predicting acute rejection (NPV 90%, PPV 64%). The main limitation of ddcfDNA for predicting acute rejection is that it is also elevated in infection, especially if the infection is associated with graft dysfunction. Multiple ongoing studies with commercial assistance are currently underway to determine the use of ddcfDNA to replace surveillance bronchoscopies and to limit chronic immunosuppression, for example.

Taking data from other transplant rejection knowledge, **Kieran Halloran, MD** presented a model to determine if known transcript sets could predict and diagnose CLAD (described in Halloran 2019 *JHLT*, https://doi.org/10.1016/j.healun.2019.01.1317).

Finally, **Vibha Lama, MD, MS** presented data regarding radiologic markers to determine CLAD at an earlier stage. Using parametric response mapping for quantifying small airway disease, we may be able to diagnose obstructive CLAD before spirometric changes more accurately. Further research is being completed to determine if we can apply predictive radiologic measures from other disease entities.

In summary, research continues to find ways to help providers prognosticate, diagnose, and treat acute and chronic rejection to improve survival after lung transplant. While many presented during this session are still in experimental or early phases of research, ddcfDNA is correlated with rejection and is in more advanced trials to determine its clinical use alongside current procedures.

– Summary by Grant Turner, MD, MHA

Donor-Specific T Cell Responses
John McDyer, MD, UPMC, Pittsburgh, PA USA

Micro-RNA Dysregulation in Lung Transplant Rejection
Alessandro Palleschi, MD, Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico, Milan, Italy

Cell-Free DNA in Lung Transplantation
Mark Nicolls, MD, Stanford University, Stanford, CA USA

Molecular Pathways of Allograft Rejection
Kieran Halloran, MD, University of Alberta, Edmonton, AB Canada

Small Airway Rejection: Diagnosis by Cytology Brush
John R. Greenland, MD, PhD, UCSF, San Francisco, CA USA

Artificial Intelligence Imaging Analysis to Detect Allograft Dysfunction
Vibha N. Lama, MD, MS, University of Michigan, Ann Arbor, MI USA

VIEW SESSION DETAILS

SESSION 03: Through the Looking Glass: Advanced Lung Assessment During EVLP

EVLP is a novel method to optimize marginal lung donors thus increasing donor availability for lung transplants. Nowadays, it is widely adopted in transplant centers and continues to be a hot topic at ISHLT. It is exciting to see several studies on donor lung assessment during EVLP in order to predict suitability of donor lungs, which may improve the outcomes of lung transplants.

cfDNA Levels in Ex Vivo Lung Perfusate Are Associated with the Prognosis of Donor Lungs

Haruchika Yamamoto, MD, PhD, University Health Network, ON Canada

Starting the session, Dr. Yamamoto demonstrated that the level of cell-free DNA (cfDNA) in EVLP perfusate samples can predict the prognosis of lungs on EVLP. The study showed that the higher the level, the more likely that those lungs will be declined. Moreover, the level is also associated with the outcome post-lung transplant defined by extubation after 72 hours in the recipient. cfDNA could potentially be a new biomarker to predict donor suitability.

Standardized Radiographic Evaluation of Human Donor Lungs During Ex Vivo Lung Perfusion Predicts Lung Injury and Lung Transplant Outcomes

Bonnie T. Chao, BASc, University Health Network, Toronto, ON Canada

In this study, the investigators reviewed radiographic features in EVLP which provide pristine and unobstructed images of donor lungs. They developed novel scores called radiographic lung scores using 5 radiographic features (consolidation, infiltrates, atelectasis, nodules, and interstitial lines). They found that RLS at 1 and 3 hours can predict the decision to transplant with AUC of 90% and 88%, respectively. This score may provide key information in lung donor evaluation for transplant.

Pulmonary Dead Space Fraction: A Predictive Factor for Transplant Suitability in Clinical Ex Vivo Lung Perfusion

Ichiro Sakanoue, MD, Cleveland Clinic, Cleveland, OH USA

The purpose of the study was to investigate lung weight gain as a predictor of transplant suitability of EVLP lung using porcine lung model. 15 pigs were randomized into 3 groups: control (no warm ischemia) or donation after circulatory death groups with 60 or 90 min of warm ischemia (n = 5, each). Out of 15, 9 cases were deemed suitable for transplant and 6 cases were not suitable. Lung weight gain was significantly higher in non-suitable lungs compared to suitable lungs at 40 minutes (48.3 ± 49.9 vs. -8.8 ± 25.7 g, $P < 0.05$). Lung weight gain was also found to correlate with P/F ratio, Peak inspiratory pressure, shunt ratio. Real time lung weight gain can be used as an early indicator of transplant suitability during EVLP.

Real-Time Lung Weight Measurement to Assess Pulmonary Function During Cellular Ex Vivo Lung Perfusion

Ryo Kosaka, PhD, Natl Inst of Advanced Industrial Science and Technology (AIST), Tsukuba, Ibaraki, Japan

This study aimed to study relationship of dead space fraction (DSF) and donor lung transplant suitability during EVLP. The investigators calculated DSF from total 80 donor lungs undergoing EVLP. DSF was then stratified into quartiles. Out of 80 cases, 53 cases were deemed suitable for

transplant. They found that lungs in the highest quartile (Q4) had higher peak airway pressure, lower PF ratio, lower dynamic compliance during EVLP, and higher lung weight. Transplant suitability decreased with higher DSF. DSF could be used as a predictor of lung transplant suitability during EVLP.

Donor Airway Bile Acid as a Biomarker of Aspiration and Predictor of Post Lung Transplant Outcomes

Rayoun Ramendra, BSc, Ajmera Transplant Center, Toronto, ON Canada

Emesis and aspiration in donor contribute to donor lung damage and may contribute to post-transplant allograft dysfunction. However current assessment of aspiration in donors has limitations as the interpretation is subjective, does not assess the severity and does not assess microaspiration. Total bile acid (TBA) from bronchial wash could be used to objectively assess for aspiration. Investigators obtained TBA from bronchial wash from 605 lung donors. They found that the level of TBA from bronchial wash is higher in lungs deemed not suitable for transplant compared to those suitable for transplant or those requiring EVLP. TBA with the cut point of 1245 nM was able to differentiate donor lungs suitable for transplantation with 90% specificity, AUC of 0.726. Higher donor TBA was also associated with worse lung physiology on EVLP with lower PO2 and higher PVR. Moreover, higher level of TBA was associated with longer time to extubation and lower allograft survival.

InsighTx: A Machine-Learning Model That Accurately Predicts Transplant Outcomes During Ex Vivo Lung Perfusion

Andrew T. Sage, Ph.D, Toronto General Hospital Res Inst, Toronto, ON Canada

And lastly, study from Dr. Sage showed us that artificial intelligence could be a huge asset in clinical decision-making on EVLP donor selection. The model has good performance to predict 3-outcome classification for EVLP - unsuitable, transplant-resulting in extubation >/=72 hours, transplant-resulting in extubation < 72 hours.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SESSION 20: Coming to a Bedside Near You: Translational Studies in Lung Organ Perfusion

This **oral abstract session** provided new translational research focused on improving donor lungs using novel organ perfusion strategies.

Time to Try Something New: Establishing Rat Models of Lung Transplantation Under ECMO Support
Xiucheng Yang, MD, Wuxi People's Hospital Affiliated to Nanjing Medical University, Wuxi, China
Dr. Yang showed us how his team developed rat models of lung transplantation under both VV and VA ECMO support. Their model was shown to adequately oxygenate during the left single lung transplantation procedure. The intraoperative hemodynamic and blood gas parameters were stable. He also pointed out that vascular cannulation technology is key to establishing ECMO.

Lung Function and Inflammatory Profiling of Damaged Rat Donor Lungs Following EVLP Heat Stress with Different Temperatures
Anne Debonneville, MSc, Lausanne University Hospital, CHUV, Lausanne, Switzerland
EVLP is a technique allowing graft assessment and treatment for donor lungs to make them suitable for lung transplants. Adaptation to heat stress is a protective mechanism that causes cellular resistance to further stress by inducing cytoprotective heat shock proteins, autophagy, and unfolded protein response to maintain protein homeostasis. The investigator hypothesized that heat stress applied during EVLP may improve lung quality by reduction of oxidative stress, cell death, and inflammation. This trial was performed on male rats which were randomized into 5 groups - control, and 4 heat stress group at different heat stress (41.5 c, 42 c, 42.5 c or 43.5 c). Lungs were kept in situ for 1 hour then harvested and kept at 4 c for 1 hour then placed on the EVLP system for 3 hours. They found that heat stress during EVLP at 41.5 offers the most favorable conditions including elevated HSP72, autophagy, and unfolded protein response. Markers for apoptosis, endothelial damage, inflammation, and oxidative stress were also reduced in the 41.5 c group. These findings correlate with physiology outcomes which showed that static compliance was significantly increased at 41.5 c group. Lung weight was significantly reduced in the 41.5 c group. Heat stress could be an innovative strategy to recondition lung grafts before transplant.

Transient Heat Stress During Ex-Vivo Lung Perfusion Induces the Heat Shock Response and Preserves Lung Function in Pig Model
Thorsten Krueger, MD, PhD, CHUV, Center Hospier Univire Vaudois, Lausanne, Switzerland
Heat shock response is an adaptive response to thermic stress that has cytoprotective and anti-inflammatory action. The investigator performed a study on pig lungs that was assigned to 2 groups: the control group (kept on EVLP at 37 c for 4 hours) and the thermal precondition (TP) group (EVLP at 37 c for 2 hrs, then 42 c for 30 min, then back to 37 c for 1.5 hr). Lungs in TP group increase mRNA of heat shock proteins from lung tissue, reduction of biomarkers for cell damage such as CK18-M30, LDH from bronchoalveolar lavage fluid. Lungs in TP group were also shown to have better function compared to control with higher P/F ratio, lower peak airway pressure, lower PVR, and higher static pulmonary compliance.

The Combination of Post-Mortem Sevoflurane Ventilation and In Situ Topical Cooling Provides Improved 6h Lung Preservation in an Uncontrolled DCD Porcine Model

Edson Brambate, MD, UHN, Toronto, ON Canada

Uncontrolled donation after cardiac death (uDCD) has been reported successful transplantation and may help increase the donor pool for lung transplantation. The investigators aimed to study the effect of combining sevoflurane preconditioning on lung grafts and in situ lowering of intrathoracic temperature in a porcine model. They found that lungs in the group with sevoflurane preconditioning and intrapleural topical cooling had better physiology on EVLP (lower peak airway pressure, higher dynamic compliance, and higher P/F ratio). Levels of pro-inflammatory cytokines (IL-6, IL-8) and apoptosis were shown to be lower in this group. They went on to the second phase of this study which they transplanted lungs from this group. Post-transplant lungs were shown to have good oxygenation function up to hours post perfusion. This strategy could be a practical way to optimize uDCD lung graft in order to increase donor pool given that the cost is relatively low, and equipment/medication is already available in ED/ICU.

Report of the GUARDIAN-LUNG Registry: An Analysis of Advanced Hypothermic Preservation on Lung Transplantation

Matthew Hartwig, MD, Duke University, Durham, NC USA

The Global Utilization And Registry Database for Improved preservAtion of doNor LUNGs (GUARDIAN-LUNG) study is a multi-center retrospective-prospective registry assessing clinical outcomes after lung transplantation. Dr. Hartwig presented the initial report of a study comparing two methods of hypothermic storage (total patients = 120): patients with donor lungs preserved by the LUNGguard and patients with donor lungs preserved by conventional preservation methods (ice). The results demonstrated that LUNGguard (LG) provided safe and reliable static cold storage for donor lungs. Though not statistically significant, the rate of grade PGD and post-operative support needs appeared to be lower in the LG cohort. The trial is currently ongoing with a plan to enroll more patients and follow them for a longer period.

Sequential Ex Vivo Lung Perfusion for Prolonged Lung Preservation: Does the Second EVLP Reset the Lung Conditions?

Ichiro Sakanoue, MD, Cleveland Clinic, Cleveland, OH USA

The purposes of the study are to investigate the potential benefits of sequential EVLP by comparing lung function between sequential EVLP and conventional cold static preservation and to examine whether EVLP can improve graft quality. Ten porcine lungs were procured and randomized to 2 groups: the control group (underwent 16 CIT and 2 hrs EVLP) and the sequential EVLP group (underwent 4hours of CIT, 2 hrs of EVLP (EVLP1), 10 hrs of CIT, then 2 hrs of EVLP (EVLP2)). Lungs in EVLP 2 group were shown to have significantly higher P/F ratio, lower shunt fraction, lower A-a gradient, and lower lung weight compared to the control group. ATP and HIF level was also higher in EVLP2 group. Histologically, EVLP2 group has significantly reduced intra-alveolar edema. Findings from electron microscope also suggest better preserved morphological structure of lungs. Sequential EVLP might be a feasible way to prolong lung preservation time to

overcome limitations of the geographic allocation range of donor lungs.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

MINI ORAL 02: COVID-19 Disease and Vaccination Issues Relevant to Lung Transplantation

COVID-19 has been a prevalent component of lung transplant care for the past two years, creating a new need for lung transplant in COVID-19 survivors and plaguing post-lung transplant patients with a high mortality rate. This **mini oral abstract session's** topics ranged from outcomes and complications for lung transplantation in COVID-19 ARDS/fibrosis to effects of COVID-19 and vaccination strategies in post-lung transplant patients.

First, we discussed the findings of a case study from Latin American countries using lung transplant for COVID-19 ARDS. They cite that transplant is used less in these countries due to lower donor rates but demonstrated the successful use of bilateral lung transplant in 13 patients for COVID-19 disease. Interestingly, their survival was 54% at 60 days follow up, 75% at 30 days, disparate from experience in the US, where mortality has mirrored other indications for transplant at ~90-100% at one year.

Presenting from Stanford, **Shravani Pasupneti, MD** discussed their findings on the use of extracorporeal membrane oxygenation (ECMO) as a bridge to transplant in COVID-19 vs. non-COVID-19 transplant recipients. Their data demonstrated 100% survival for both but a higher return to the operating room and use of dialysis post-transplant. **Deepika Razia, MBBS**presented their experience from Norton Thoracic Institute comparing 11 cases of COVID ARDS transplant to 121 restrictive lung disease controls and demonstrated higher morbidity but similar mortality between the groups. **Sharanya Kumar, MD** from India presented data on airway complications in their cohort of 23 transplants; they found a high incidence of airway complications requiring dilation and stent placement.

Moving to issues after lung transplant with COVID-19, **Stanley Wolfe, MD** presented data examining patients who died due to COVID-19 after lung transplant. Their team found that COVID mortality was more likely to be a contributing cause of death in Black and Hispanic patients, with a HR of 2.18 for Hispanic lung transplant recipients who contracted COVID-19.

How can we help predict lung transplant recipients who might have early or late issues after COVID-19? **Adrian Lawrence, MD** presented data using the CARE Score, which looks at a chest radiograph at the time of diagnosis and creates a score based on ground-glass vs consolidation in lung areas. They found in a retrospective analysis that a score of 5 (range 0-6 for test) had adjusted HR of 11.63 for death from COVID-19, suggesting its use in lung transplant recipients would be helpful. In addition, **Vaidehi Kaza, MD** presented data from a small sample that lung transplant recipients who had higher levels of preformed IgG antibodies were more likely to have critical COVID-19 disease.

Finally, we discussed vaccination for lung transplant patients. It is known that due to the complex immunosuppression lung transplant recipients require that the effect of vaccination has been significantly reduced. **Sandhya Bansal, PhD** presented data from their lab demonstrating that after

vaccination, lung transplant recipients had elevated IFN gamma levels secreted from T cells, suggesting some level of protection. **François Michel Carlier, MD, PhD** presented data from their lab confirming poor anti-SARS-CoV-2 antibody production after mRNA vaccination, especially if on mycophenolate or higher doses of prednisone.

– Summary by Grant Turner, MD, MHA

Lung Transplantation for Post COVID-19 End Stage Lung Failure: A Case Series from 3 Latin American Countries
Pedro Felipe Undurraga, MD, Clinica Las Condes, Santiago, Chile

Racial Disparities in Death Due to SARS-CoV-2 in the United States: An Analysis of the OPTN Database
Stanley B. Wolfe, MD, Massachusetts General Hospital, Boston, MA USA

Comparing Outcomes of COVID-19 vs NonCOVID-19 Lung Transplant Recipients on ECMO as a Bridge to Transplant
Shravani Pasupneti, MD, Stanford University Hospital, Stanford, CA USA

A Comparison of Short-Term Morbidity and Mortality Among Inpatient Lung Transplant Recipients Transplanted for COVID-19 and Other Restrictive Lung Diseases
Deepika Razia, MBBS, Norton Thoracic Inst, St. Joseph's Hospital and Medical Center, Phoenix, AZ USA

Airway Complications After Lung Transplant for Post Coronaviral Disease (COVID-19) Acute Respiratory Distress Syndrome (ARDS) Related End Stage Lung Disease: Single Centre Experience
Sharanya Kumar, MD, KIMS, Hyderabad, India

CARE Score on Chest Radiograph at Diagnosis Predicts Early and Late Outcomes Among Lung Transplant Patients with COVID-19
Adrian Lawrence, MD, University of Texas Southwestern, Dallas, TX USA

Autoantibodies and Severity of COVID-19 in Lung Transplant Recipients
Vaidehi Kaza, MD, University of Texas Southwestern Medical Center, Coppell, TX USA

Lung Transplant Recipients with SARS-CoV-2 Infection Induce Circulating Exosomes with SARS-CoV-2 Spike Protein S2 Which Are Immunogenic in Mice
Sandhya Bansal, PhD, St. Joseph's Hospital and Medical Center, Phoenix, AZ USA

Analysis of Humoral and Cellular Immunity of Lung Transplant Recipients Following SARS-CoV-2 Infection and BNT162b2 mRNA Vaccination
Sandhya Bansal, PhD, St. Joseph's Hospital and Medical Center, Phoenix, AZ USA

Immunogenicity of Two Doses of ChAdOx1 nCoV-19 Vaccine in Lung Transplant Recipients

François Michel Carlier, MD, PhD, CHU UCL Namur, Yvoir, Belgium

VIEW SESSION DETAILS

Featured Abstract 3 at Plenary 2: Evaluation of 10°C as the Optimal Storage Temperature for Injured Donor Lungs in a Large Animal Transplant Model

Presenter: ***Aadil Ali, PhD****, Latner Thoracic Surgery Res Labs, University Health Network, Toronto, ON Canada*

What is the best temperature to store lungs for transportation? While many centers currently use 4°C, recent literature challenges that 10°C may improve outcomes for lung transplant. In this research presentation, Dr. Ali presented the findings from the Toronto group on the use of 10°C in damaged lungs from pigs or transplantation.

Why is this being researched? By using less extreme temperatures, ischemic reperfusion could be alleviated while also allowing transplant centers to overcome geographical hurdles, add time-dependent therapeutics, allow for better immunological matching, change lung transplant to semi-elective, and have a socio-economic benefit for both transplant centers and patients.

Previous work from their group has demonstrated that 10°C exerts some of its effects by protecting mitochondrial health, causing less oxidative damage and less DNA release. A recent publication also details the successful use of ideal human lungs stored at 10°C (DOI: 10.1126/scitranslmed.abf7601).

Based on this research, their group asked: could 10°C be used to store damaged lungs for transplant? Using a pig model, they caused damage using gastric juices, harvested lungs, stored them at either 4°C or 10°C, and measured clinically relevant outcomes. After transplant, lungs held at 10°C had significantly improved oxygenation and compliance and decreased cell-free mitochondrial DNA, suggesting less reperfusion injury (see image for further details).

Further research will need to be completed to determine if this association remains true in human lungs and a larger, randomized trial in humans to determine if there are significant benefits from utilizing 10°C instead of the standard of care 4°C.

VIEW FULL ABSTRACT

– Summary by Grant Turner, MD, MHA

SUNRISE 02: The Path Forward in Developing Novel Therapies in Lung Transplantation

Improving Clinical Trial Design in Lung Transplantation

Ramsey Hachem, MD, Washington University SoM, St. Louis, MO USA

The goal of clinical trials in lung transplantation is to improve clinical outcomes. Given that there is only a small pool of lung transplant recipients to recruit, we need to learn as much as possible from clinical trials. In addition to the primary goal which is to assess the efficacy and safety of a specific treatment, ancillary and mechanistic studies should also be performed.

A traditional randomized controlled trial is usually a design of choice when conducting a clinical trial. However, it is expensive, time-consuming, and requires dedication from all stakeholders. Moreover, it is difficult to calculate sample size and power as sometimes the effect of treatment is not available.

One of the solutions is to start from a pilot clinical trial to assess the feasibility of a larger trial. The results from the pilot trial can guide the design and conduct of the pivotal trial. Another interesting option is to conduct an adaptive trial. An adaptive trial uses results from interim analyses to modify the ongoing trial without undermining its integrity or validity.

An adaptive trial can help refine sample size, change allocation ratios, identify patients most likely to benefit, focus recruitment on these patients, and lastly, adaptive trials can be stopped early for success or lack of efficacy. For the above-mentioned reasons, it can improve the efficiency of RCTs. Although, it is complex as blinding during interim analysis is necessary and it also needs statistical adjustment for multiple testing. Therefore, adaptive trial requires a specific analysis and biostatistician with experience.

Is Rejection the Best Endpoint? Where Do We Stand on Biomarkers as Endpoints?

Stijn Verleden, PhD, University of Antwerp, Leuven, Belgium

Rejection is an important problem in lung transplantation. However, the current limitation of using rejection as an endpoint includes

1. **Power:** Sometimes it is difficult to enroll sufficient patients to power the study as we do not know who will develop CLAD.
2. **CLAD phenotypes:** Lung transplant patients suffer in different kinds of rejections (BOS, RAS, and mixed/undefined). Patients with RAS and mixed rejection have worse survival. Moreover, BOS and RAS also have different pathophysiology. Thus, there is a heterogeneity in CLAD trajectories which complicates trial design when using CLAD as an endpoint.
3. Once CLAD is diagnosed, only temporary stabilization can be obtained.

PFT could be used as an endpoint in lung transplant trial. However, it is important to deal with missing values when using pulmonary function trajectory analysis.

Biomarker is another option to use as endpoint. However, there are few important points to

consider. Biomarker must be present in peripheral tissue and/or fluid (BAL, peripheral blood), easy to detect or quantify in an affordable and robust way. Its appearance must be associated as specifically as possible, preferably in a quantifiable way. DSA could be a very important endpoint in lung transplant trials. It can be obtained from blood and can be quantified by MFI. Moreover, there is evidence showing that there is strong association between DSA and graft loss.

Removing Impediments to Clinical Trial Success: A Regulatory Body View

Yuan-Di Halvorsen, PhD, Massachusetts General Hospital, Boston, MA USA

Clinical studies that require regulation include studies of new drugs (never been approved), or studies of approved drugs with new indication with same or new regimen. Once a study is determined that it qualifies for regulation, next step is to prepare a dossier for regulatory submission which include Investigation new drug application (IND) (to be submitted to FDA), informed consent form (ICF) (to be submitted to IRB/ethic committee), and a detailed protocol (to be submitted to both FDA and IRB). The FDA will review protocol and IND within 30 days. If investigators do not hear back from the FDA, it means study protocol and IND are approved. IRB/ethic committee will give a written approval to investigators once they approve the study. Once study is approved by both FDA and IRB, drug and device shipment process can be started, and then proceed to consent and enroll study subjects.

IND may be waived if the drug is lawfully marketed in United States, has the same indication and regimen, the purpose of study is not to support promotion of the drug, no change in risk assessment, and lastly, the study is compliant to IRB requirements.

To pivot the idea successfully, investigators should envision the big picture and educate the reviewers, articulate the hypothesis and rationale for the proposed study clearly and concisely, and outline the objectives and approaches to achieve the objectives. Investigators should avoid presenting detailed data and ask for advice during formal meeting, avoid requesting for waiver of quality requirement, and avoid conducting study without an operational team.

Where Does This Leave Us? Where Do We Go From Here?

Paul A. Corris, MB, FRCP, Freeman Hospital, Newcastle upon Tyne, UK

Dr. Corris summarized the problems of clinical trial in lung transplantation as the following:

1. Many standard RCTs are long, require large numbers of patients, and are expensive.
2. Industry, regulatory bodies, and clinical academics often struggles to agree on design and endpoints of phase 2 and 3 trials.
3. Results of immunosuppression trials in kidney transplantation are not always applicable to lung transplantation.
4. Large unmet clinical need in lung transplantation to improve outcomes.
5. Novel immunosuppressive drugs in pharma development pipeline are not always made known to clinician scientists.
6. Lack of drive by pharma to develop and progress novel immunosuppressive drugs in pipeline.
7. Use of orphan status of lung transplant recipient problems are not fully exploited.

8. Lack of current opportunity for pharma, regulatory bodies, and clinical academics to meet and collaborate.

Dr. Corris gave us a successful example of the collaboration between pharma, regulatory, and academics from Pulmonary vascular Research Institute (PVRI). In 2017, The innovative Drug Development Initiative, formerly known as the PVRI Pharma Task Force was established as a collaboration between PVRI, Bayer, and Bellerophon. As a result, a series of 4 documents on clinical trial endpoints, clinical trial designs, biomarkers, and repurposing drugs were released in 2020 as a guidance for academics, drug regulators, and industry partners.

Dr. Corris proposed a similar approach to PVRI to the ISHLT Board in 2021. The ISHLT Professional Communities can be utilized to populate the initiative. He also proposed to create the ISHLT Immunosuppression Initiative to stimulate and speed up clinical trials of novel or repurposed drugs to improve clinical outcomes in lung transplantation. ISHLT board gave a full support and the ISHLT Immunosuppression Initiative or "the triple I" first meeting has taken place for agenda setting and to identify pharma and regulatory body partners.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SUNRISE 04: Challenges in Pediatric Lung Transplant: What Learning Can We Impart to Our Adult Colleagues?

Pediatric lung transplant shares many commonalities with adult lung transplant but has limitations regarding standardization and high-volume trials as significantly fewer pediatric transplants are completed yearly. These limitations, however, can demonstrate areas for innovation and potential crossover ideas for the adult population.

First, **Helen Spencer, MD** discussed when it is the right time to evaluate pediatric patients for transplant. One unique take-home point from her talk related to confirming the diagnosis. As pediatric lung diseases are rarer and transplantation would significantly limit a recipient's long-term life span, being pedantic and thorough about the diagnosis and potential treatments is critical. Additionally, she described their process for listing, including both the child and the parents being ready for possible transplant on the day of listing and a listing meeting with the entire team, including Surgery, Pulmonary, Anesthesia, nursing, etc.

How do we ensure lungs are functioning well after transplant? Determining lung function is an issue that can be especially difficult in pediatrics, where testing that requires recipient participation can be limited. **Marc G. Schecter, MD** discussed this issue and presented several unique concepts. First, pulmonary function tests (PFTs) can be completed on infants through raised volume rapid thoracoabdominal compression but requires conscious sedation, and there are relevant size limitations. Inspiratory oscillometry is another option that requires no active participation and uses frequency distortions to determine abnormalities in the small and large airways. As ionizing radiation in children is not ideal, studies are underway looking at the use of hyperpolarized gas with MRI to determine ventilation defect percentage. Finally, confocal endomicroscopy with bronchoscopy can be helpful in imaging and quantitating abnormalities of the small airways, which may help with the diagnosis of acute cellular rejection in the future.

Christian Benden, MD, MBA, FCCP presented preliminary data on a multicenter survey of pediatric lung transplant programs' monitoring post-transplant to determine if these new techniques are being utilized. Notably, no consensus definitions exist for diagnosing chronic lung allograft dysfunction (CLAD) after pediatric lung transplant, so definitions are extrapolated from adult guidelines. In his survey, Dr. Benden demonstrated that all centers queried were still using CT imaging using pediatric protocols, and 70% were continuing to undergo surveillance bronchoscopy, with 80% completing clinically indicated transbronchial biopsy. Further results of this study are forthcoming by his group.

After obtaining biopsies, how can we diagnose rejection? **Kathryn Wikenheiser-Brokamp, MD, PhD** summarized the issue with this in pediatrics. While a good amount of lung tissue is defined the same as adults, evaluation for rejection is more difficult based on smaller biopsy sizes obtained via pediatric bronchoscopy. Further research about defining antibody-mediated rejection (AMR) and a standardized approach to rejection in pediatrics is needed.

Finally, how can we ensure pediatric patients have a soft landing in a new adult program? **Ernestina Melicoff-Portillo, MD** discussed the six core elements of transition; policy, tracking and monitoring, readiness, planning, transfer/integration into adult-centered care, and completion and ongoing care with an adult clinician. These transitions in care require an understanding of the patient's developmental status, giving age and skill level appropriate directions, and knowledge from the adult program of the unique challenges.

While pediatric lung transplant comprises less than 10% of lung transplants completed globally, there are potential areas of innovation that adult programs can consider moving forward. These include novel spirometry and imaging techniques for diagnosing small airway disease, continuing work on improving biopsy techniques, and educational interventions targeting appropriate age and skill level abilities.

VIEW SESSION DETAILS

– Summary by Grant Turner, MD, MHA

Assessing Kids for Transplantation: When is the Right Time and How Do We Know?
Helen Spencer, MD, Great Ormond Street Hospital, London, UK

Novel Methods for Assessing Lung Disease: From PFTs to Imaging Modalities
Marc G Schecter, MD, University of Florida, Gainesville, FL USA

CLAD in Pediatrics versus Adult Populations: What To Do When PFTs Aren't an Option
Christian Benden, MD, MBA, FCCP, University of Zurich, Zurich, Switzerland

Challenges in Rejection Diagnostics in Pediatric Transplant and How to Overcome Them
Kathryn Wikenheiser-Brokamp, MD, PhD, Cincinnati Children's Hospital, Cincinnati, OH USA

Transitioning to Adult Services: How the Patient-Centered Multidisciplinary Team Approach in Pediatric Transplant May Benefit Adult Centers
Ernestina Melicoff-Portillo, MD, Baylor College of Medicine, Houston, TX USA

SESSION 38: Vaccination in Cardiothoracic Transplant Candidates and Recipients: The Time is Now?

While currently a hot topic because of a worldwide pandemic and efforts to vaccinate against COVID-19, vaccination for many other diseases remains a critical intervention for cardiothoracic transplant candidates and recipients. This **symposium** served as a helpful review of vaccination strategies and closed with a debate over vaccine mandates for COVID-19 in the transplant population.

Before listing a lung transplant patient, an extensive review of their vaccination history should be completed, including testing of available IgG levels to ensure response to vaccinations. The pre-transplant period is the ideal time to ensure all live vaccinations have been completed, as per your country's guidelines. Vaccination against COVID-19 is also best undertaken in the pre-transplant phase since post-transplant cardiothoracic transplant patients have poor responses to currently available vaccines. After transplant, it is common to wait 3-6 months to continue vaccinations and avoid them during augmented immunosuppression. Additionally, it is important to remind recipients that their families should not get smallpox or oral polio vaccines while around them. Their pets can get all vaccines except the intranasal live Bordetella (while they are in the room with the pet).

As a community, we have come a long way since 1796, when the idea of vaccines was first discovered with cowpox inoculations. Unfortunately, we continue to note difficulty with getting an adequate response to vaccines in some individuals, such as the elderly, obesity, chronic heart disease, kidney disease, and lung transplant recipients, but there is known discordance between seroconversion and T-cell response. Efforts to improve this response include vaccination pre-transplant, using higher doses of available vaccines and utilizing boosters, and new forms of vaccines which contain adjuvants to improve immunogenicity.

Looking to the future, new and exciting vaccines are in development. Currently available are the PCV15 and 20, allowing for easier dosing structure than previous pneumonia vaccines. There are also investigational CMV and Hep C vaccines currently being developed as well as many mRNA vaccines in trials (flu, RSV, rabies, Zika, Ebola, HIV, CMV, EBV, HSV, VZV, malaria, hMPV + PIV3, COVID + flu, etc).

Finally, and potentially the most pressing topic of the current discussion is what to do if a patient refuses vaccination against COVID-19. Should COVID-19 vaccines be mandated before activation on the transplant list?

In defense of mandates, **Osnat Shtraichman, MD** presented the staggering mortality in solid organ transplant recipients who developed COVID-19 of 20%, which may be even higher in lung transplant recipients. By vaccinating, especially pre-transplant, transplant recipients have a significantly decreased risk of morbidity or mortality. There is also a low likelihood of adverse events (0.2-0.5%). By mandating vaccines, we can determine if a patient is likely to adhere to treatment recommendations, be good stewards of the limited resource of donated organs, and

meet the ethical principles of non-maleficence and justice.

In defense against mandates, **Olivia S. Kates, MD** reviewed four concepts - what is correct, good, fair, and done well, and how this relates to mandating COVID-19 vaccination. While mandatory vaccination is correct and good, she argued that it is not necessarily fair nor done well. While transplant centers can mandate vaccination as it would increase net utility of transplantation more than any alternative, we can mitigate the risk of developing COVID-19 in other ways. Additionally, centers tolerate other risks for acute rejection and death. Unfortunately, vaccine refusal is also more common in individuals affected by broader systems of disadvantage such as income, education, and race. It has also been the target of a misinformation campaign since its inception.

While the crowd determined this debate was a tie, this debate will continue throughout transplant centers worldwide as the COVID-19 pandemic continues. The topic of vaccination will continue to be crucial to help protect our vulnerable transplant population, and with continued patient education and innovation in new vaccinations, we can continue to find the proper level of protection.

VIEW SESSION DETAILS

– Summary by Grant Turner, MD, MPH

Vaxxed and Transplanted—Not Just for COVID
Haifa Lyster, MSc, Royal Brompton Specialist Transplant Pharmacist, Middlesex, UK

From Cow Pox to COVID: A Brief Overview of Vaccination and the Immunocompromised Host
Joanna M. Schaenman, MD, PhD, UCLA School of Medicine, Los Angeles, CA USA

New Advances in Transplant Vaccinology: Current and Emerging Vaccines for Transplantation
Robin Avery, MD, Johns Hopkins, Baltimore, MD USA

Case Study: Should This Patient's Listing Require Completion of Recommended Vaccination?
Michelle Murray, MD, MSc, MRCPI, Mater Misericordiae, Dublin, Ireland

DEBATE: Transplant Programs Should Mandate Candidates Be Fully Vaccinated Prior to Activation on a Transplant List (PRO)
Osnat Shtraichman, MD, Rabin Medical Center Belinson Campus, Petach Tikva, Israel

DEBATE: Transplant Programs Should Mandate Candidates Be Fully Vaccinated Prior to Activation on a Transplant List (CON)
Olivia S. Kates, MD, Johns Hopkins, Baltimore, MD USA

SESSION 40: Take a Chance on Me: Updates in Lung Transplant Candidate Selection

This session informed us of the updated ISHLT Consensus document for the selection of lung transplant candidates, focusing on the ethical implications, the assessment of risk factors that are included in the consensus statement, and disease-specific updates for referral and listing.

Updated Recommendations for Lung Transplant Candidate Selection: Assessment of Risk Factors
Lorriana E. Leard, MD, UCSF Medical Center, San Francisco, CA USA
In this session, we learned from Dr. Leard about the updated ISHLT lung transplant candidate selection consensus document that was published in 2021. This updated version is different from the previous one as it includes an ethical framework, a recognition of the variability in acceptance of risk between transplant centers, and a recognition that risk factors need to be considered together.

Variability in acceptance of risk between lung transplant centers depends on risk tolerance, which is contributed by center volume, accreditation requirements, organ availability, and varying expertise. Some centers may develop expertise in transplanting patients with higher risks and this may help advance the field.

To assess the risk factors, three things need to be taken into account:

1. Evaluation to determine what risk factors are present (medical comorbidities, psychosocial factors, and potential for rehabilitation)
2. Valuation of risk factors (relative risk associated with risk factors, the cumulative effect of multiple risk factors)
3. Consideration of center-specific risk tolerance/expertise/experience

Risk factors for poor post-transplant outcomes are now divided into 3 categories:

1. Absolute contraindication: conditions considered too high risk of adverse outcome and would make transplant more harmful for patients
2. High or substantially increased risk: risk factors that increase the risk of poor outcome post lung transplant. Centers with expertise may consider transplant.
3. Risk factors with implications for unfavorable shot/long-term outcomes. Multiple risk factors together may increase the risk for adverse post-lung transplant outcomes.

Other considerations

- Age remains controversial. No endorsement of upper age limit but acknowledge the increased risk with increasing age. Based on the literature, carefully selected older recipients may have the same short-term survival as younger recipients but have decreased longer-term survival, especially in those aged above 70 years old.
- Malignancy: The updated consensus acknowledges that not all cancers are the same. Each patient should be evaluated to determine the stage-specific risk of recurrence or progression. So, it is very important to work closely with an oncology specialist.

- Timing: early referral is very important in order to allow time to optimize any modifiable ones.
- Transparency is essential: the center should provide reasons if patients are deemed not a candidate. Patients should be given information about alternatives and referred to centers that may consider transplants.

Psychosocial Considerations in the Selection of Lung Transplant Candidates
Patrick J. Smith, PhD, MPH, Duke University Medical Center, Durham, NC USA
In this session, Dr. Smith discussed psychosocial considerations in lung transplant candidate selection. Given that psychosocial data are probabilistic by nature, they must not be interpreted in isolation. He pointed out that psychosocial domains are multidimensional and need to integrate multiple factors when possible. Assessment domains should link to target behaviors (adherence, abstinence). Transplant teams should make decisions regarding patient selection with attention to the dangers of implicit bias against subsets of patients.

The recommendation regarding substance use is similar to the 2018 consensus guideline. For cognitive impairment, the most concerning factor is progressive decline as it can impact adherence, lower survival, and lesser quality of life benefit from transplant. Milder cognitive impairments are common and variable such as impairment due to hypoxemia, poly pharmacy, frailty and these may be improved following transplant. Depression has been shown to be associated with worse outcomes, especially when recurrent and refractory. Anxiety is less associated with outcomes. It is often reactive and may associate with disease burden during preoperative.

Pediatric Specific Considerations for Lung Transplant Candidate Selection
Melinda Solomon, MD, FRCPC, Hospital for Sick Children, Toronto, ON Canada
Dr. Solomon updated us on the change in pediatric consideration in the new consensus statement compared to the 2015 guideline.

First, CF referral guidelines are more conservative when it comes to earlier referral—especially for young adolescent females with rapid decline. Second, the pediatric PH referral guideline is also updated, based on the latest guideline from the European Pediatric Pulmonary Vascular Disease Network in 2019. Third, infant transplantation is highlighted in this updated version.

There are several considerations in pediatric lung transplantation. Waiting time may be longer for infants/children due to the challenge of acquiring suitable-sized organs, so early referral is important. Common indications for a lung transplant in pediatrics are different from adults, for example, CF is a leading indication in age 6-17 years old, increasing numbers with IPAH, which is the most indicated in 1-5 years old. The common indications in infants are different, the leading indications include surfactant B deficiency and pulmonary hypertension due to congenital heart disease.

Other indications that should be referred for transplant and were highlighted in the document include ABCA3 deficiency (insufficient surfactant), ACD with misalignment of pulmonary veins,

childhood interstitial lung diseases, and bronchiolitis obliterate. Some rare entities with very poor prognoses will require urgent evaluation/listing such as alveolar capillary dysplasia, pulmonary vein stenosis refractory to intervention, and pulmonary Veno-occlusive disease (PVOD). Ongoing assessment of non-adherence should occur as they progress through different developmental stages. The transition of care is also important and required careful planning if done while on the waiting list or early after the transplant. Lastly, growth can be affected by medications such as steroids post-transplantation.

Infectious Disease Risk Factors in Lung Transplant Candidates
Silvia V. Campos, MD, Heart Institute of Sao Paolo Medical School, Sao Paolo, Brazil
Dr. Campos updated us on infectious risk factors in lung transplant candidates. There are still absolute contraindications which include active tuberculosis infection, HIV infection with detectable viral load, and active extrapulmonary or disseminated infection. Although multi-drug resistant organisms are no longer absolute contraindication due to novel tests and broad-spectrum antibiotics to treat, these organisms can still increase morbidity and mortality post-transplant and should be still taken into account.

Non-tuberculous mycobacteria increase morbidity and mortality in lung transplants due to their intrinsic resistance to treatment and their high risk of relapse. However, there is a case series showing successful management and good outcomes after transplant.

Burkholderia cepacia complex has been shown to be associated with poor outcomes in lung transplants due to higher virulence. It is important to evaluate for *B. Cepacia* complex and identify species as the virulence is different and results in different lung transplant outcomes.

Non-aspergillus molds, including *Scedosporium apiospermum* or *Lomentospora prolificans*, which are emerging multi-resistant pathogens and require prolonged anti-fungal therapy. Incidence of these is rising, especially in Australia and Spain. These may be due to the widespread use of posaconazole for fungal prophylaxis in some lung transplant centers.

There is some good news for virus organisms. There is more evidence treatment may be possible for Hepatitis B virus before or after transplant with a good outcome. There is an increased rate of sustained virology response (SVR) in patients with hepatitis C infection from 62% (Peg-intereron+ribavirin) to 100% (with direct-acting antiviral). Now it is also possible to use D+ to R- HCV. With the pan-genomic antiviral treatment, all lung transplant patients in the small study achieved SVR at 24 weeks.

There is still a small number of lung transplants in HIV patients. Data from a lot of case series showed that HIV patients (with undetectable viral load and CD4 count > 200) have good outcomes/survival post lung transplantation. One important consideration in the HIV population is a drug interaction between immunosuppressive agents and efavirenz or ritonavir. Lastly, COVID-19, it is reasonable to accept patients suffering from ARDS from COVID infection for 4-6 weeks.

Ethical Principles to Guide the Selection of Lung Transplant Candidates and Allocation of Lungs
Are Holm, MD, PhD, Oslo University Hospital, Oslo, Norway
Dr. Holm updated us on ethical principles to guide the selection of lung transplant candidates and the allocation of lungs. The 2015 consensus document focused on how to select the lung transplant candidate based on only the principle of beneficence or who would benefit from lung transplant as if the number of organs was unlimited. In the 2021 consensus, in addition to beneficence, the consensus also focuses on distributive justice or how to say no despite beneficence based on rationing due to the scarcity of donor lungs, societal responsibility (to consider net survival gain for society as a whole), and center variability.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SESSION 26: Rejection Revelations: Novel Insights into Lung Transplant Rejection

Is Acute Rejection Truly Acute or an Exacerbation of an Underlying Disease?

Sean Agbor-Enoh, MD, PhD, National Heart, Lung, and Blood Institute, Bethesda, MD USA

Acute rejection (AR) is viewed as an acute event. However, most patients progress to chronic lung allograft dysfunction (CLAD) despite receiving treatment for AR. The investigators hypothesized that AR is not an acute event, but rather, an exacerbation of an ongoing early post-transplant disease. Donor-derived cell-free DNA (ddcfDNA) was used as a marker to define post-transplant allograft injury patterns associated with AR. 141 lung transplant patients were enrolled and grouped as AR or no rejection (NR) as determined per diagnostic criteria. Allograft injury was measured by ddcfDNA via shotgun sequencing in plasma samples. Of 141 patients, 51 developed 87 episodes of AR at a median of 7.6 months post-transplant. %ddcfDNA was high after transplant, then declined. In the AR group, baseline ddcfDNA levels were higher than NR group. At AR diagnosis, the levels increased to 2-fold higher than subject baseline level and 6 times higher than time-matched NR. After treatment, levels reduced but remained higher than NR group. In conclusion, AR patients had higher baseline allograft injury that worsened during diagnosis of AR.

The Relationship Between Soluble PD-L1 and Viral Infection, ACR, and CLAD

Eric Morrell, MD, University of Washington, Seattle, WA USA

Respiratory viral infection (RVI) is a risk factor for chronic lung allograft dysfunction (CLAD). The one-year incidence of CLAD after RVI is about 30% and mechanisms are poorly understood. PD-L1 plays a key role in host immune response to viruses. Investigators hypothesized that higher serum levels of soluble PD-L1 (sPD-L1) are associated with a higher one-year incidence of CLAD.

They performed a retrospective cohort study of lung transplant patients with serum collected at the time of suspicion for RVI or ACR. 40 patients had RVI and 27 patients had ACR without RVI. RVI groups had 1.73 times higher levels of sPD-L1 levels, compared to subjects with ACR (without RVI). They also found that doubling of the sPD-L1 levels in subjects with RVI was associated with a higher risk of CLAD at 1 year post-infection with RR of 4.96. There was no association between sPD-L1 levels at ACR (without RVI) and the development of CLAD.

Currently, the investigators are validating the findings with a prospective cohort and found similar findings that sPD-L1 levels were significantly higher in RVI group. However, BAL fluid concentrations of sPD-L1 were not different between groups. sPD-L1 may play roles in the development of CLAD and may be a target of treatment to modulate lung inflammation and improve outcomes of lung transplant.

Molecular Insights into the Role of BAL-EVs in Lung Transplant Rejection

Alessandro Palleschi, MD, University of Milan and Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico, Milan, Italy

Extracellular vesicles play a role in intracellular communication and involve in multiple immune responses and are capable of eliciting and potentiating innate and adaptive immunity in lung

transplant rejection. This study aimed to study BAL-extracellular vesicles (BAL-EVs) as pathomolecular signaling that precede and drives graft rejection.

BAL-EVs were isolated from ACR patients (n=3), CLAD patients (n=3), and matched lung disease, donor-type, and time of BAL from lung transplantation. BAL-EVs then were co-cultured with human primary bronchial cells for 48 and 72 hours, then secreted cytokines were analyzed. They found that ACR-EVs induced a transient up-regulation of cytokines after 48 hours of co-cultures, after which 7 cytokines remained up-regulated at 72 hours. CLAD-EVs induced secretion of cytokines, especially after 72 hours of co-culture. Up-regulation of IL-32 at 72 hours was a common effect of ACR- and CLAD- BAL EVs. Pathway analysis (STRING) of cytokines induced by ACR and CLAD BAL-EVs evidences their involvement in pro-inflammatory processes and allograft rejection.

These data indicate that BAL-EVs vehicular functional signals into recipient bronchial cells with a role in the onset and perpetuation of inflammatory processes. Targeting IL-32 might prevent the onset of an unfavorable environment for lung allograft. This study suggested that at the cellular level, compensatory mechanisms may be induced to counteract the extracellular pro-inflammatory environment.

Detection of Directly Alloreactive Graft Antigen-Specific CD4+ T Cells in Peripheral Blood

Stephen J. Huddleston, MD, University of Minnesota, Minneapolis, MN USA

The investigators are interested in CD4 T cell activation. There are three classic pathways of antigen presentation: direct pathway, indirect pathway, and semi-direct pathway. In the direct pathway, peptide antigens that directly activate alloreactive CD4 T cells are not known. The investigators hypothesized that a panel of human peptides presented by mismatched human leukocyte antigens (HLA) can be used to directly detect alloreactive CD4+ T cell in peripheral blood.

The investigators developed a panel of 18 human peptides presented by HLA-DRB1*04(DR4) to generate phycoerythrin(PE)- and allophycocyanin(APC)-labeled 18p:DR4 tetramers. They found that 100-fold more 18p:DR4tet+ CD4+ T cells were detected directly ex vivo in peripheral blood mononuclear cells (PBMC) from DR4- individuals than in DR4+ individuals. Ten-fold peptide-dependent expansion of 18p:DR4tet+ CD4+ T cells was also seen from PBMC from DR4- but not DR4+ individuals. Directly alloreactive CD4+ T cells specific for human peptides are detectable directly ex vivo in PBMC of HLA-mismatched individuals. This tool will be used to detect and characterize directly alloreactive CD4+ T cells in the PBMC, BAL, and pleural fluid in order to better diagnose allograft rejection.

High Volume Centers Have Lower Incidence of Acute Cellular Rejection in Pediatric Lung Transplant Recipients and Better Survival After Treatment

Alia Dani, MD, MPH, Cincinnati Children's Hospital Medical Center, Cincinnati, OH USA

Acute cellular rejection (ACR) is a common form of allograft rejection in pediatric recipients after lung transplant (Ltx), mostly occurring during the first post-transplant year. This study aimed to determine if center volume at pediatric centers and induction therapy impacted outcomes in

children that required treatment for ACR during the first post-Tx year.

The investigators included 1,338 pediatric patients (<18 years) from OPTN/UNOS Registry from 1987 - September 2020 and divided into ACR (n=271, 20.3%) and non-ACR groups. ACR cohort was defined as patients receiving treatment for ACR episodes in the first year post-LTx. Patients were categorized according to average center LTx volume/year. ACR cohort was found to be significantly older, more commonly female, more commonly diagnosed with cystic fibrosis, and had higher LAS at LTx. KM survival of ACR vs nonACR cohorts trended towards lower survival at 5-yr and 10-yr post-Tx (p=0.06). ACR occurred more frequently at low volume centers. ACR treated at high volume centers had better post-transplant survival than low volume centers but similar to medium volume centers. No significant difference in survival was observed in medium vs low volume centers.

In conclusion, higher volume centers have lowest ACR incidence with superior post-ACR treatment survival outcomes compared to low volume centers.

Higher Levels of Donor-Derived Cell-Free DNA Are Associated with Acute Cellular Rejection but Not with Severe PGD After Lung Transplantation

Kentaro Noda, PhD, University of Pittsburgh, Pittsburgh, PA USA

Circulating donor-derived cell-free DNA (dd-cfDNA) levels have been proposed as a potential tool for the diagnosis of graft injury (rejection, infection, ischemia/reperfusion injury). This study aimed to investigate dd-cfDNA plasma levels and their association with severe primary graft dysfunction (PGD) at 72 hours and acute cellular rejection (ACR) in the first month after lung transplant.

Thirty-five lung transplant patients were included in the study and PGD was graded according to ISHLT criteria. Surveillance bronchoscopy with transbronchial biopsy at three weeks post-transplant was performed per protocol. Blood samples were collected at several time points before and after the lung transplant. Dd-cfDNA in samples were measured using AlloSure dd-cfDNA test kits. Dd-cfDNA in blood of recipients rapidly increased and peaked at 72 hours after lung transplantation compared to baseline then decreased during the first two weeks. The peak values of dd-cfDNA varied among subjects and had no association with PGD grade 3 occurrences at 72 hours. There was an association between levels of dd-cfDNA from blood collected at the time of transbronchial biopsy and the histological diagnosis of ACR at 3 weeks. Plasma dd-cfDNA levels are associated with ACR early after transplantation but not with severe PGD at 72 hours and can be a less invasive tool to estimate graft rejection after lung transplantation.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SESSION 29: Survival of the Fittest: BMI and the Frailty Construct as Risk Factors for Lung Transplantation

Finding modifiable risk factors for lung transplantation and how to mitigate them is a crucial way to continue to advance our ability to offer this life-saving intervention to more individuals. In this session, presenters discussed the topics of frailty and weight, including how they are defined, how they are measured, and potential interventions to reduce risk.

First, we discussed frailty, defined as "a biologic syndrome of decreased reserve and resistance to stressors," and identified in consensus opinion to be an important factor for determining lung transplant candidacy. Unfortunately, there is no agreed-upon single operational definition for frailty—should we go based on phenotype, clinical judgment, and/or cumulative deficit? **Jonathan P. Singer, MD, MS** and his group developed a novel physical frailty measure, reflecting on the contemporary understanding of frailty, designed for use in patients with advanced lung disease. By evaluating currently available measurement tools and potential blood biomarkers, they created a basic lung transplant frailty index including balance, weak hand grip, slow gait, and C-reactive protein. Additional indexes with higher hazard ratios also included measures of sarcopenia and additional biomarkers.

Thinking about frailty in an alternative way, Dr. Singer's group also used latent class analysis to determine if there are differential phenotypes within the frailty cohort. They found two distinct phenotypes, with the cohort at higher risk being more sarcopenic with higher levels of inflammation and more likely to be hospitalized.

Moving toward nutrition, **Kei Matsubara, MD** presented data on the Prognostic Nutrition Index (PNI), an index utilizing albumin and total lymphocyte count to predict postoperative prognosis. In Japan, where the waiting list is based on a first-come first-serve basis, determining the time for listing can be difficult. Based on their research, PNI could be useful to help determine urgency or when to list a patient with advanced lung disease.

While it is known that the extremes of weight (both under and over) are associated with worse post-transplant outcomes, it is not clear the cause of mortality for these patients. In their retrospective review of the UNOS dataset, **Michaela R. Anderson, MD** and their team found that recipients with BMI >36 or <24 were more likely to die of acute respiratory failure, chronic rejection, and primary graft dysfunction. This study was limited by one in five patients having an unknown cause of death and the cause of acute respiratory failure being unclear. Additional work by **Noah Weingarten, MD** and their group demonstrated a significant risk of morbidity and mortality in morbidly obese patients bridged with extra-corporeal support, with a hazard ratio of 2.36 from their review of the UNOS database.

Finally, **Irina Timofte, MD, MS** and their group demonstrated a potential intervention for frail, malnourished patients. In a small pilot study, they demonstrated a standardized nutrition and therapy plan, which decreased intubation time, ICU length of stay, and hospital length of stay.

While further research is needed to determine the best way to approach the frail patient in the pre-lung transplant setting, we continue to make strides toward defining and risk stratifying those at the highest risk.

VIEW SESSION DETAILS

– Summary by Grant Turner, MD, MHA

Preliminary Development of the Lung Transplant Frailty Index
Jonathan P. Singer, MD, MS, University of California San Francisco, San Francisco, CA USA

Molecular Phenotypes of Frailty in Lung Transplant Candidates
Jonathan P. Singer, MD, MS, University of California San Francisco, San Francisco, CA USA

Impact of Prognostic Nutrition Index on the Waitlist Mortality of Lung Transplantation
Kei Matsubara, MD, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Body Mass Index and Cause-Specific Mortality After Lung Transplantation in the United States
Michaela R. Anderson, MD, University of Pennsylvania, Philadelphia, PA USA

Morbid Obesity is Associated with Significantly Higher Risk of Death After Lung Transplant in Recipients Bridged on Extra-Corporeal Support
Noah Weingarten, MD, Cleveland Clinic, Cleveland, OH USA

Post-Transplant Metabolomics Profiles in Patients Undergoing Lung Transplantation
Irina Timofte, MD, MS, University of Texas Southwestern, Dallas, TX USA

SESSION 48: Cut to the Chase: Lung Transplantation from the Operating Room to the ICU

Clamshell Incision for Lung Transplantation

Mani Daneshmand, MD, Emory University, Atlanta, GA USA

Dr. Daneshmand started the session by telling us a history of clamshell incision that was first described in the early 1900s as a good technique to repair thoracic vessels injury from trauma. In the early 1990s, it was brought into lung transplant and allowed massive growth in the field. However, there are some disadvantages of a clamshell incision. First, it is a big incision and causes a lot of tissue damage, thus more bleeding and transfusions. It causes significant pain compared to median sternotomy.

There are several advantages to a clamshell incision as well. Clamshell incision provides excellent exposure, so it is good for teaching trainees. Adhesion in pleural space is easier to be removed by this technique. It is easier for concomitant heart surgery such as CABG or MV repair if needed. It also facilitates off-pump bilateral sequential lung transplant. Studies have shown that vital capacity post-lung transplant is lower compared to median sternotomy. However, there was no difference in survival.

Median Sternotomy for Lung Transplantation

John Dark, MB, FRCS, Newcastle University, Newcastle-upon-Tyne, UK

Next, Dr. Dark discussed median sternotomy for a lung transplant. He started by telling us the advantages/disadvantages of median sternotomy. To open and close is rapid/easy for median sternotomy. It also facilitates central cannulation and provides good access to hilar structures. Median sternotomy was used regularly to perform heart-lung transplants in the 1990s. It was utilized in the setting of single lung transplant after previous pneumonectomy. It is also a technique used in older patients with COPD for bilateral lung transplant, as the incision will be smaller compared to clamshell as the chest is bigger in this population. It initially was always done with cardiopulmonary bypass, then with ECMO, and more recently off-pump bilateral lung transplant.

Dr. Dark also shared his clinical experience in Newcastle from 1995-2020. He compared the outcome of lung transplant between clamshell (n=448) and median sternotomy (n=177) and found that early lung function (FEV1 and FVC) was better in the median sternotomy group and there was no difference in 30-day survival, one year but no long-term benefit from median sternotomy.

Minimally Invasive Lung Transplantation

Pedro Catarino, MD, Cedars-Sinai, Los Angeles, CA USA

Dr. Catarino then introduced us to minimally invasive lung transplantation. Given that lung transplant is a big, long operation, usually done in elderly patients with frailty, we should not only focus on incision but look at patients as a whole. Sometimes, a bigger incision that gives better exposure and allows the surgery to be done more quickly with less operative time is better for patients.

He defined “minimally invasive” as an incision that the surgeon could not put the hand in, usually 6-8 cm. This technique was introduced in Cedars Sinai in March 2021. Since March 2021, a total of 75 cases of lung transplants were performed at Cedars Sinai, and 41 cases were performed using a minimally invasive technique. The indications for lung transplant were not different between the non-minimally invasive group and minimally invasive group, and the most indication was ILD. ECMO support was required in less than 50% of the minimally invasive group. Above 50% of the minimally invasive group were older than 65 years old.

At Cedars Sinai, patients who underwent lung transplants with this technique required fewer analgesics and less ICU length of stay. Although the time to implant the lungs are higher in the minimally invasive group (65 minutes vs 55 minutes), There were no patients who developed primary graft dysfunction in this group.

Finding the Way In: Transplant After Previous Thoracic Surgery
Goran Dellgren, MD, PhD, Sahlgrenska University Hospital, Goteborg, Sweden
Dr. Dellgren then discussed risk assessment, operative techniques, and challenges to consider in patients with prior chest surgery. In previous studies, the outcomes (PGD and survival) were not different in patients who underwent previous thoracic surgery compared to patients without previous thoracic surgery, although the ICU length of stay was longer in the group with previous thoracic surgery. Similarly, post-transplant survival of patients with previous lung volume reduction surgery (LVRS) was not different from patients without LVRS.

On the contrary, in re-transplantation, the outcomes were shown to be significantly worse. Lung re-transplantation was shown to have a median survival of only 2.5 years. It was usually done during the first month of primary lung transplant due to PGD, graft failure, or airway complications. Data from registry and a study from Scandinavian countries showed that the survival of lung re-transplantation has improved in later years compared to the earlier years of lung transplantation. There is no clear data on whether it should be done by a single or bilateral lung transplant. Data from one single center showed that most lung re-transplants (80%) were performed with single lung transplant. HR was 1.7 for mortality at one year in the re-transplant group compared to primary lung transplant.

There is no consensus on how to do re-transplantation. In patients with a previous single lung transplant, contralateral re-single lung transplantation should be considered. For patients with previous double lung transplants, consider re-transplant as single in patients above 50-55 years old, on the side with fewer adhesions and worse function (deemed by V/q scan). While patients < 50-55 years old, re-double lung transplant can be considered. Re-transplantation is questionable in patients above 60-65 years old, in those with dialysis, in those who are on ventilator or ECMO due to the poor outcome.

Post-Operative Pain and Analgesic Strategies
Theresa Gelzinis, MD, Presbyterian Hospital, Pittsburgh, PA USA
Dr. Gelzinis discussed pain and analgesic strategies in post-operative lung transplantation. Pain

control in lung transplant is challenging due to the variety in patient population and diagnosis, surgical approaches (clamshell incision is associated with the highest pain and anterolateral thoracotomy is least painful), and whether ECLS was used or not (nerve blocks is contraindicated in anticoagulated patients).

Inadequate postoperative analgesia can lead to hemodynamic instability and respiratory complications. It also impairs immunologic response, metabolism, hemostasis, and cognitive function. It has been shown to increase ICU length of stay and development chronic post-thoracotomy pain. There is no standard regimen as most data/evidence came from small observational/retrospective studies.

Common strategies for pain control include:

1. Intravenous opioid or non-opioids (ketamine, lidocaine, gabapentin, acetaminophen, ketorolac). These agents need to be used with caution given systemic side effects, especially opioids, which can cause respiratory depression, cough suppression, drowsiness, ileum, and urinary retention. Long-term use is associated with reduced lung function and survival.
2. Nerve block:
    1. Neuraxial technique: Thoracic epidural anesthesia and analgesia (TEA) is the gold standard of neuraxial technique. TEA prevents excessive sedation, allows early extubation, and reduces the incidence of pulmonary complications. However, the failure rate is 23% due to difficulty in placement. It cannot be placed in anti-coagulated patients. It can cause hypotension, motor weakness, pruritus, urinary retention, and epidural abscess/hematoma. Paravertebral nerve block (PVB) can be performed unilaterally for patients with single lung transplant to preserve contralateral intercostal muscle function. it has similar efficacy to TEA, but patients require higher opioids compared to TEA.
    2. Truncal nerve block (intercostal, serratus anterior, erector spinae) provides less analgesia than neuraxial blocks but has a lower complication rate.

Lastly, Dr. Gelzinis presented a study by Lewis et al, who developed an opioid-sparing technique with intercostal nerve block with liposomal bupivacaine and adjunctive therapy (gabapentin, acetaminophen, ketorolac, methocarbamol) and found that patients receiving this technique had better pain control and required fewer opioids for breakthrough pain.

Respiratory Mechanics After Lung Transplantation

Monique Malouf, MD, St. Vincent's Hospital, Sydney, Australia

Dr. Malouf discussed the impact of lung transplantation on lung physiology in this talk. Lung mechanic and physiologic changes can occur over months to years following lung transplantation. These changes can be due to changes in chest wall mechanics from a surgical incision, and structural injury (such as phrenic, vagus, recurrent laryngeal, and sympathetic nerve injury) during transplantation. So surgical incision plays a role in post-transplant lung mechanics.

Evidence from previous studies showed that lung function was significantly worse in clamshell

incisions compared to sternotomy or minimally invasive approaches. This may be explained by the restriction of chest wall expansion and compliance caused by the weakness and paralysis of accessory respiratory muscles from rib cage deformation due to this type of incision and the fact that patients with clamshell incision required longer ventilator support.

Mechanical ventilation after lung transplant is also important, as studies showed that recipients of undersized grafts were exposed to higher tidal volume than recipients of oversized grafts, which could be explained by a higher risk of ventilator-induced injury. Undersized allograft was shown to be associated with increased rates of primary graft dysfunction and mortality. Ventilator management based on donor details should be implemented in post-lung transplant care. Lastly, postoperative complications in recipients that fail to achieve predicted lung function may also impact lung function.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SESSION 55: Improving Quality of Lung Transplant Care: Survival is Only the Beginning

The main outcome that every transplant center focus on is survival. However, there are other metrics that significantly impact transplant success which were discussed during **this session**.

What is a Relevant Survival Metric After Lung Transplant?
Jasvir Parmar, PhD, FRCP, Royal Papworth Hospital, Cambridge, UK
Survival is the most common metric used to assess the performance of lung transplant centers. It is binary and easy to collect, and provides longitudinal data. But it does not reflect the quality of life of survived patients, as they may suffer from complications of lung transplantation, prolonged intubation, and side effects of immunosuppressive agents. WHO defines quality of life as an individual's perception of their position in life in the context of culture and value systems and in relation to their goals, expectations, standard, and concerns.

Other aspects to consider when considering the outcome of lung transplants are graft function, treatment burden, comorbidities, financial pressure, and social function. The Lung Transplant Quality of Life (LT-QOL) Survey was developed in 2019 by Singer et al. It is a multidimensional instrument that characterizes and quantifies health-related quality of life (HRQL) in lung transplant recipients. Integrating HRQL in lung transplantation routine clinical care could improve patients' quality of life, patient-physician communication, and direct clinical management.

How to Define Benefit and Success from Lung Transplant Beyond Survival Tools
Joshua Diamond, MD, University of Pennsylvania, Philadelphia, PA USA
Dr. Diamond pointed out that point of view matters when considering lung transplant success. Success in the point of view of SRTR, researcher, and patients may be different. We need to incorporate patients' points of view into the determination of success and this information can be obtained by asking patients what they think is the most important.

The success of lung transplants is more than survival. It can be viewed as a combination of success prior to lung transplant (success in addressing disparities in transplantation, increasing donor allocation) and success after lung transplant (survival, quality of life). Finally, we need to keep in mind that success metrics are not independent and connected with each other.

Assessing Physical Functioning Post-Lung Transplant: How, When and Who Benefits?
James Walsh, PhD, BPhty, The Prince Charles Hospital, Brisbane, Australia
One of the goals of lung transplantation is to improve patients' physical function. Many measures can be used to assess physical function, including CPET, 6MWT, physical activity, the impact of frailty, sarcopenia, or muscle weakness, and health-related quality of life. These measures are usually performed to assess patients at pre-transplantation and the first 12 months post-lung transplantation.

Pre-transplant physical function can significantly impact post-transplant physical function, so

exercise rehabilitation pre-transplant is essential, although there is no data on the optimal structure. The transplant course also impacts physical functioning post-transplant. However, data is limited as most studies exclude patients with prolonged ICU/hospital stay, and recovery for these patients is more difficult. Post-transplant exercise rehabilitation most likely impacts physical functioning post-transplant. However, more studies are needed to determine program modalities, length, and structure.

The Impact of Nutritional State on Post-Transplant Success

Marion Seabaugh, MPH, RD, Stanford Health Care, Stanford, CA USA

Nutritionists are essential members of a multidisciplinary team, and are significantly involved in patient evaluation/patient care during both the pre- and post-transplant phases.

During the pre-transplant phase, patients will be evaluated by a nutritionist for nutritional status, diet, and weight gain/loss history. Nutritionists also perform a nutrition-focused physical examination and assess patients' BMI and frailty. Abnormal BMI (< 18.5, > 35) has been shown to be associated with lung transplant mortality.

Frailty is also common in patients with chronic lung diseases undergoing lung transplant evaluation. It has been shown to be associated with disability and increases the risk of delisting and death. There are several tools used to assess frailty including short physical performance battery (SPPB) and fried frailty phenotype (FFP). SPPB has a stronger association with disability, risk of delisting, and death than FFP. Patients with malnutrition/frailty will be labeled as high risk and targeted for aggressive intervention. In addition to a nutritionist consult, patients will be evaluated and treated by a physical therapist; and evaluated by a social worker to identify other factors such as polypharmacy, lack of social support, or cognitive impairment that can contribute to the problem.

During the post-transplant phase, the nutrition goal is early feeding within 48 hours of admission to ICU to attenuate catabolic response and facilitate recovery of patients in order to participate in rehabilitation. Early feeding maintains integrity and modulates stress and systemic immune response and has been shown to reduce mortality, infection morbidity, hospital length of stay, and the likelihood of discharge to the facility.

Post-Transplant Medication Adherence as an Outcome and a Risk Factor

Fabienne Dobbels, MSc, PhD, University Hospital Leuven, Leuven, Belgium

Non-adherence to immunosuppressive agents post-transplant is a widespread problem. A systematic review of 12 studies before April 2015 reported a non-adherence rate of 2.7-72.3%. However, these studies used different measures (most studies used self-report) and definitions for non-adherence. The observation period also ranged from four weeks to two years. Consensus is needed on how to measure and define non-adherence to be used in clinical practice, and research, and to obtain good clinical outcomes.

Non-adherence is a risk factor for poor outcomes, as data from the UNOS registry showed that the rate of non-adherence in the first year post-lung transplantation was 3.1% and increased to 10.6%

at 2-4 years post-transplantation. The non-adherence group had shorter median survival compared to the adherence group. Adherence has also been shown to increase graft loss and mortality rate at five years post-transplantation.

Studies showed that non-adherence can be modified with intervention and may improve long-term outcomes. In conclusion, adherence is a key outcome and should be integrated into all future drug and outcome studies. Investing in adherence supportive interventions should be prioritized as non-adherence is a risk for poor clinical outcomes.

How to Analyze Psychosocial Benefit for Patients and Caregivers Post-Transplant
Melissa Sanchez, BScHons, PGDip, DClinPsy, MSc, Harefield Hospital, Harefield, Middlesex, UK
A psychosocial benefit may be defined by health-related quality of life, absence of psychological difficulties, active engagement in family life, return to education and employment, or active engagement in sexual intimacy.

There are three approaches to analyzing psychosocial outcomes: a quantitative approach, a qualitative approach, and building positive relationships. Each approach has its own advantages and limitations. Choosing the right approach for analysis depends on who you are conducting the analysis for (patients/caregivers) and what the goal is. Transplant centers may choose to use a combination of approaches for different needs over time.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SESSION 62: Save the Beans: Recognition and Protection of Renal Function in Lung Transplantation

Kidney injury and eventual failure seem all but inevitable for many lung transplant patients. In **this session**, presenters discussed potential opportunities for determining which recipients are at the highest risk for renal failure and potential strategies to mitigate this risk.

First, thinking about evaluating renal function in pre-transplant candidates, **Timothy Whelan, MD**, presented helpful information regarding creatinine and its pitfalls. Measuring the true function of the kidney is difficult, and GFR is assessed via clearance markers such as creatinine, cystatin C, or inulin. While creatinine is widely available, a large number of conditions can alter the level without reflecting changes in GFR. Another marker, Cystatin C, can be more reliable as it is less affected by muscle mass but can be affected by smoking, obesity, inflammation, thyroid disease, and use of glucocorticoids, and may not be widely available. A new measurement of estimated GFR using CKD-EPI combines the use of cystatin C and creatinine and may be more accurate in the assessment of renal function.

Assessment of the renal function both pre- and post-transplant is critical in determining when acute kidney injury (AKI) may be occurring. **Alberto Benazzo, MD**, discussed potential strategies to prevent AKI in the peri- and post-operative period, the incidence of which is estimated to be 12-68%, including volume management, transfusion management (oxygen delivery), and drug management to limit nephrotoxic agents. Primary graft dysfunction (PGD) likely has a relationship with AKI as well, and thus attempting to prevent PGD may have a protective effect. Molecular biomarkers which are more sensitive may allow for better prediction, definition of AKI in the future.

Can we impact renal function by changing the maintenance immunosuppression used in our transplant patients? **Jens Gottlieb, MD**, reviewed the available literature regarding this known issue in lung transplant, often because of the use of tacrolimus and standard triple therapy immunosuppression. Retrospectively comparing the use of tacrolimus, cyclosporine, and types of cell-cycle inhibitors demonstrated no difference in renal function. Some centers will use mTOR inhibitors (everolimus or sirolimus) to decrease the dosage of tacrolimus, which helps in early renal function but not in long term outcomes (NOCTET, 4EVERLUNG studies). Belatacept is being used in other solid organ transplants to allow for withdrawal of tacrolimus, but this has not been shown to be an effective immunosuppressant in lung transplant. More research is being completed to determine if an extended-release tacrolimus would benefit renal function, and looking at torque tenovirus viral load for better determination of optimal immunosuppression.

Beyond immunosuppression, what can we do to alter the course of chronic kidney disease? **Anil Chandraker, MD, MBChB**, presented potential strategies, including treating any underlying factors continuing to cause kidney injury, blood pressure management including RAAS blockade, reducing salt intake, and treatment of metabolic acidosis.

Finally, **Miranda Paraskeva, MBBS, FRACP, MD**, discussed whether renal dysfunction should be a contraindication to lung transplant. Currently, multi-organ transplantation with lung and kidney is uncommon, and more likely to happen in younger diabetic patients. In those with pre-existing renal dysfunction, there is known high waitlist mortality in absence of concurrent kidney transplant, and kidney transplantation confers survival advantage. Ethical issues exist with this use of multiorgan transplantation, however, since it bypasses the existing waitlist, and the majority of multiorgan transplants will die with a functioning kidney, disturbing the balance between justice and utility.

VIEW SESSION DETAILS

– Summary by Grant Turner, MD, MHA

Into the Looking Glass: Evaluating Renal Function in Pre-Transplant Candidates
Timothy Whelan, MD, Medical University of South Carolina, Charleston, SC USA

Putting Up a Shield: Protective Peri- and Post-Operative Strategies to Prevent Acute Kidney Injury
Alberto Benazzo, MD, Medical University of Vienna, Vienna, Austria

Clinical and Molecular Epidemiology of AKI and CKD Post-Transplant
Michael Shashaty, MD, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA USA

Diving Deep: Maintenance Immunosuppression Strategies for Renal Protection
Jens Gottlieb, MD, Hannover Medical School, Hannover, Germany

Tricks of the Chronic Kidney Disease Trade

Anil Chandraker, MD, MBChB, Brigham & Women's Hospital, Boston, MA USA

To Transplant or Not to Transplant?
Miranda Paraskeva, MBBS, FRACP, MD, Alfred Hospital, Melbourne, Australia

SESSION 66: Navigating the COVID Pandemic: Clambering into the Lung Transplant Life Raft

Many questions exist regarding the ongoing COVID-19 pandemic: how can we protect our patients with advanced lung disease, how can we prevent infection in our lung transplant population, and when is the right time to consider lung transplant for COVID-19 infection? **This session** attempted to answer many of these questions with a review of available data.

First, **Kathleen Murphy, MD**, discussed how we can prevent COVID-19 infection. Evaluation of the risk of infection is crucial, especially finding those which are modifiable such as vaccination. The currently available COVID-19 vaccines are known to have variable immunogenicity in solid organ transplantation, increasing the discussion on how we can optimize this key component of risk mitigation. Potential strategies discussed included the optimal boosting interval, finding variant-specific boosters, improving immune response by mixing vaccine platforms, and potentially decreasing immunosuppression around the time of vaccination. Additionally, the use of pre-exposure prophylaxis (PrEP) with Evusheld to reduce the risk of serious illness is key. Finally, counseling patients on safe living is crucial by ensuring close contacts are vaccinated, maintaining awareness of community transmission rates, continuing the use of masking, and undergoing risk assessment for crowded events.

While COVID-19 is known to cause severe acute respiratory failure, what other organ systems is it known to affect? **Olivier Manintveld, MD**, reviewed these complications in depth. From a cardiac standpoint, COVID-19 is known to have direct viral toxicity, causing an inflammatory response and thrombosis, as well as potential long-term consequences of recurrent myocarditis, heart failure, arrhythmias, etc. COVID-19 may increase the risk of gastroesophageal reflux and induce a change in the gut microbiome. Neurologically, it has been correlated with loss of taste and smell, cognitive impairment, and hearing loss. The virus itself and the global pandemic have also caused significant mental health concerns with increased rates of depression, anxiety, insomnia, OCD, and agoraphobia. Finally, COVID-19 has been implicated in reproductive health issues with potential impaired fertility and adverse pregnancy outcomes.

For those patients with COVID-19 ARDS, it can be difficult to know when the optimal time is to consider lung transplantation. **Konrad Hoetzenecker, MD, PhD**, reviewed this topic, first thinking about the history of lung transplant for ARDS; data from Europe demonstrates 30 transplants with 60% five-year survival in those with a pre-transplant diagnosis of ARDS. UNOS's criteria include no improvement despite optimized therapy for a minimum of two weeks, absence of signification ECMO-related complications or extrapulmonary disease, no neurological damage, and adequately treated infection, all while meeting the agreed-upon international criteria for listing. While not standardized, most centers have selection criteria for COVID-19 ARDS lung transplant which include: negative PCR for COVID-19, no improvement on mechanical ventilation or ECMO for 4-6 weeks, persistent consolidation or severe fibrotic changes of the lungs affecting all lobes, single organ failure without severe comorbidities, and potential for long-term recovery.

Unfortunately, our advanced lung disease patients on the lung transplant waiting list occasionally develop COVID-19. **Erika Lease, MD**, reviewed strategies to optimize such patients. The general consensus of the community is to avoid transplant in acute or very recent COVID infection. The COVIDSurg collaborative group studied the optimal timing of any surgery after COVID infection and found seven weeks to be the time when mortality was no longer increased compared to non-COVID infected controls. ISHLT guidelines suggest awaiting clinical resolution of symptoms and >21 days in the immunocompetent and one negative PCR (can decrease to 14 days if high risk of mortality), or >14 days with negative PCR if asymptomatic.

Finally, we discussed the management of post-lung transplant patients who developed COVID-19. **Cameron R. Wolfe, MBBS, MPH**, reviewed the currently available information, which of note is an ongoing and ever-changing issue. The NIH guidelines are a helpful resource for up-to-date recommendations (available here: **https://www.COVID19treatmentguidelines.nih.gov/**). At the time of the conference, four treatments currently exist including Paxlovid, Remdesivir, Bebtelovimab, Molnupiravir. Unfortunately, Paxlovid, an oral treatment, has significant drug-drug interactions which severely limit its use, especially in lung transplant patients secondary to tacrolimus. Currently, no post-exposure prophylaxis currently exists, but Evusheld should be given for PrEP in all who qualify.

VIEW SESSION DETAILS

– Summary by Grant Turner, MD, MHA

COVID-19 Vaccination and Prevention Strategies
Kathleen Murphy, MD, Penn Medicine, Philadelphia, PA USA

It's Not Just the Lungs: Extrapulmonary Manifestations of COVID-19
Olivier Manintveld, MD, Erasmus Medical Center, Rotterdam, Netherlands

Recipients with COVID-19: When Can/Should We Transplant?
Konrad Hoetzenecker, MD, PhD, Medical University of Vienna, Vienna, Austria

Optimization of the COVID-19 Infected Lung Transplant Candidate
Erika Lease, MD, University of Washington, Seattle, WA USA

Management of the COVID-19 Infected Lung Transplant Recipient
Cameron R. Wolfe, MBBS, MPH, Duke University Medical Center, Durham, NC USA

SESSION 45: Molecular Assessment of Lung Allograft Injury

While bronchoscopies with transbronchial biopsies and bronchoalveolar lavage (BAL) are the standard of care for evaluation of rejection and infection in lung transplant recipients, research is underway to identify new modalities that might add additional information to the evaluation of allograft injury post-lung transplant patients. First up in this Friday **oral session**, we discussed the use of donor-derived cell-free DNA (ddcfDNA). How can we determine the right cutoff for allograft injury? Prospectively, **Justin Rosenheck, DO**, and his lab at The Ohio State University used samples from multiple centers that were correlated with transbronchial biopsies; their group aimed to determine the statistical cutoffs for three levels of ddcfDNA cutoffs - 0.5%, 0.85%, and 1%. They found that while the performance of ddcfDNA at timepoints less than six months post-transplant was poor, a ddcfDNA threshold of 0.5% achieved a high negative predictive value at six months post-transplant for acute histological allograft injury.

Challenging the use of current use of donor fraction (%) of ddcfDNA as the only clinically significant cutoff, Dr. Rosenheck then presented data from his group reviewing the use of absolute ddcfDNA quantity (cp/mL) to improve the test performance. Using samples from their center with known bronchoscopic outcomes, they were able to demonstrate similar test characteristics with higher levels of absolute ddcfDNA as compared to % donor fraction. His group posits the use of the absolute amount of ddcfDNA in the evaluation of allograft health, with further research needed. Later, the concept of adding a metagenomics next-generation sequencing panel to ddcfDNA to identify potentially pathogenic viral, bacterial, and fungal genomic markers in samples that could be contributing to allograft injury was presented. In this pilot study, using BAL fluid, a significant number of potentially pathogenic microbial targets were identified, which could affect the ultimate “clinical-pathological diagnosis” when combined with TBBx/BAL in 22.5% of cases.

Adding to this, **Mena Botros, MD**, also from The Ohio State University, summarized data from the same center looking at tissue gene expression in acute cellular rejection and found specific genes upregulated related to adaptive immune system recruitment and chemotaxis. Analysis of tissue gene expression in these patients may also assist in identifying potential therapeutic targets moving forward.

Next, we explored primary graft dysfunction (PGD) and natural killer (NK) cells. While PGD is well defined and risk factors are known, the molecular etiology behind it is unclear. Presented by **Daniel R. Calabrese, MD**, his group at the University of California San Francisco has hypothesized that NK cells mediate PGD via recognition of stress molecules. In sham models of PGD in mice, NK cells were upregulated along with NKG2D, a stress molecule, and MICB. This was then confirmed in human samples, with elevated NKG2D and MICB being elevated in the BAL fluid of patients who developed PGD and was associated with poor clinical outcomes. The hope from this study is that NKG2D may be an attractive therapeutic target for patients with PGD to prevent the poor outcomes related to PGD, or potentially prevent PGD from ever occurring.

Finally, we reviewed the topic of aspiration and its relation to chronic lung allograft dysfunction (CLAD) in a presentation from **Rayoun Ramendra, BSc**. It is known that gastroesophageal reflux disease (GERD) is associated with increased bacterial pulmonary biomass, likely due to aspiration and bacterial overgrowth. Increased bacterial load in BAL fluid has also been associated with CLAD progression in lung transplant recipients. In this study, it was theorized that aspiration of Lipopolysaccharide (LPS), a major component of the gram-negative bacterial cell wall, causes innate immune activation resulting in an increased risk of adverse outcomes in lung transplant recipients. By examining BAL fluid, they were able to demonstrate that LPS was associated with gram-negative infection and bacterial colonization, GERD and markers of aspiration, activation of the innate immune system, and an increased risk of CLAD.

VIEW SESSION DETAILS

– Summary by Grant Turner, MD, MHA

Performance of Donor-Derived Cell-Free DNA (dd-cfDNA) for Discriminating Acute Lung Allograft Injury in a Multicenter Cohort
Jamie L. Todd, MD, MHS, Duke University Medical Center, Durham, NC USA

Quantitative Donor-Derived Cell-Free DNA Levels Reflect the Variability in Lung Allograft Cellular Injury
Justin Rosenheck, DO, The Ohio State University, Columbus, OH USA

Donor-Derived Cell-Free DNA Plus Tissue Gene Expression Profiling of Lung Allograft Injury
Mena Botros, MD, The Ohio State University, Columbus, OH USA

Metagenomic Next Generation Sequencing (mNGS) Can Complement Fractional Donor-Derived Cell-Free DNA in Lung Allograft Assessment: Pilot Data
Justin Rosenheck, DO, The Ohio State University, Columbus, OH USA

Bronchoalveolar Lavage MICB is Associated with Severe Primary Graft Dysfunction, Prolonged Mechanical Ventilation, and Low Post-Transplant FEV1 in Lung Transplant Recipients
Daniel R. Calabrese, MD, University of California San Francisco, San Francisco, CA USA

Pulmonary Endotoxin is Associated with Reflux, Inflammation, and Adverse Outcomes in Lung Transplant Recipients
Rayoun Ramendra, BSc, Ajmera Transplant Center, Toronto, ON Canada

SESSION 59: Age, Size, Location: Studies in Survival after Lung Transplant

Are the LAS Models Accurate Predictors of Mortality?

Carli J. Lehr, MD, MS, Cleveland Clinic, Cleveland, OH USA

The aim of this study was to evaluate the overall and subpopulation prediction accuracy of LAS models and compare results to alternative modeling. This study found that all models had high discrimination performance for the waitlist model. The discrimination performance decreased with increased forecasted time. Post-transplant discrimination performance was similar across models and stable with increasing forecasting times. No alternative model clearly performed better than the LAS. Strategies to optimize discrimination and calibration in lung allocation models are essential to accurate prediction of transplant benefits.

The Impact of Geographical Distance on Survival in Adult Cystic Fibrosis Lung Transplant Recipients

Shivani U. Patel, BS, Johns Hopkins University, Baltimore, MD USA

The aim of this study was to assess the association of geographical distance with survival among adult cystic fibrosis lung transplant recipients (CF LTx) in the US. This was a retrospective study using SRTR including 2,838 adult CF LTx from 2005-2019. The geographical distance was determined between the recipients' zip code and their transplant center zip code. Patients were stratified into three groups based on distance.

The study found that there was a significant difference in survival by distance traveled. Patients who lived within 50-150 miles or more than 150 miles of the transplant center had a higher risk of mortality with an HR of 1.2 and 1.29, respectively. Geographical distance is an important factor in consideration of access to care post-lung transplant. Further investigations of the causes that contribute to this observation may help improve the survival rate of CF LTx.

Recipient Outcome After Lung Transplantation from Older Donors (⩾70 Years) Equals Younger Donors (< 70 Years): A Propensity-Matched Analysis

Cedric Vanluyten, BSc, University Hospital Leuven, Leuven, Belgium

This study aimed to examine and compare short- and long-term outcomes of lung transplantation (LTx) between the younger donors (<70 years) and older donors (⩾70 years) using propensity-matched analysis. A total of 695 LTx were performed between 2010 and 2020. 69 with donors ⩾ 70 years were identified. 1:1 matching was performed for donor and recipient characteristics.

The study found that there were no significant differences observed in the length of ventilatory support, ICU, or hospital stay. PGD grade 3 rates were similar (26.1% vs 29%, p=0.85). Reoperation rate and anastomotic complications were comparable. The 5-year survival was 73.6% in the older donor group (73.1% in the younger donor group, p=0.72). CLAD-free 3- and 5-year survival were also comparable. Short- and long-term outcomes were similar between LTx from donors ⩾ 70 years and LTx from younger donors < 70 years.

Actual Size Mismatch in Lung Transplantation for Restrictive Lung Disease

George Gill, MD, Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA USA

Donor-recipient size mismatch is associated with worse outcomes in lung transplantation. Donor to recipient predicted TLC ratio is increasingly used for size matching in lung transplantation, but this can overlook the reduction in actual TLC in restrictive lung diseases. FVC is a surrogate for actual TLC and may better predict actual lung size mismatch. The aim of this study was to evaluate donor-predicted : recipient actual FVC ratio as a metric for quantifying size match in lung transplantation for restrictive lung disease using the UNOS database.

The investigators included a total of 7,572 patients with restrictive lung diseases undergoing bilateral lung transplantation from 2005-2021. Lung size mismatch was quantified by donor : recipient FVC ratio, and divided into quintiles. They found that the highest quintiles of FVC ratio was an independent predictor of mortality in multivariable analysis (HR=1.2, 95%CI 1.1-1.4). Spline analysis indicated that an FVC ratio > 3.45 significantly predicted a worse outcome. Undersizing and oversizing with respect to recipient actual FVC results in worse adjusted long-term survival, emphasizing the importance of considering recipient actual lung volumes in donor-recipient matching.

Long-Term Weaning of Mechanical Ventilation After Lung Transplantation: Patient Characteristics and Impact on Survival

Lucille Hu, MPH, Case Western Reserve University, Cleveland, OH USA

This study aimed to characterize post-lung transplantation (LTx) patients with the prolonged postoperative course, including long-term weaning of mechanical ventilation; to identify risk factors of prolonged mechanical ventilation (PMV); and to study the impact on survival. This was a retrospective study that included 1,138 adult LTx performed in single center from January 2008 and January 2009. Of 1,138 adult LTx, 58 patients (5%) underwent PMV > 60 days. Risk factors for PMV were bridging on MV, double LTx, concomitant cardiac procedure, re-exploration for bleeding, and higher grade primary graft dysfunction.

At the listing time, these patients had higher LAS, greater chest wall soft tissue to pectoral muscle thickness, lower 6MWD, and increased bridging on MV. One-year survival was lower in this group (59% vs 86%, p<0.01). However, three- and five-year survival were not different. Lex recipients with PMV have baseline characteristics and underwent more complex procedures which resulted in complicated peri-operative course, and worse early outcomes and survival. Identifying these risk factors of PMV may help optimize candidate selection for LTx.

Long-Term Outcome and the Radiological Evaluation of Lung Growth After Living-Donor Lobar Lung Transplantation in Pediatric Patients

Satona Tanaka, MD, Kyoto University Hospital, Kyoto, Japan

This study aimed to evaluate the short- and long-term outcome and longitudinal functional and radiographic change of transplanted adult lobe in growing pediatric recipients undergoing Living-Donor Lobar Lung Transplantation (LDLLT). Thirty pediatric LDLLT cases between 2008 and 2020 were reviewed (12 unilateral transplantation of the right lower lobe, 13 bilateral transplantation of 2 lower lobes, and 5 others including segmental and middle lobe transplantation).

Ten-year overall survival was 76.8%, while CLAD-free survival was 64.4%. In 12 recipients who

were followed up for more than five years, the mean increase in height, vital capacity, and graft volume were 15.9, 14%, and 55.4% respectively. The transplanted graft volume exceeded the original volume in the donor's chest in 11 of 12 recipients. Radiologic graft weight increased by 6.6% at three years post-LDLLT. Pediatric LDLLT provides satisfactory long-term outcomes. Graft function is sufficiently maintained long-term after LDLLT with the radiological evidence of lung growth.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SESSION 78: Human Versus Beast: Advances in Translational Models of Lung Transplant

Animal models could be used to study the processes and investigate underlying mechanisms and therapeutic interventions of lung transplant disease pathogenesis. A variety of lung transplant models was reviewed and discussed in **this session** on how we can use animal models to improve our understanding of lung transplant pathophysiology.

Rat Models: A Window of Opportunity

Dong Tian, MD, The University of Tokyo Graduate School of Medicine, Tokyo, Japan

The ideal animal should be able to provide physiological and anatomical similarities to the human disease process. It should be cost-efficient, technically stable, and easy to handle. The rat model was first developed in 1971 and has since been used to study several lung transplantation models. The advantages of the rat model include weight and size, which allows one performer to develop the model compared to larger animals. Complicated techniques such as EVLP and re-transplantation can be applied in the rat model, and serial blood sampling is more feasible in rats, compared to the mice model (researchers are able to obtain more blood from rats).

Another advantage of the rat model is low surgical complexity. There is no technical difficulty in heterotypic or orthotropic tracheal or bronchial implantation. Orthotopic left lung transplantation can be done by Dr. Tian's group's "Pendulum" model within 48 minutes without intraoperative failing. The cost of the rat model is cheap, and this is helpful when trying to screen novel treatments prior to proceeding to large animal models.

The short gestation period and life span of rats also allows investigators to increase sample size in a short timeframe, which increases the replicative value in research, leading to more robust and credible results. A rat model has been used to develop a model to study ischemia-reperfusion injury, allograft rejection, ex vivo lung perfusion, and decellularization (bioartificial lung).

Mouse Models: The Golden Standard?

Andrew E. Gelman, PhD, Washington University School of Medicine, St. Louis, MO USA

Dr. Gelman discussed the murine model in lung transplantation in this session. The mice model has been used in lung transplantation research due to the similarity of general anatomic organization of human and mouse lungs, the cost-effectiveness of the model, and the opportunities to investigate genetic manipulations.

The first model using mice (heterotrophic tracheal transplantation) was developed in 1993 by a group of investigators at the University of Minnesota. This model produces a histopathological appearance of obliterative bronchiolitis in seven days, and continues to be a highly used BOS model due to technical ease. The drawback of this model is that the airway was not vascularized, and there is a lot of immunologic stress.

Orthotopic tracheal transplantation from a mice model was developed at Mount Sinai in 2002

with an end-to-end anastomosis. This model demonstrates a loss of ciliated cells and high amounts of lymphocyte infiltrate by three weeks, and subbasement fibrosis by four weeks. The drawback of this model is allografts undergo recipient-derived re-epithelialization, which does not happen in humans.

Orthotopic lung transplantation was developed in 2006 at Washington University. It is technically challenging and took about six months to learn. It has been used to study PGD, ACR, AMR, and CLAD. There are several drawbacks of the mice model. The regenerative response to lung tissue injury is prominent in this model. Mice have a different spatial distribution of club cells, and immune system dissimilarities. Finally, an altered microbiome and sterile facility housing can alter the immune response.

Xenotransplantation and Beyond
Megan Sykes, III, MD, Columbia Center for Translational Immunology, Columbia, NY USA
Xenotransplantation is transplantation from another species. It could provide unlimited organ supply, alleviate organ shortages, and allow transplants to be performed electively as there is no need to wait for donors. Organ survival in xenotransplantation has improved since the 1980s from minutes to months due to better immunosuppression.

There are three major approaches to overcoming immune barriers to xenograft: immunosuppression, genetic engineering, and tolerance. Recent studies showed that the survival time of xenotransplantation of a heart from pigs to non-human primates lasted for about six months. In 2021, that has been prolonged to nine months by using an organ from genetic modification "10-GE pig," including growth hormone receptor knockout. This is the same approach that lead to the first pig to human heart transplantation that was performed recently in the United States.

For lung and liver xenotransplantation, the graft survival was only two and four weeks, respectively. Tolerance is necessary to get permanent graft survival without excess immunosuppression. There are two approaches for xenograft tolerance: mixed chimerism and thymic transplantation. Mixed chimerism involves the coexistence of donor and recipient hematopoietic systems. It can tolerate most of the immune system (T cell, B cell, and partial NK cell tolerance). The second technique of xenograft tolerance is thymic transplantation. The combination of these two techniques using further genetic modification could make xenotolerance clinically achievable and safe.

The Ex-Vivo Lung as an Experimental Mechanistic Model of Transplant
Ciara Shaver, MD, PhD, Vanderbilt University Medical Center, Nashville, TN USA
Ex vivo lung perfusion (EVLP) provides a platform for transcriptomic, proteomic, and metabolic assessment of potential donor lungs. Moreover, advanced assessment can be performed in EVLP to evaluate gas exchange, biomarkers, and imaging studies. The possible disadvantages are variability between lungs (especially if using declined donor lungs), limited duration, and logistic challenges. EVLP with declined human donor lungs is a useful tool for mechanistic research.

Injury can be induced in this model by either intravenous or intrabronchial instillation by infectious or sterile insults, and injury can be detected within two hours. This model can test the causal roles of molecules and pathways. However, the current EVLP systems are limited by 6-8 hours due to mitochondrial injury, altered glucose utilization, impaired amino acid clearance, and shift in lipid utilization. Bioenergetic and metabolic support is limited to 6-12 hours and is associated with lung health deterioration. Temperature management and xenogeneic platforms may facilitate organ recovery and rehabilitation.

Clinical Interventions with Ex-Vivo Perfused Lungs
Marcelo Cypel, MD, Toronto General Hospital, Toronto, ON Canada
Dr. Cypel reviewed existing evidence for EVLP therapeutic interventions, and covered novel interventions in EVLP. EVLP allows the transplant team to assess and optimize organs prior to transplantation. The conditions of organs that could be optimized by EVLP include pulmonary edema, pneumonia, aspiration, chronic viral infection (HCV), or long warm ischemia in controlled and uncontrolled DCD.

Treatment strategies that have been studied in EVLP are perfusion therapy (solution with UVC light for HCV treatment, Rituximab for EBV infection), drugs (high dose antibiotics to reduce bacteria), inhaled gases (high dose inhaled nitric oxide above 200 ppm acts as an antimicrobial through nitrosylation of bacterial chromosome), cell therapy, immuno-cloaking, and gene therapy (conversion human donor blood type ex vivo).

In the future, EVLP could be a platform for major advances in organ transplantation including cell and genetic modification, organ modification in xenotransplantation, and a platform for patients' own organ repair.

How Well Do Animal Models Mimic the Human Condition?
Fiorella Calabrese, MD, University of Padova, Padova, Italy
Dr. Calabrese concluded the session with things we should consider when using animal models to conduct a study on lung transplantation. The ideal animal model should provide strong physiological/anatomical similarity to a human disease process.

Unfortunately, the ideal model does not exist yet. Investigators should know the lung anatomy of animal models, which animal (small, large, genetically modified) is suitable for which disease pathologies, and graft pathology lesions. In conclusion, there is no perfect animal model and continuous effort should be made to collect translatable data to select an appropriate model.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH

SESSION 72: COVID Consequences: Can We Protect the Lung?

The effect of COVID-19 on lung transplant patients remains an intense research focus. In **this abstract session**, presenters discussed the use of lung transplant for COVID-19 fibrosis, findings from COVID-19 explants, the effect of COVID-19 on transplant function, and continued discussions regarding the effectiveness of COVID vaccination.

First, **Donna K. Phan, MD, MPH**, of Montefiore Medical Center in New York, NY USA presented the experience in the United States of the use of lung transplant for COVID-19 fibrosis. Broadly, outcomes in this cohort are limited due to the time period since COVID-19 has existed, but they were able to extract 30-day mortality, length of stay, and adverse events. Reviewing the UNOS/OPTN database from Jan 2018 through July 2021 and comparing COVID fibrosis patients to patients with IPF, individuals transplanted for COVID-19 were: younger, more likely to get a bilateral transplant, three times more likely to be Hispanic, and had shorter times on the waitlist with a higher allocation score. Most notably, the IPF vs COVID-19 cohorts had no significant differences in 30-day mortality and hospital length of stay.

Moving forward to autopsy studies of COVID-19 lungs, Sravanthi Nandavaram, MD, of the University of Kentucky in Lexington, KY USA described the damage that is caused by the viral infection as diffuse alveolar damage that is heterogeneous with organizing pneumonia, pulmonary hemorrhage, and microthrombi. Alveolar capillary microthrombi are 9x more prevalent in COVID ARDS than in influenza ARDS. Looking at a cohort of COVID-19 patients, most had traction bronchiectasis (84%) and consolidations (80%) on CT imaging, and on pathology had NSIP (76%), pulmonary vascular injury (72%), and alveolar hemorrhage (56%).

Thinking now of lung transplant patients who developed COVID19, **Elizabeth Roosma, MD**, of Martini Ziekenhuis in Groningen, Netherlands, described a review of 74 COVID-19 lung transplant recipients and their outcomes. Out of their cohort, 57% were hospitalized, 45% in the ICU, and 64% survived (overall mortality 20%). Of those were not hospitalized for their disease, mortality was 0%. Long term, they noted that FEV1/FVC was significantly decreased at three and six months, but there was no significant difference in hospitalized vs non-hospitalized patients. Finally, they did note a trend towards higher mortality in transplant recipients with pre-existing CLAD.

Next, **Gaelle Dauriat, MD**, from Marie Lannelongue Hospital in Le Plessis Robinson, France, presented the French experience with vaccine response in lung transplant recipients, including Pfizer, Moderna, and AstraZeneca vaccines. Their primary outcome was to determine the proportion of patients with a protective level of antibody, with a secondary outcome to determine the proportion of patients with COVID-19 infection and severity of disease. They noted four factors are associated with vaccine response: younger, delay between transplant and vaccination, not being on steroids or MMF. Interestingly, they noted no difference in COVID-19 infection or severity in vaccine responders vs non-responders.

An additional factor for determining vaccine responsiveness may be the level of torque tenoviremia. **Erik Verschuuren, MD, PhD**, of UMC Groningen Transplant Center in Groningen, Netherlands, presented his work on this subject. Torque tenovirus (TTV) load has previously been described as a directly related marker for level of immunosuppression. In their study of 103 transplant patients receiving the Moderna COVID-19 vaccine, the TTV load did have a correlation with vaccine response, contributing to known data.

– Summary by Grant Turner, MD

The United States Experience of Lung Transplantation in Recipients with COVID-19 Fibrosis: A UNOS/OPTN Analysis
Donna K. Phan, MD, MPH, Montefiore Medical Center, Albert Einstein School of Medicine, Bronx, NY USA

Radiographic and Histopathologic Lessons from COVID-19 Explants
Sravanthi Nandavaram, MD, University of Kentucky, Lexington, KY USA

The Effect of COVID-19 Infection on Transplant Function and Development of CLAD in Lung Transplant Patients: A Multicenter Experience
Elizabeth Roosma, MD, Martini Ziekenhuis, Groningen, Netherlands

SARS-CoV-2 Vaccine Response in Lung Transplant Recipients: A French Multicenter Study
Gaelle Dauriat, MD, Marie Lannelongue Hospital, Le Plessis Robinson, France

TTV Load is Associated with SARS-CoV-2 Vaccination Response in Lung Transplant Recipients
Erik A.M. Verschuuren, MD, PhD, UMC Groningen Transplant Center, University of Groningen, Groningen, Netherlands

Variances in Humoral Responses to Different Spike Protein Domains After SARS-CoV-2 Vaccination in Lung and Heart Transplant Recipients
Jasper Sauer, Medical School Hannover, Hannover, Germany

VIEW SESSION DETAILS

SESSION 75: A Cure for CLAD? Update on CLAD Therapeutics

Treatment of De Novo DSA with IVIG Monotherapy After Lung Transplantation

Skye J. Castaneda, PharmD, Spectrum Health, Grand Rapids, MI USA

De novo donor-specific anti-HLA antibodies (DSA) increase the risk of CLAD and decrease survival. This study aimed to evaluate IVIG monotherapy for de novo DSA without allograft dysfunction or clinical antibody-mediated rejection (AMR). This is a retrospective study that included 32 lung transplant recipients who were treated with IVIG for de novo DSA with no evidence of AMR. Of 32 patients, 18 patients cleared de novo DSA (defined as sum MFI < 1,000) and 14 patients did not clear at the end of IVIG therapy. There was no significant difference in baseline characteristic, transplant indication or type, cPRA, HLA mismatch, or PGD. There was no difference in CLAD or survival. However, ACR and AMR tended to be more frequent during follow-up in the group that did not clear de novo DSA.

Carfilzomib versus Rituximab for Treatment of De Novo Donor Specific Antibodies in Lung Transplant Recipients

Deepika Razia, MBBS, Norton Thoracic Institute, St. Joseph's Hospital and Medical Center, Phoenix, AZ USA

De novo donor-specific antibodies (DSA) increase risk of ACR, AMR, and CLAD in lung transplant recipients. Carfilzomib (CFZ) and rituximab (RTX) can lower the mean fluorescent intensity (MFI) of DSA. This study aimed to compare the degree and duration of DSA depletion with carfilzomib (CFZ) and rituximab (RTX). Forty-four lung transplant recipients with 53 drug events were identified and divided into two groups, CFZ (n=17) and RTX (n=36). Both CFZ and RTX were shown to significantly lower the MFI at DQ locus. The median of change in MFI was comparable. However, the median interval to DSA rebound was shorter in CFZ group. CLAD-free survival was comparable in the 2 groups.

Efficacy and Safety of the Janus Kinase 1 Inhibitor Itacitinib (ITA) in Patients with Bronchiolitis Obliterans (BOS) Syndrome Following Double Lung Transplant

Joshua M. Diamond, MD, MSCE, University of Pennsylvania, Philadelphia, PA USA

This study aimed to evaluate the efficacy and safety of the Janus Kinase 1 inhibitor ITA in patients with BOS after lung transplantation. This is an open-label, phase 1/2 randomized control trial to evaluate three doses of ITA in adult lung transplant recipients with a diagnosis of BOS stage 1-3 in the past year.

Twenty-three patients were randomized to take ITA 300 mg BID (n=7), 400 mg QD (n=7), 600 mg QD (n=8), or 200 mg QD (n=1, enrolled under previous protocol version). There was no difference in baseline characteristics. Mean FEV1 was 1.61 L at study enrollment across all doses of ITA (n=23). No clear dose-related trends were seen; therefore, results are reported as pooled across all doses.

Post-enrollment mean FEV1 increased at subsequent time points (1.69 L at week 4, 1.76 L at week 8, 1.86 L at week 12). Protocol-defined FEV1 response was observed in 5 patients (21.7%).

The overall incidence of treatment-emergent adverse events (AEs) was similar across all doses (87.0%). The most common AEs were cytomegalovirus (CMV) reactivation/viremia, diarrhea, and fatigue. Infections of any cause occurred in 14 patients (60.9%).

In conclusion, lung function stabilized or improved in a subset of BOS patients who were treated with ITA. Although AEs were frequent, they were generally not dose-limiting.

An Investigational Inhaled rhIL-1Ra (ALTA-2530) Demonstrates Distribution to Distal Regions of Lung and High Affinity IL-1 Receptor Blockade Supporting Development as a Treatment for Bronchiolitis Obliterans Syndrome

Michelle Palacios, PhD, Altavant Sciences, Cary, NC USA

Dysregulated expression of interleukin-1 (IL-1), and downstream cytokines, has been shown to involve in the development of bronchiolitis obliterans syndrome (BOS). Blocking the IL-1 receptor type 1 (IL-1R1) is proposed to reestablish the physiologic immune regulation. The aim of this study was to assess potency and characterize distribution of ALTA-2530 in the lung in the animal model (rat and non-human primate).

ALTA-2530 is inhaled from of a recombinant human IL-1Ra (rhIL-1Ra) that binds competitively to IL-1R1 to block signaling of IL-1a/IL-1b. Bronchoalveolar lavage fluid (BALF) and lung tissue samples were collected from rats and non-human primates after seven daily inhaled doses of ALTA-2530.

The study showed that a daily dose of ALTA-2530 provided more than 24-hour exposure in BALF. The nebulized form of ALTA 2530 achieved delivery of IL-1Ra to dial parts despite narrow airway. The affinity of IL-1Ra bound to IL-1R1 with over 100 times greater affinity than endogenous IL-1 agonists IL-1a. Inhaled ALTA-2530 distributes to distal regions of the lung and inhibits downstream signaling which is supportive of therapy for BOS.

Long-Term Pirfenidone for Restrictive Allograft Syndrome: A Case Series

Hanne Beeckmans, MD, KU Leuven, Leuven, Belgium

The study aimed to report the outcomes of restrictive allograft syndrome (RAS) patients treated with off-label pirfenidone (PFD). The investigators identified four of 30 patients RAS patients who were on long-term PFD—mean duration of 5.2±1.1 years (range 3.8-6.3 years).

Three out of 4 are currently alive (total follow-up was 10.4±3.1 years). The survival post-RAS diagnosis was 6 years (4.9-7.6). FVC and FEV1 did not significantly change during PFR treatment. TLC and DLCO did not significantly differ over time. PFD may attenuate PFT decline in RAS patients.

Extracorporeal Photopheresis in CLAD: A 15-Year Single Centre Experience

Mark Greer, MB Bch, Hanover Medical School, Hanover, Germany

In this study, the investigators summarized their experience of using extracorporeal photopheresis (ECP) in chronic lung allograft dysfunction (CLAD) over 25 years at their center and assess the outcomes and determining treatment duration. A total of 372 patients who received

ECP for CLAD were included in the analysis. The investigators used latent class mixed effect models to identify the phenotype of treatment response.

There was a total of 5 classes (easy, intermediate, advanced progressive, advanced chronic, fulminant). Twenty-five patients (7%) were in the fulminant group, which did not respond to treatment. In advanced groups (progressive and chronic), patients were older and had underperforming grafts. Survival of these three groups (fulminant, advanced progressive, and advanced chronic groups) was worse compared to the other two groups (early and intermediate). ECP appears to offer a survival benefit in some CLAD phenotypes.

VIEW SESSION DETAILS

– Summary by Prangthip Charoenpong, MD, MPH