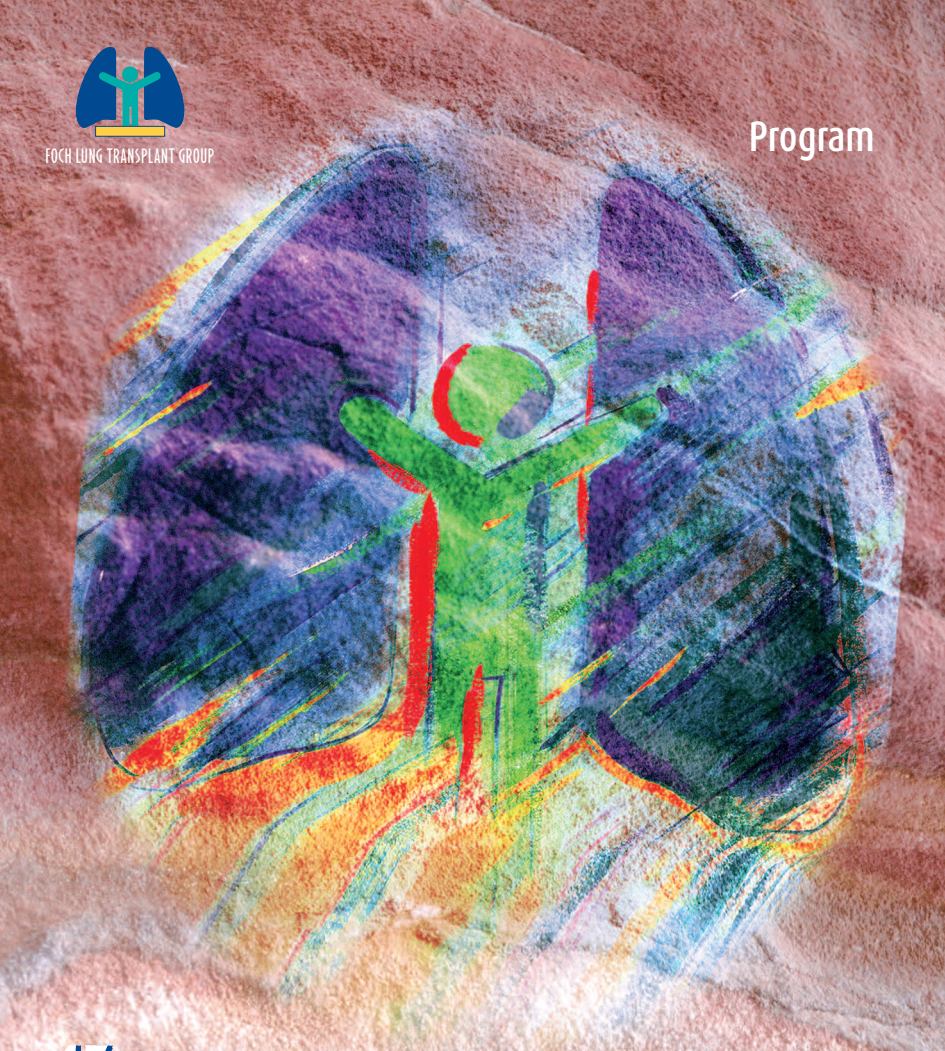
FOCH LUNG TRANSPLANT GROUP

Program



13th International Congress on LUNG TRANSPLANTATION

Paris, september 13-14, 2018

Espace Richelieu - 60 rue de Richelieu - 75002 Paris

www.lungtransplantation.org

FONDATION FOCH

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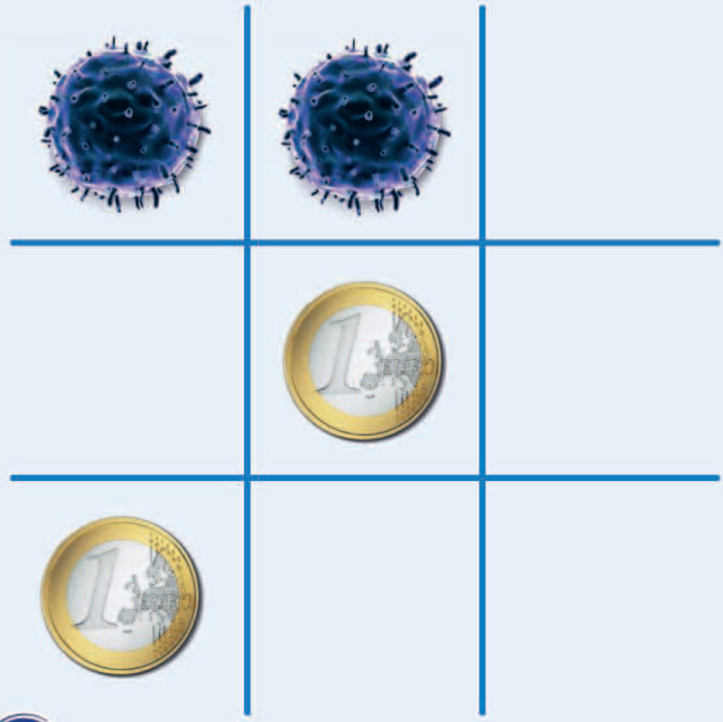

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FOCH LUNG TRANSPLANT GROUP

13th International Congress on LUNG TRANSPLANTATION

Paris, september 13-14, 2018

under the Patronage of

Marshal Foch Foundation
A French American Medical Foundation

Contents

Welcome Address

Dear Colleagues,

The 13th edition of the International Congress on Lung Transplantation is headed by our two presidents: Pr. Ramsey Hachem from Saint-Louis, MO, and Pr. Dirk Van Raemdonck from Leuven, eminent leaders of two bestknown teams in the field of lung transplantation.

The scientific program includes this year again new subjects in addition to classic topics. Our hope is that the numerous lectures and debates will be fruitful and have a positive impact for the future activity of each participant.

Best regards

Dr. Antoine ROUX,
Dr Edouard SAGE,
Dr. Marc STERN

Secretariats

Administrative Secretariat

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43 rue de l'Abbé Groult - 75015 Paris
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✱ If you are a chairperson

You must be in your session room 10 minutes prior the beginning of the session.
Make sure that all speakers observe timing.
Participants should not speak without permission.
They should first clearly state their name, institution and country.

✱ If you are a speaker

Locate your session room in due time.
Speakers must go to the preview room and turn in their slide computer assisted presentations that will be handed out to the session room. **Laptops will not be allowed in the meeting room**.
In the session room, strictly follow instructions from the chairperson, in particular those regarding the timing of your presentation.

Administrative Secretariat

Office hours:

Thursday, September 13	7:30 a.m. - 6:30 p.m.
Friday, September 14	7:30 a.m. - 4:30 p.m.

After the Congress:

VBCE - Lung Transplantation Congress
43 rue de l'Abbé Groult
75015 Paris - France
Phone: +33 (0)1 45 33 60 46
e-mail: secretariat-vbce@vbce.fr

Badges

For security and regulation reasons, all participants will be required to wear their badge at all time throughout the Congress.

Certificate of attendance

A certificate of attendance for registered participants will be available after the congress, from September 24, on the congress website.

Technical Exhibition

The technical exhibition is located close to the conference rooms. Please plan to visit the exhibits regularly, and especially during the breaks.

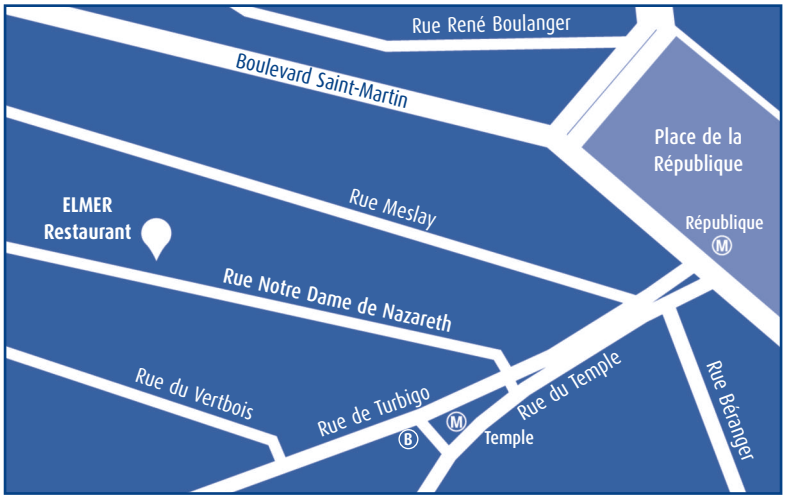
✱ Thursday, September 13

DINNER at the Elmer Restaurant
19 rue Notre Dame de Nazareth
75003 Paris

8:00 p.m.

Price per person: 75 €
Reservation on site is possible upon availability.

Enjoy a gastronomic dinner proposed by a young talent Chef Simon Horwitz.
Very nice cuisine with a selection of artisanal products, carefully chosen.



Ⓜ Métro Stations: Temple (line 3), République (lines 3, 5, 8, 9, 11)

Ⓑ Bus Station: Turbigo-République (lines 20, 75)

Exhibitors' List

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Scientific Program

	Room 1	Room 2
8:30	**Welcome**	
8:45	**Rejection** Chairs: Gerald Berry, Ramsey Hachem p 14	
10:10	Coffee Break	
10:30	**Frontiers in lung transplantation: Extremes of age, how to manage?** Chairs: Christian Benden, Mark Greer p 14	10:30 **Antibody mediated rejection** Chairs: Deborah Levine, Antoine Roux p 14
12:30		12:35
12:45	Symposium One Lambda - A Thermo Fisher Scientific Brand **AMR but no HLA DSA: What to do next?** p 14	
13:45		
14:00	**Chronic lung allograft dysfunction** Chairs: Jens Gottlieb, Clément Picard p 14	14:00 **Primary graft dysfunction** Chairs: Christine Falk, Dirk Van Raemdonck p 14
16:00	Coffee Break	16:00 Coffee Break
16:20	**Oral presentations** Chairs: Jérôme Le Pavec, Deborah Levine p 14	16:20 **Oral presentations** Chairs: Matthieu Glorion, Gregor Warnecke p 14
17:30		17:30

Friday 14

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10:00	Coffee Break	10:00 Coffee Break
10:30	**Next future** Chairs: Christophe Pison, Edouard Sage p 14	
12:00		
12:30	**Symposium Biotest** **CMV**	
13:30		
14:00	**Microbiology of lung transplantation** Chairs: Laurent Nicod, François Parquin p 14	14:00 **Managing pretransplant conditions** Chairs: Mark Greer, Jean-François Mornex p 14
16:00	**Meeting conclusion**	16:00
16:10		

8:30 → 8:45 **Room 1**

Welcome

Presidents of the Congress:
Ramsey Hachem (Saint-Louis, USA), Dirk Van Raemdonck (Leuven, Belgium)
Presidents of the Local Organizing Committee:
Antoine Roux, Edouard Sage (Suresnes, France)

8:45 → 10:10 **Room 1**

Rejection

Chairs: Gerald Berry (Stanford, USA),
Ramsey Hachem (Saint-Louis, USA)

8:45 **Physiopathology**
Olivier Thaunat (Lyon, France)

9:10 **Improve diagnosis through big data**
Alexandre Loupy (Paris, France)

9:35 **New therapeutic approach**
Menna Catworthy (Cambridge, UK)

10:00 **Questions-Debate**

10:30 → 12:30 **Room 1**

Frontiers in lung transplantation: Extremes of age, how to manage?

Chairs: Christian Benden (Zurich, Switzerland),
Mark Greer (Hanover, Germany)

10:30 **Specificity of elderly patient**
Ramsey Hachem (Saint-Louis, USA)

10:50 **Ethical issues**
Dirk Van Raemdonck (Leuven, Belgium)

11:10 **How to evaluate frailty before lung transplantation**
Angela Koutsokera (Lausanne, Switzerland)

11:30 **Extremes of age decrease survival after lung transplant**
Carli Lehr (Cleveland, USA)

11:50 **Pediatrics: Lung transplant medical specificities**
Christian Benden (Zurich, Switzerland)

12:10 **Pediatrics: Lung transplant surgical specificities**
Alexis Slama (Essen, Germany)

10:30 → 12:35 **Room 2**

Antibody mediated rejection

Chairs: Deborah Levine (San Antonio, USA),
Antoine Roux (Suresnes, France)

10:30 **Diagnosis of antibody-mediated rejection (AMR) on lung transplant biopsies: A retrospective single-centre case study** **O1**
S. Geleff, G. Fischer, P. Jaksch (Vienna, Austria)

10:37 **Graft donor-specific anti-human leukocyte antigen antibodies (DSA) in phenotypes of chronic lung allograft dysfunction** **O2**
A. Sacreas, J.L. Taupin, R. Vos, M.P. Emonds, L. Daniëls, G. Verleden, B. Vanaudenaerde, A. Roux, S. Verleden (Leuven, Belgium)

10:45 **Still a place for C4d? Pro/Cons**
Gerald Berry (Stanford, USA) vs. Desley Neil (Birmingham, UK)

11:20 **Should we treat asymptomatic DSA? Pro/Cons**
Ramsey Hachem (Saint Louis, USA) vs. Deborah Levine (San Antonio, USA)

11:55 **What clinician should know about complement for lung transplantation?**
TBC

12:15 **DQ matching for lung transplantation**
Jussi Tikkanen (Toronto, Canada)

12:45 ➜ 13:45 Room 1

AMR but no HLA DSA: What to do next?

Symposium sponsored by One Lambda – A Thermo Fisher Scientific Brand

Chairs: Deborah Levine (San Antonio, USA),
Antoine Roux (Suresnes, France)

Speaker: Nicole M. Valenzuela, PhD, D (ABHI)
Assistant Director at the UCLA Immunogenetics Center and Assistant Professor in the Department of Pathology and Laboratory Medicine

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14:00 → 16:00 **Room 1**

Chronic lung allograft dysfunction

Chairs: Jens Gottlieb (Hanover, Germany),
Clément Picard (Suresnes, France)

14:00 **COLT: results**
Adrien Tissot (Nantes, France)

14:20 **Bronchiectasis as prognostic factor in bronchiolitis obliterans syndrome after lung transplantation** **O3**
A. Van Herck, A. Sacreas, T. Heigl, S. Verleden, B. Vanaudenaerde, W. De Wever, G. Verleden, R. Vos (Leuven, Belgium)

14:27 **A closer look at chronic rejection in the murine model of orthotopic lung transplantation** **O4**
T. Heigl, J. Kaes, A. Sacreas, G. Van de Velde, A. Van Herck, E. Verbeken, G. Verleden, S. Verleden, R. Vos, B. Vanaudenaerde (Leuven, Belgium)

14:34 **Diagnostic challenges of restrictive allograft syndrome in single-lung transplantation recipients: characterization of functional, immunological and CT scan patterns for early diagnosis** **O5**
Q. Philippot, M.P. Debray, J. Frijat, V. Bunel, L. Morer, J. Mourin, G. Dauriat, G. Jebrak, H. Mal, O. Brugière (Paris, France)

14:40 **What the best way to phenotype your CLAD?**
Stijn Verleden (Leuven, Belgium)

15:00 **Azithromycine: Hematopoietic stem-cell transplantation experience**
Anne Bergeron (Paris, France)

15:20 **New therapeutic option/strategy for CLAD**
Robin Vos (Leuven, Belgium)

15:40 **What is the best strategy for lung retransplantation?**
Mark Greer (Hanover, Germany)

14:00 → 16:00 **Room 2**

Primary graft dysfunction

Chairs: Christine Falk (Hanover, Germany),
Dirk Van Raemdonck (Leuven, Belgium)

14:00 **Primary graft dysfunction: New classification**
Greg Snell (Melbourne, Australia)

14:20 **Primary graft dysfunction: Mechanistic review**
Christine Falk (Hanover, Germany)

14:40 **Routine use of intraoperative ECMO leads to excellent postoperative graft function**
Konrad Hoetzenecker (Vienna, Austria)

15:00 **VA or VV ECMO to treat primary graft dysfunction ?**
Gregor Warnecke (Hanover, Germany),
Konrad Hoetzenecker (Vienna, Austria)

15:40 **VV-A ECMO for severe primary graft dysfunction**
Matthieu Glorion (Suresnes, France)

16:20 → 17:30 **Room 1**

Oral presentations

Chairs: Jérôme Le Pavec (Le Plessis Robinson, France),
Deborah Levine (San Antonio, USA)

16:20 **The molecular landscape of transbronchial biopsies from patients diagnosed with CLAD** **06**
M. Parkes, K. Halloran, I. Timofte, G. Snell, G. Westall, R. Hachem, D. Kreisel, E. Trulock, A. Roux, S. Juvet, S. Keshavjee, P. Jaksch, W. Klepetko, P. Halloran (Edmonton, Canada)

16:27 **Torque Teno Virus as a novel biomarker targeting the efficacy of immunosuppression after lung transplantation** **07**
P. Jaksch, M. Kundi, I. Görzer, G. Muraközy, C. Lambers, A. Benazzo, K. Hoetzenecker, W. Klepetko, E. Puchhammer-Stöckl (Vienna, Austria)

16:34 **Extravesicles and lung transplantation: New prospective in the evaluation of injury and function of the graft** **08**
L. Rosso, I. Righi, M. Barilani, P. Mendogni, A. Mazzucco, V. Musso, L. Lazzari (Milano, Italy)

16:41 **CD9+ Regulatory B lymphocytes induce effector T cell apoptosis** **09**
C. Brosseau, M. Durand, E. Durand, A. Foureau, P. Lacoste, M.A. Cheminant, A. Magnan, S. Brouard (Nantes, France)

16:48 **Bile acid aspiration is associated with airway infections: A targeted metabolomic approach** **010**
A. Urso, F. Briganti, J. Costa, R. Nandakumar, H. Robbins, L. Shah, J. Sonett, S. Cremers, S. Arcasoy, F. D'Ovidio (New York, USA)

16:55 **Bile acid aspiration modulates cholinergic and serotonergic responses of the distal airways** **011**
A. Urso, J. Perez-Zoghbi, C. Emala, N. Bunnett, F. D' Ovidio (New York, USA)

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17:02 **Control of Kaposi's sarcoma after lung transplantation with inhibitor of mTOR** **O12**
A.M. Rabain, F. Philit, J.F. Mornex (Lyon, France)

17:09 **An integrated pharmacist-led medication review service to support outpatient care of thoracic transplant patients** **O13**
P. Ly, K. Habibi-Parker, R. Betmouni, M. Carby, A. Reed, A. Simon, H. Lyster (Harefield, UK)

17:16 **Conversion from tacrolimus twice-daily to tacrolimus once-daily in stable lung transplant recipients: effects on lung function** **O14**
L. Godinas, L. Hulst, R. Vos, B. Vanaudenaerde, S. Verleden, D. Van Raemdonck, A.P. Neyrinck, G. Verleden (Leuven, Belgium)

16:20 → 17:30 **Room 2**

Oral presentations

Chairs: Matthieu Glorion (Suresnes, France),
Gregor Warnecke (Hanover, Germany)

16:20 **First experience with ex-vivo lung perfusion for initially discarded donor lungs in the netherlands, a single center study** **O15**
Z. Zhang, V. Van Suylen, J. Van Zanden, C. Van De Wauwer, E. Verschuuren, W. Van Der Bij, M. Erasmus (Groningen, Netherland)

16:27 **Six-year experience of ex-vivo lung perfusion at Milan Lung Transplantation Centre** **O16**
L. Rosso, V. Rossetti, M. Nosotti, L.C. Morlacchi, E. Scotti, A. Palleschi, P. Tarsia, M. Mendogni, G. Ruggeri, D. Tosi, A. Zanella (Milano, Italy)

16:34 **Absorbable sternal pins for sternal closure following lung transplantation** **O17**
A. Olland, J. Reeb, S. Guinard, J. Seitlinger, N. Santelmo, P.E. Falcoz, G. Massard (Strasbourg, France)

16:41 **Lung transplantation for pulmonary hypertension presenting with giant aneurysm of the pulmonary trunk** **O18**
S. Schwarz, A. Benazzo, H. Prosch, H. Hager, T. Schweiger, B. Moser, J. Matilla, G. Lang, S. Taghavi, P. Jaksch, W. Klepetko, K. Hoetzenecker (Vienna, Austria)

16:48 **Cost-effectiveness of lung transplant for end-stage cystic fibrosis: Evidence from a french observational study** **O19**
T. Renaud, N. Kaboré, A. Roux, M. Stern, J. Wittwer (Bordeaux, France)

16:55 **Development and validation of an instrument to measure knowledge in transplant recipients** **O20**
V. Shaevers, S. Berentsen, M. De Vos, S. Stulens, K. De Bondt, F. Dobbels (Leuven, Belgium)

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17:02 **Outcome after lung transplantation using repeatedly declined marginal donor lungs** **021**
S. Schwarz, M. Muckenhuber, A. Benazzo, O. Glueck, M. Evermann, L. Beer, T. Schweiger, B. Moser, J. Matilla, G. Lang, S. Taghavi, P. Jaksch, W. Klepetko, K. Hoetzenecker (Vienna, Austria)

17:09 **Right single lung transplantation for emphysema has better survival than left single transplant: A single center experience** **022**
J. Costa, D. Piloni, L. Benvenuto, A. Urso, L. Shah, H. Robbins, J. Sonett, S. Arcasoy, F. D'Ovidio (New York, USA)

17:16 **Central versus peripheral cannulation of extracorporeal membrane oxygenation support during double lung transplant for pulmonary hypertension** **023**
M. Glorion, O. Mercier, D. Mitilian, A. De Lemos, L. Lamrani, S. Feuillet, P. Pradère, J. Le Pavec, D. Lehouerou, F. Stephan, L. Savale, D. Fabre, S. Mussot, E. Fadel (Suresnes, France)

17:23 **Better pulmonary function in upper lobe than in lower lobe in a porcine DCD donor lung model using cellular ex vivo lung perfusion** **024**
H. Niikawa, T. Okamoto, K. Ayyat, Y. Itoda, C. Farver, K. McCurry (Cleveland, USA)

8:00 → 10:00 **Room 1**

Rejection: New tools

Chairs: Gerald Berry (Stanford, USA),
Ramsey Hachem (Saint-Louis, USA)

8:00 **Standardized analysis GRID and new staining**
Fiorella Calabrese (Padova, Italy)

8:25 **Molecular microscope**
Philip Halloran (Edmonton, Canada)

8:50 **Nanostring**
Michael Mengel (Edmonton, Canada)

9:15 **Cell free DNA**
Sean Agbor-Enoh (Bethesda, USA)

9:40 **Discussion**

8:00 → 10:00 **Room 2**

Increasing donor pool-graft allocation

Chairs: Andrew Fisher (Newcastle, UK),
Dirk Van Raemdonck (Leuven, Belgium)

8:00 **UK superurgence system**
Andrew Fisher (Newcastle, UK)

8:20 **Italian Urgent List Transplant Program: Monocentric experience** **025**
F. Damarco, L. Rosso, M. Montoli, M. Nosotti, V. Musso, L. Santambrogio (Milano, Italy)

8:30 **Ex vivo lung perfusion is relevant to bypass adverse logistics** **026**
A. Olland, J. Reeb, S. Guinard, J. Seitlinger, N. Santelmo, P.E. Falcoz, G. Massard (Strasbourg, France)

8:40 **Ex vivo lung perfusion for deceased donor**
Dirk Van Raemdonck (Leuven, Belgium)

9:00 **OCS experience**
Gregor Warnecke (Hanover, Germany)

9:20 **Size matching**
Jason Christie (Philadelphia, USA)

9:40 **Category III Donation after Circulatory Death (DCD) lung donors for pediatric lung transplantation: Increasing the lung donor pool with excellent outcomes** **027**
B. Levvey, D. Mc Giffin, G. Westall, G. Snell (Melbourne, Australia)

10:30 → 12:00 **Room 1**

Next future

Chairs: Christophe Pison (Grenoble, France),
Edouard Sage (Suresnes, France)

10:30 **How to build a lung?**
Darcy Wagner (Lund, Sweden)

10:55 **Artificial lung**
Olaf Mercier (Le Plessis Robinson, France)

11:20 **Data scientist**
Martin Daniel (Paris, France)

11:45 **Revisiting ischemia paradigm**
Didier Journois (Paris, France)

12:30 → 13:30 **Room 1**

CMV

Symposium sponsored by Biotest

Chair: Antoine Roux (Suresnes, France)

12:30 **CMV biology and specific immune response**
Hanna Kaminski (Bordeaux, France)

13:00 **New therapeutics**
Sophie Alain (Limoges, France)

14:00 → 16:00 **Room 1**

Microbiology of lung transplantation

Chairs: Laurent Nicod (Lausanne, Switzerland),
François Parquin (Suresnes, France)

14:00 **Role of microbiome in lung transplantation**
Laurent Nicod (Lausanne, Switzerland)

14:25 **Non tuberculosis mycobacteria: The new recommendations**
Claire Andrejak (Amiens, France)

14:45 **CMV hyperimmune globulins as salvage therapy in patients with CMV infection following lung transplantation: The French multicentric experience** **028**
C. Roy, F. Parquin, O. Brugiere, S. Hirchsi, T. Degot, S. Feuillet, J. Le Pavec, E. Camps, M. Leguen, E. Sage, A. Hamid, A. Roux (Suresnes, France)

14:55 **Isavuconazole for the treatment of fungal infections in lung transplant recipients: Case series from a single centre** **029**
N. Pagani, H. Lyster, D. Armstrong-James, M. Carby, A. Simon, A. Reed (London, UK)

15:05 **Fungal infection in lung transplantation: A new paradigm?**
Shahid Husain (Toronto, Canada)

15:30 **Solid organ transplantation for HIV positive patient: What to learn from renal transplantation?**
Anne Scemla (Paris, France)

14:00 → 16:00 **Room 2**

Managing pretransplant conditions

Chairs: Mark Greer (Hanover, Germany),
Jean-François Mornex (Lyon, France)

14:00 **New antifibrotic drug**
Jens Gottlieb (Hanover, Germany)

14:25 **CFTR modulator and antimicrobial drug for multiresistant microorganism**
Peter Jaksch (Vienna, Austria)

14:50 **Influence of plasmapheresis on hemostasis and hemorrhage intraoperatively in pulmonary transplantation** **030**
J. Fessler, A. Mailloux, F. Parquin, A. Roux, E. Sage, M. Fischler, M. Le Guen (Suresnes, France)

14:57 **Cystic fibrosis-related diabetes before lung transplantation impacts survival but not long term renal function** **031**
S. Jardel, S. Touzet, S. Poupon-Bourdy, R. Nove-Josserand, J.F. Mornex, F. Philit, I. Durieu, Q. Reynaud (Lyon, France)

15:04 **Development of a cumulative deficit frailty index for cystic fibrosis lung transplant candidates to predict post-transplant survival** **032**
A. Koutsokera, J. Sykes, O. Theou, K. Rockwood, A. Stephenson, L. Singer (Lausanne, Switzerland)

15:11 **Prevalence and prognosis of coronary artery disease in high risk patients referred for lung transplantation** **033**
A. Bertolotti, R. Ahumada, JM. Osses, G. Wagner, G. Parrilla, C. Zambrano, J. Caneva, RR. Favaloro (Buenos Aires, Argentina)

15:18 **Patients outcome according to the induction therapy for renal transplantation in patients with history of previous cardiac or pulmonary transplantation** **034**
L. Meyer, S. Varnous, R. Guillemain, J. Le Pavec, L. Houyel, C. Picard, D. Bodez, N. Arzouk, V. Audard, A. Dürrbach, C. Legendre, M. Delahousse, P. Rieu, E. Thervet (Paris, France)

15:25 **mTORs inhibitors use and lung transplantation**
Jean-François Mornex (Lyon, France)

16:00 ➜ 16:10 **Room 1**

Meeting conclusion

Presidents of the Congress:
Ramsey Hachem (Saint-Louis, USA), Dirk Van Raemdonck (Leuven, Belgium)
Presidents of the Local Organizing Committee:
Antoine Roux, Edouard Sage (Suresnes, France)

Abstracts

DIAGNOSIS OF ANTIBODY-MEDIATED REJECTION (AMR) ON LUNG TRANSPLANT BIOPSIES: A RETROSPECTIVE SINGLE-CENTRE CASE STUDY

S. Geleff[2], G. Fischer[1], P. Jaksch[3]

1- Department of Blood Group Serology and Transfusion Medicine ; 2- Department of Pathology, Medical Universitiy of Vienna, Vienna General Hospital ; 3- Department of Thoracic Surgery, Medical University of Vienna, Vienna General Hospital, Vienna, Austria

AMR is increasingly recognized as an important form of lung rejection and contrary to its cellular counterpart it lacks specific features. Diagnostic criteria according to ISHLT guidelines include clinical evidence of graft dysfunction, presence of de novo donor-specific antibodies (DSAs) and histology suggestive of AMR with or without deposition of complement 4d (C4d). We examined the incidence of AMR as a clinical indication for biopsy between 2011 and 2017. In this period 736/49 patients underwent lung transplant/retransplantation procedures at the Vienna General Hospital. In the first year after surgery AMR was suspected in 22 out of 82 patients who developed allograft dysfunction. We observed DSAs in these 22 patients prior to or concomitantly with diagnostic biopsy. No evidence of higher-grade cellular rejection, infection, drug reactions or other injuries was seen in these patients. Histologic features included diffuse alveolar damage (DAD) (n=15), capillaritis (n=3) and neutrophilic septal margination (n=2). C4d deposition in the endothelium (50% or more capillaries stained) was seen in 5 grafts. Out of 22 patients with DSAs diagnostic certainty of AMR was 'definite' in 5, 'probable' in 10 and 'possible' in 7.

Although any process associated with complement activation can induce C4d deposition, positive staining without other proof of AMR was rarely seen in our collective. The only 2 cases presented as DAD related to severe infection and higher-grade (A2) cellular rejection. We concluded from this study that definite AMR according to ISHLT is a rare occurrence in our center and that the majority of cases with suspected AMR rank as probable/possible.

GRAFT DONOR-SPECIFIC ANTI-HUMAN LEUKOCYTE ANTIGEN ANTIBODIES (DSA) IN PHENOTYPES OF CHRONIC LUNG ALLOGRAFT DYSFUNCTION

A. Sacreas[1], J.L. Taupin[4], R. Vos[1], M.P. Emonds[2], L. Daniëls[2], G.M. Verleden[1], B.M. Vanaudenaerde[1], A. Roux[3], S.E. Verleden[1]

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Purpose

Following lung transplantation (LTx), 10-50% of patients develop anti-HLA donor specific antibodies (DSA), which increases the risk of chronic lung allograft dysfunction (CLAD), especially restrictive allograft syndrome (RAS), and mortality. Post kidney transplantation, intragraft DSA (gDSA) are considered a severity marker of antibody-mediated rejection; while post lung transplantation gDSA were able to identify pathogenic DSA. Therefore, we aimed to assess the presence of gDSA in lungs from patients with different phenotypes of CLAD to establish their relevance.

Methods

Explant lungs from patients with bronchiolitis obliterans syndrome (BOS, n= 18) and RAS (n=18) were collected, inflated and fixed in the fumes of liquid nitrogen. Per lung, two tissue cores were selected from distinct regions and assessed for tissue % using microCT, and subsequently homogenized. Intragraft IgG antibodies were eluted (Gamma ELU-kit II, Immucor) and anti-HLA Class I and II antibodies were identified via Luminex (LABScreen LS1A04 and LS2A01 Single Antigen HLA test, One Lambda). gDSA data were correlated to serum DSA (sDSA) profiles, known for all patients included in this study.

Results

Overall, there was a good agreement between the gDSA and sDSA (31/36, 86%). In BOS, 1 patient had both sDSA and gDSA, while in 1 patient there were (weak) sDSA and in 1 patient gDSA only. In RAS, 7 patients (39%) showed both sDSA and gDSA, while in 1 patient sDSA were found, but no gDSA; and in 2 patients gDSA but not sDSA. There were differences in gDSA detection between the different biopsies from the same lung. When results of sDSA and gDSA were combined, 10 patients with RAS (56%) had DSA, in contrast to only 3 BOS patients (17%) (p=0.015). The majority of DSA were directed against HLA-DQ. Interestingly, from the 3 patients that showed gDSA only, in 2 patients sDSA against the first graft were detected 2-4 years following their redo-transplantation.

Conclusion

DSA are more prevalent in RAS compared to BOS patients. gDSA can provide complementary information to sDSA finding. The relevance and applications of gDSA needs further investigation to demonstrate their relevance.

BRONCHIECTASIS AS PROGNOSTIC FACTOR IN BRONCHIOLITIS OBLITERANS SYNDROME AFTER LUNG TRANSPLANTATION

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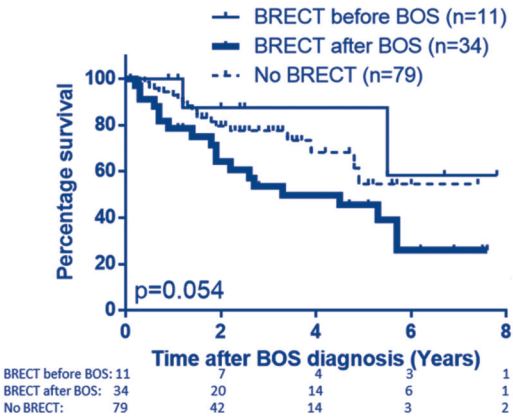
Long-term survival after lung transplantation (LTx) is hampered by chronic lung allograft dysfunction, with bronchiolitis obliterans syndrome (BOS) as its most common phenotype. We investigated whether development and timing of bronchiectasis (BRECT) has prognostic significance in BOS patients.

Patients transplanted between 2004-2015 with a survival of >90 days who developed BOS (n=124) were included. BOS was defined as a persistent FEV_1 decline of ≥20% compared to baseline, in absence of restrictive pulmonary function tests or persistent infiltrates. BOS patients were retrospectively classified according to presence and timing of BRECT development (before vs. after BOS diagnosis) using chest CT during follow-up. Primary outcomes were overall survival and post-BOS survival.

In 36% of BOS patients BRECT were identified, of which 24% developed BRECT at a median of 331 days before BOS and 76% at a median of 654 days after BOS diagnosis. Patients who developed BRECT after BOS, had worse overall (p=0.0031) and post-BOS (p=0.030) survival compared to those without BRECT. Patients who developed BRECT before BOS, had similar overall (p=0.40) and post-BOS survival (p=0.52) compared to those without BRECT. BOS patients with BRECT had more infections (p=0.0030) and were more colonized with Pseudomonas Aeruginosa (p=0.013) compared to those without BRECT.

Development and timing of BRECT has prognostic significance in BOS.



A CLOSER LOOK AT CHRONIC REJECTION IN THE MURINE MODEL OF ORTHOTOPIC LUNG TRANSPLANTATION

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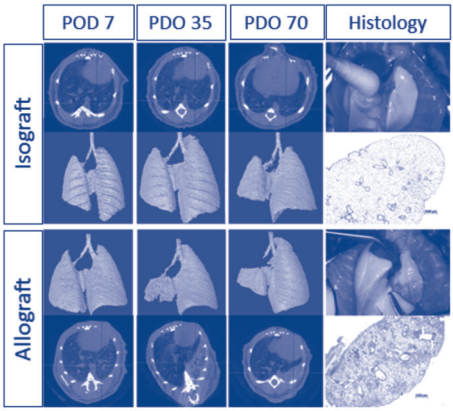
Introduction: Survival after lung transplantation (LTx) remains poor, with chronic rejection being the most important cause of mortality. The controlled setting of a proper preclinical animal model would be of great value to investigate chronic rejection in more depth. Our aim was to have a closer look at chronic rejection within the murine orthotopic left lung transplant model by serial follow-up micro-computed tomography (microCT).

Materials & Methods: Murine orthotopic single lung transplantations were performed using a cuff technique. Groups consisted of isografts (n=8) (C57BL/6N to C57BL/6N) and major mismatched allografts (n=8) (Balb/c to C57BL/6N). Both groups received daily immunosuppression. Animals underwent respiratory-gated time resolved microCT at post-operative week 1, 5, 10 to image pathology and quantify lung density and volume using company software (SkyScan 1278, Bruker micro-CT, Kontich, Belgium). Mice were sacrificed after the last scan for histopathological analysis.

Results: MicroCT of isografts showed normal lung parenchyma after 1, 5 and 10 weeks with a stable lung volume (p=0.23) and density (p=0.23) and normal histology. Within allografts, we observed graft loss (necrosis/apoptosis) in 4 animals; non-rejection related severe pathology in 2 animals and rejection in 2 animals all confirmed on histopathology. The density of the transplanted lung increased (p=0.027), while volume decreased (p=0.016). The native lung density was stable during the follow-up (p=0.15), however the volume increased (p=0.052). The allografts native lung increased in volume to compensate for the loss of the transplanted lung.

Conclusions: Longitudinal microCT might be very important to assess disease progression chronic rejection n the mouse model as transplanted allografts became smaller and tissue density increased. The combination of our animal model with its major genetic mismatch, immune suppressive regime and longitudinal microCT follow up holds great promise to tackle the complex problem of chronic rejection after lung transplantation.



DIAGNOSTIC CHALLENGES OF RESTRICTIVE ALLOGRAFT SYNDROME IN SINGLE-LUNG TRANSPLANTATION RECIPIENTS: CHARACTERIZATION OF FUNCTIONAL, IMMUNOLOGICAL AND CT SCAN PATTERNS FOR EARLY DIAGNOSIS

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Purpose of the study: Restrictive allograft syndrome (RAS) has recently been identified as a chronic lung allograft dysfunction (CLAD) phenotype with the worth prognosis after lung transplantation (LTx). Diagnosis criteria of RAS have been proposed in double-LTx (DLTx), but how to apply these criteria in single-LTx (SLTx) remained debated due to the contribution of the native lung with highly variable volume of initial disease. Hence, there is an urgent need to validate these criteria of RAS in SLTx in the aim of early diagnosis and therapeutic intervention in this population.
The aim of these study is to investigate functional, allosensitization, and CT-scan abnormalities patterns in single-LTx recipients with ultimate diagnosis of RAS during follow-up.

Methods: We retrospectively reviewed data from all LTx recipients who survived at least 6 months and were diagnosed with CLAD onset during the 2009-2017period at Bichat hospital. We hypothesized that patients with SLTx could potentially been misdiagnosed by strict application of functional criteria used for RAS diagnosis in DLTx.
RAS phenotype of the graft lung in SLTx was ultimately identified at last follow-up, using both graft lung volume calculation outcome after Tx and standard functional/CT-scan criteria used for this diagnosis of RAS in BLTx. Outcome of PFTs (Vital capacity, FEV1, Tiffeneau index), repeated CT-scan patterns (Qualitative RAS parenchymal score and CT-volume calculation), and anti-HLA donor-specific antibodies detection were assessed at 3 time points: (1) at the date of CLAD onset, retrospectively defined at first irreversible decline of PFTs, of graft CT-volume, or first irreversible onset of pleuroparenchymal abnormalities reflected by RAS parenchymal score; (2) at last available CT-scan and/or PFTs; (3) at an intermediate date closest between the midtime of time 1 and 2.

Results: 19 SLTx were identified with RAS diagnosis, with initial diagnosis of emphysema (n=6), fibrosis (n=11), or other diseases (n=2). Mean survival after RAS diagnosis was 552 days. Patterns of functional, immunological, and CT-scan outcomes during RAS development will be reported at the 13th International congress on LTx.

Discussion: Our hypothesis is that specific early criteria of RAS diagnosis in SLTx might be refined from those proposed in DLTx, with potential additional CT-scan volume measurements. This will be assessed and discussed.

THE MOLECULAR LANDSCAPE OF TRANSBRONCHIAL BIOPSIES FROM PATIENTS DIAGNOSED WITH CLAD

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Background: Chronic lung allograft dysfunction (CLAD), the major obstacle to improving transplant outcomes, is a clinical and functional diagnosis that has been difficult to characterize by histology. Deeper understanding of its biology is essential to develop strategies for prevention and management. In the INTERLUNG study we used microarrays to examine phenotypes associated with CLAD in transbronchial biopsies.

Methods: We processed 152 highly alveolated single-piece transbronchial biopsies from 7 centers using the Molecular Microscope (MMDx-Lung) algorithms (manuscript submitted for publication). We examined relationships between CLAD and MMDx-Lung scores for normalness (S1normal), TCMR (S2TCMR), an ABMR-like phenotype (S3ABMR), and an injury-like phenotype (S4injury). The top transcripts associated with clinically diagnosed CLAD (n=36) vs no CLAD (n=116) at biopsy were identified and their functional pathway annotations were examined. We also compared expression of published pathogenesis-based transcripts (PBTs) in CLAD vs. no CLAD. PBT sets reflect biological processes related to rejection and injury-and-repair, and were originally defined in human cell lines, mouse models, and human biopsies.

Results: Using MMDx-Lung algorithms, CLAD was associated with higher S2TCMR and S3ABMR scores, and with lower S1normal and S4injury scores ($p<0.05$; Figure 1).
The most highly increased PBT sets in CLAD vs. no CLAD reflected immunoglobulin transcripts (IGT), IFNG effects (GRIT1), T cells (QCAT, TCB), endothelial changes (ENDAT), DSA-selective transcripts (DSAST), and NK cells (NKB). The IGTs were not statistically significant ($p=0.11$) despite their fold change being the greatest, presumably reflecting plasma cell infiltrates in only a subset of the dysfunctional grafts. Differences in NKBs also lacked statistical significance ($p=0.43$) (Table 1).
Pathway analysis using the top 100 unique genes (by p-value) increased in CLAD vs. no CLAD returned top gene ontology terms relating to antigen processing and presentation and regulation of immune response ($p<0.05$) (Table 2). Angiogenesis and extracellular matrix organization were among the top 10 annotated processes, potentially reflecting the injury-repair responses.

Conclusions: CLAD is associated with IFNG effects, endothelial changes/angiogenesis, T cell infiltration, and probably with plasma cell infiltration (a feature of active scarring). Some of these features may be related to various disease states that cause CLAD, including rejection. These findings reinforce the concept of CLAD as a response to wounding. Increased ENDATs and DSASTs in CLAD may indicate endothelial changes in CLAD pathogenesis that are reminiscent of but not necessarily caused by ABMR. Molecular phenotyping of CLAD is a promising avenue for creating a more precise and accurate diagnostic system for detecting, classifying, and understanding this critical process.

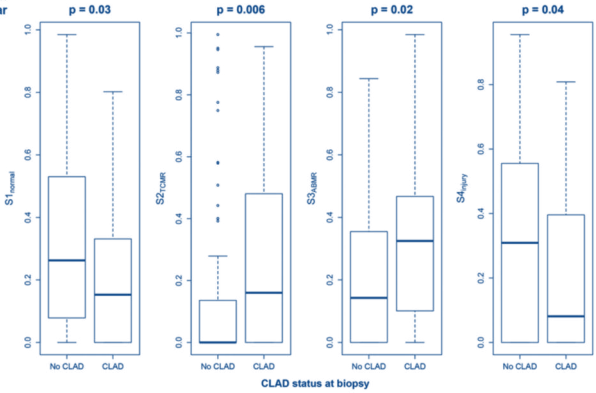

Figure 1. Relationships between CLAD and MMDx-Lung molecular scores.

Boxplots are given for S1, S2, S3, and S4 scores in CLAD vs. no CLAD (scores reflect normalness, TCMR, an ABMR-like phenotype, and an injury-like phenotype, respectively). Mann-Whitney U test p values are reported at the top of each plot.

Table 1. Pathogenesis-based transcript expression in CLAD

Pathogenesis-based transcript (PBT) set	Fold change, CLAD vs. No CLAD	Welch's p-value
IGT - *Immunoglobulin transcripts*	1.28	0.11
TCB - *T cell burden*	1.21	0.02
QCAT - *Cytotoxic T cell transcripts*	1.16	0.02
GRIT1 - *Interferon-gamma effects*	1.12	0.01
eDSAST - *Endothelial DSA-selective transcripts*	1.10	0.04
DSAST - *DSA-selective transcripts*	1.09	0.04
NKB - *NK cell burden*	1.07	0.43
ENDAT - *Endothelial cell transcripts*	1.06	0.02
IRIT5 - *5 day kidney isograft injury-and-repair transcripts*	1.05	0.08
AMAT1 - *Alternatively activated macrophage transcripts*	1.02	0.71
IRIT3 -*3 day kidney isograft injury-and-repair transcripts*	1.02	0.20
QCMAT - *Constitutive macrophage transcripts*	1.00	0.97
IRRAT - *Non-rejecting human kidney injury transcripts*	0.94	0.14

Statisically significant ($p<0.05$) results are highlighted. Results are sorted by decreasing fold change in CLAD vs. no CLAD.

Table 2. Pathway analysis of top 100 CLAD-associated transcripts

Gene ontology term	Hits in gene list	Fold enrichment	P-value	Benjamini-Hochberg corrected p-value
Immune response	13	5.7	2.5E-06	1.7E-03
Antigen processing and presentation of exogenous peptide antigen via MHC class I, TAP-independent	4	82.0	1.2E-05	4.3E-03
Antigen processing and presentation of peptide antigen via MHC class I	5	30.8	1.9E-05	4.5E-03
Extracellular matrix organization	8	7.5	8.7E-05	1.5E-02
Protection from natural killer cell mediated cytotoxicity	3	110.7	2.8E-04	3.9E-02
Regulation of immune response	7	7.3	3.9E-04	4.5E-02
Signal transduction	17	2.7	4.1E-04	4.0E-02
Inflammatory response	9	4.4	9.7E-04	8.2E-02
Angiogenesis	7	5.8	1.3E-03	9.4E-02
Antigen processing and presentation	4	13.4	3.2E-03	2.0E-01

TORQUE TENO VIRUS AS A NOVEL BIOMARKER TARGETING THE EFFICACY OF IMMUNOSUPPRESSION AFTER LUNG TRANSPLANTATION

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Introduction

Monitoring immunosuppression (IS) after organ transplantation (TX) is still challenging. Torque teno viruses (TTV) are small DNA viruses, of the genus Alphatorquevirus, whose replication is linked to immune status. Hence alphatorquevirus-load may be an indicator for efficacy of IS in lung transplant recipients (LTRs).

Patients and Methods

In a prospective single-center study 143 LTRs were followed up for 197-1612 days and tested by quantitative alphatorquevirus-DNA PCR. Between 10 and 47 alphatorquevirus measurements were performed during follow-up. Using multivariate Cox regression with time-dependent covariates and assuming an Andersen-Gill counting process, contribution of alphatorquevirus load to the occurrence of severe infections, chronic lung allograft dysfunction (CLAD), acute cellular rejection (ACR), and death was assessed.

Results

During follow-up 28 (20%) patients developed infections with a rate of 7.7 per 100 patient-years (%-PY). The hazard ratio (HR) associated with a one log10 increase of maximal alphatorquevirus load during a time-window of 3 months before the event was 5.05 (95% confidence interval - CI: 2.94-8.67). CLAD occurred with a rate of 6.0 %-PY with 22 (15%) LTRs affected. HR for a one log10 increase of the lowest alphatorquevirus level during a 3 months' time-window before the event was 0.71 (95% CI: 0.54-0.93). For ACR the minimum three-month alphatorquevirus level was a significant predictor (HR: 0.48, 95% CI: 0.26-0.88). ROC analysis based on the moving window data revealed a threshold of 9.2 log10 copies/ml and of 8.1 log10 copies/ml predicting infections and CLAD, respectively.

Conclusion

Alphatorquevirus load predicts clinical events associated with the level of immunosuppression and may be useful to monitor and optimize IS during the first years of follow-up of LTRs.

EXTRAVESCICLES AND LUNG TRANSPLANTATION: NEW PROSPECTIVE IN THE EVALUATION OF INJURY AND FUNCTION OF THE GRAFT

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Purpose of the study

Lung transplantation is a consolidated surgical therapy of end-stage pulmonary failure, when maximal medical therapy fails. One of the most critical problems is the shortage of donor pool available for transplantation: it is estimated that only 15-20% of the multi-organ donors have suitable lungs. To assess the quality of the graft, in clinical practice chest x-ray, arterial recipient gas analysis and smoking history are currently used, but often these factors do not allow a proper evaluation of the real cellular damage. In the donor, aspiration of gastric content, brain-death induced cellular damage, or initial intensive care infections not detectable at x-ray, affect transplant outcome especially in the first 72 hours. Furthermore, after the retrival, ischemia-reperfusion lung injury (IRI), has a key role in the development of post-transplant complications such as primary grafts dysfunction (PGD) or chronic lung allograft dysfunction (CLAD). Therefore, there is an urgent need for simple, time-sensitive, validated, and non-invasive methods to monitor the quality of the explanted lungs to minimize and hopefully avoid the IRI.

Statements of methods

Our idea is that we have to move from the macro clinical considerations to a micro system, getting back to the single cells that form the lung tissue. In our opinion the definition of appropriate biomarkers able to indentify the quality of the organ at a micro level will be crucial as predictors of the post transplantation lung graft. This is why we focused our attention on the cell-to-cell communication, mainly on microvesicles and exosomes, that are the extracellular nanoparticles release by all the tissues. These extracellular vesicles contain tissue-specific proteomic and RNA signature profiles that reflect the status of their tissue of origin.

Conclusions

Therefore, the identification and the modulation of this specific signature can be predictive of the IRI and can represent the biomarker that the thoracic surgeons are looking for to quantify the organ damage.

CD9+ REGULATORY B LYMPHOCYTES INDUCE EFFECTOR T CELL APOPTOSIS.

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Introduction

Several observations highlight the relevance of regulatory B cells (Breg) to clinical transplantation. We have identified CD9-expressing B cells as a new predictive biomarker of bronchiolitis obliterans syndrome–free survival in a cohort of lung transplanted patients. This new Breg population expressing the CD9 is able to block T cell proliferation. The aim of our study was to decipher the molecular mechanism induced by this CD9+ Breg cell population in the control of effectors T cells.

Materials and methods

CD19+CD9+, CD19+CD9- B cells and CD3+CD4+CD25- effector T cells from the spleen of Balb-c mouse were sorted using a FACSAria III and activated for 48h (a-CD40+LPS for B cells and IL-2 for T cells). CD3+CD4+CD25- effector T cells were co-cultured with CD19+CD9+ or CD19+CD9- for 48h. CD3+CD4+CD25- effector T cells alone were used as control. Cell death, cell cycle arrest, apoptosis, and mitochondrial depolarization were determined by Yellow Dye, propidium iodide, Annexin V and JC-1 staining respectively. Caspases cleavage and protein expression of the Bcl-2 family members were estimated by western blotting. MAPK activation was measured by flow cytometry.

Results

CD19+CD9+, but not CD19+CD9- cells, induce CD3+CD4+CD25- effector T cells death, and inhibit their proliferation with a cycle arrest in G0/G1 via IL-10 secretion. CD19+CD9+ Bregs activate CD3+CD4+CD25- effector T cell apoptosis through both intrinsic and extrinsic apoptosis pathways as illustrated by the mitochondrial depolarization and the cleavage of caspase 8-9 and PARP. CD19+CD9+ Bregs induce expression of pro-apoptotic members of the Bcl-2 family such as Bax and downregulate expression of anti-apoptotics such as Bcl-2, Bcl-XL and Mcl-1. Finally, CD19+CD9+, but not CD19+CD9- cells induce MAPK phosphorylation, showing that MAPK are the main actors of apoptosis activation in this process of regulation.

Discussion

These data show that CD19+CD9+ Breg cells, but not CD9- CD19+ B cells, are able to exert a powerful anti-inflammatory function by inducing effector T cell apoptosis via secretion of IL-10. CD19+CD9+ Breg cells and possibly their production of IL-10 may contribute to create a favorable environment that might be essential for the maintenance of long-term stable lung graft function. These results highlight the use of Bregs as major target for future therapeutic strategies.

BILE ACID ASPIRATION IS ASSOCIATED WITH AIRWAY INFECTIONS: A TARGETED METABOLOMIC APPROACH

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Introduction

Gastroesophageal reflux and bile acids (BAs) aspiration are risk factors for chronic lung allograft dysfunction. BAs may compromise the broncho-alveolar innate immunity by deranging the lipid surface barrier and/or by direct modulation of macrophage activity. Targeted BAs metabolomics and bacterial, fungal and viral cultures were investigated in post lung transplant surveillance bronchial washings (BW).

Methods

BW (238 samples) prospectively collected from 111 lung-Tx patients were retrospectively assayed by liquid chromatography-mass spectrometry for BAs: primary unconjugated (CA, CDCA) and conjugated (TCA, GCA, TCDCA, GCDCA); and secondary unconjugated (LCA, DCA) and conjugated (TLCA, GLCA, TDCA, GDCA, UDCA). BW cultures for bacterial, fungal or viral infection were monitored. Statistical analysis was performed via Mann Whitney test. Data shown as 25th to 75th percentile boxplot, with bars representing 10th and 90th percentile.

Results

Bile acids were detected in 94% (224/238) of samples. Positive Bacterial cultures were in 71%(170/238) of BW and showed greater levels all BAs (p=0.0003); Unconjugated (p=0.0002); Conjugated (p=0.01); Primary (p=0.0015); Secondary (p=0.002). Positive Fungal cultures were in 14%(35/238) of BW with greater Primary BAs (p=0.045). Positive Viral cultures were n 6%(15/238) of BW: No difference noted for BAs levels.

Conclusion

Bile acid aspiration is strongly associated with airway bacterial infections. We speculate BAs aspiration may inhibit macrophage activity via TGR5 receptor in lung, affecting its broncho-alveolar innate immunity consequently facilitating bacterial and possibly fungal infections.

BILE ACID ASPIRATION MODULATES CHOLINERGIC AND SEROTONERGIC RESPONSES OF THE DISTAL AIRWAYS

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Introduction

Gastro-esophageal reflux and bile acids (BAs) aspiration is associated to chronic lung allograft dysfunction (CLAD). We investigated for the first time the reactivity of small airways to a comprehensive panel of BAs as detected in post lung transplant bronchial washings.

Methods

Precision-cut lung slices (PCLS) were prepared from human and mouse lungs. Changes in distal airway luminal area were studied with video phase-contrast microscopy in response to superfusion of 30µM BAs both alone (CA, TCA, GCA, CDCA, TCDCA, GCDCA, DCA, LCA, TLCA, GLCA, TDCA, GDCA, UDCA, CDCA) and in the presence of known bronchoconstrictors: 300nM acetylcholine (ACh), 300nM histamine (His) and 300nM serotonin (5-HT).

Results

Perfusion of BAs alone did not alter basal airway lumen area. However, BAs caused up to ~58% relaxation of airways pre-contracted with ACh (Fig 1 A-F). In contrast, BAs caused up to ~120% further constriction of airways pre-contracted with 5-HT in mouse, and ~30% further constriction in airways pre-contracted with His in human.

Conclusion

Our results demonstrate a dynamic interaction between BAs and distal airways, with secondary BAs showing greater effect. The action mechanism through which BAs affect the cholinergic and serotonergic responses of distal airways is under investigation, although we speculate important in CLAD pathophysiology.

CONTROL OF KAPOSI'S SARCOMA AFTER LUNG TRANSPLANTATION WITH INHIBITOR OF MTOR

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A 37 years old Caucasian man underwent left lung transplantation in march 2009 for pulmonary emphysema (alpha1-antitryptin deficiency PiZ).. The patient was HIV and HHV8 seronegative. Post-operative immunosuppression consisted of tacrolimus use to maintain whole bloods level at 12-15 µg/L, mycophenolate mofetil (2 g qd) and prednisone (0.5 mg/kg qd). During follow up mycophenolate mofetil was reduced due to leucopenia (500 mg qd).

During follow-up, a mild stenosis of the left main bronchial anastomosis was balloon dilatated then stented. Eventually the FEV1 declined from 1.5 L to 1.0 L; diagnosis of Kaposi's sarcoma was performed on the biopsy of a stenosis next to the endobronchial stent; HHV8 DNA was detected by PCR. Antibodies to HHV8 were detected in the blood of the donor. Other locations of Kaposi included a purplish blue nodular supra-pubic skin lesion and a liver nodular lesion on CT.

Conversion to everolimus was initiated (1 mg qd) throughout treatment, mycophenolate mofetil was ceased and the through level of tacrolimus was reduced to a target range of 4 to 6 µg/L. Because of the initial severity 3 courses of IV liposomal doxorubicin were administrated. This resulted in the regression of the clinical symptoms and the reduction of the bronchial stenosis. Chest and abdominal CT showed a marked reduction of the infiltration (40%).

6 month later cutaneous examination showed purplish blue nodular lesion of the legs and CT showed pleural and pericardial effusions. We reduced again the target range of tacrolimus of 3 to 5 µg/L, increased the dose of rapamycin inhibitor (2 mg qd) and added 6 courses of IV liposomal doxorubicin.

Seven years later is in good clinical condition without evidence of recurrence (TEP-CT, bronchoscopy, cutaneous examination) and a preserved FEV1.

AN INTEGRATED PHARMACIST-LED MEDICATION REVIEW SERVICE TO SUPPORT OUTPATIENT CARE OF THORACIC TRANSPLANT PATIENTS

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Purpose: Poor adherence with medication, particularly immunosuppression, is associated with adverse outcomes after thoracic transplantation (allograft rejection, renal impairment, death). Thoracic transplant patients receive multiple interventions to promote adherence in the early post-transplant period, however, with the growing population of long-term survivors there is a need for repeat measures to support adherence over many years. Therefore a pharmacist-led medicine review service was started as part of our long-term follow-up program, which began in January 2017.

Methods: A retrospective analysis of the first 7 months experience was performed to identify the issues that occur in long-term thoracic transplant patients and possible interventions. Subsequent analysis is currently on going.

Results: 403 medication reviews were performed in 332 patients (275 Bilateral Sequential Single Lung Transplants; 38 Heart and Lung Transplants; 19 Single Lung Transplants). A total number of 382 interventions were made. The median age of patient seen was 53 (range 19-77) years and the median time post-transplant was 4 (range 0-33) years.

Categories of Interventions made	Number of Interventions
Medication knowledge assessment/education	95 (24.7%)
Review of immunosuppression and prophylactic medications against protocol	68 (17.9%)
Identification and monitoring of patients requiring treatment which can cause drug interactions	15 (3.9%)
Non-adherence identification	16 (4.2%)
Queries with supply of Medication (Including Homecare delivery service)	56 (14.7%)
Medicines Reconciliation (Corrections made)	22 (5.8%)
Identifying or checking for an adverse effect of a medication	17 (4.5%)
Review of Blood Pressure control (protocol driven management)	51 (13.4%)
Cholesterol Management	8 (2.1%)
Electrolyte Management	13 (3.4%)
Renal Function – dose adjustment of Medication	12 (3.1%)
Patient Referred to another service (e.g. Dermatology/Pain)	5 (1.3%)
Other	4 (1.0%)

Limitations: This study was restricted to the work of the outpatient pharmacy medicines review service. There were difficulties collecting all intervention data retrospectively.

Conclusion: This work has identified many pharmaceutical care issues and interventions in the long-term care of the thoracic transplant patient, in particular supporting continued medication education and identifying those patients who are non-adherent to their medication regimen for closer follow-up. It will guide further studies to determine the impact of the interventions made in the pharmacist-led medicines review service in this group of patients.

CONVERSION FROM TACROLIMUS TWICE-DAILY TO TACROLIMUS ONCE-DAILY IN STABLE LUNG TRANSPLANT RECIPIENTS: EFFECTS ON LUNG FUNCTION

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Purpose: Immunesuppressive maintenance therapy after lung transplantation (LTx) is based on calcineurin inhibitors. Prolonged-release formulation of tacrolimus has been developed to improve patient adherence in solid organ transplantation. However, no study has been performed in LTx to assess if the once-daily tacrolimus (ODT) was equivalent to twice-daily tacrolimus (TDT) regarding allograft function. The aim of this study was to evaluate the effect of conversion from TDT to ODT on lung function in stable LTx patients.

Methods: This retrospective study included all consecutive stable LTx recipients switched from TDT (Prograft®, Astellas) to ODT (Advagraf®, Astellas) between March 2016 and December 2016. FEV_1 (ml), FEV_1 (% pred), FVC (ml) and FVC (% pred) were assessed 6 months before (T0), 3 months before (T1), 1 week after (T2), 3 months after (T3) and 6 month after (T4) conversion. Rate of function decline before and after conversion were also assessed (T0-T1 and T3-T4). Lung function variables were compared using paired test (RM one-way ANOVA) with subsequent multiple comparisons (Holm-Sidak's multiple comparisons test). Rate of function decline were compared using Wilcoxon test.

Results: A total of 372 LTx recipients were included (191M/181F; aged at time of LTx 49y (13-67); 349 BLTx/11 SLTx/12 HLTx; 187 COPD/78 CF and non-CF Bronchiectasis/61 Pulmonary Fibrosis /22 Pulmonary Hypertension/9 OB/15 other), who were converted from TDT to ODT 5.3 (0.5-25) years after LTx. Most patients were converted using a 1mg:1mg (89% ratio), the others at >1mg:1mg ratio (av. 0.8mg; 4%) or a >1mg:1mg ratio (av. 1.6mg, 7%) based upon the treating physicians' discretion. Baseline (T0) FEV_1 (ml), FEV_1 (% pred), FVC (ml), FVC (% pred) were respectively 2482±903ml, 86±26%, 3375±997ml and 96±23%. At T4, FEV_1 (ml), FEV_1 (% pred), FVC (ml) and FVC (% pred) were respectively 2403±945ml, 84±28%, 3343±1034ml and 97±24%. Through T0 to T4, a progressive decrease in FEV_1 (ml and % pred) were observed ($p<0.0001$ and $p=0.0004$, respectively). However, rate of lung function decline was not statistically different between the periods pre- (T0-T1) and post- (T3-T4) use of ODT, except for FVC (% pred) where a slightly significant decreased rate was observed between T0-T1 and T3-T4 (respectively, +1.2 % vs +0.3 % , $p=0.0330$).

Conclusion: Shift from TDT to ODT does not alter the rate of lung function decline in stable LTx recipient. ODT is a safe option for the management of immunosuppression in LTx recipients.

FIRST EXPERIENCE WITH EX-VIVO LUNG PERFUSION FOR INITIALLY DISCARDED DONOR LUNGS IN THE NETHERLANDS, A SINGLE CENTER STUDY

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Purpose

Despite ongoing progress in lung transplantation (LTx) techniques, a shortage of donor lungs persists worldwide. A waiting list mortality of 10,2% in the Netherlands is currently the reality. However, the most recent advancement, Ex-vivo lung perfusion (EVLP), might bring change. EVLP is a technique that evaluates, optimizes and enables transplantation of lungs that would otherwise have been discarded. Here we present our center's first EVLP experiences.

Methods

We retrospectively studied our single-center, prospectively collected database in the period between 2012 and 2016. The EVLP group (n=9) consisted of recipients who received initially discarded donor lungs that were reconditioned using EVLP. The non-EVLP (N-EVLP) group (n=18) consisted of cases that were matched to the EVLP group based on similar surgery dates, sex, extracorporeal circulation (ECC) use, the recipients' underlying lung disease, donor type and type of transplantation performed (primary LTx, bilateral LTx, EVLP or N-EVLP and donation after brain death or donation after cardiac death category 3). All N-EVLP group patients received standard quality lungs in the traditional way. Both groups were compared on primary graft dysfunction (PGD) grades 0-3, lung function, chronic lung allograft dysfunction (CLAD) and survival.

Results

PGD differences were non-significant. In the EVLP group, 33% developed PGD1 at 72 hours post-LTx. In the N-EVLP group, 11% developed PGD1, 6% PGD2 and 11% PGD3 at 72 hours post-LTx. At 3 and 24 months post-LTx, FEV1 as percentage of predicted was similar in the EVLP (78% & 92%) and N-EVLP group (69% & 89%). (Fig.1) Forced vital capacity as a percentage of predicted was comparable in the EVLP (77% & 93%) and N-EVLP group (68% & 101%). (Fig.2) CLAD was diagnosed in one N-EVLP patient at two years post-LTx. Three-year survival was 78% (EVLP group) versus 83% (N-EVLP group).

Conclusion

These results are in line with existing literature that suggest transplantation of previously discarded lungs recovered by EVLP, leads to equal outcomes compared to traditional LTx methods. Furthermore, this study also supports evidence for safe prolonged ischemic times.

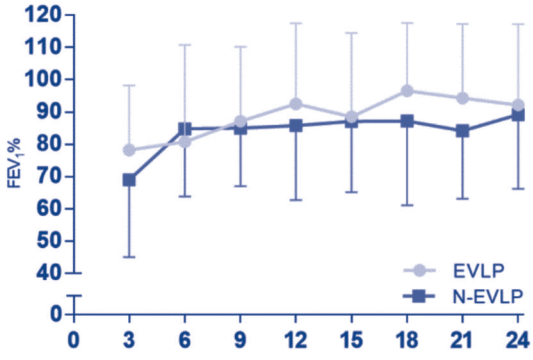

Figure 1

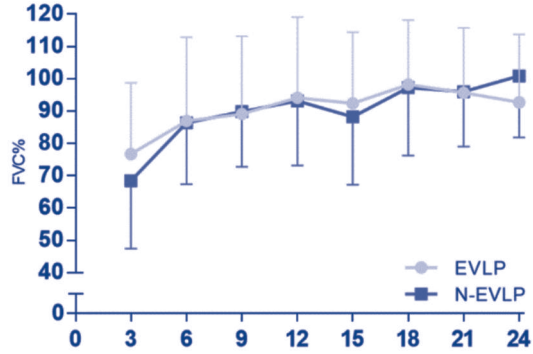

Figure 2

SIX-YEAR EXPERIENCE OF EX-VIVO LUNG PERFUSION AT MILAN LUNG TRANSPLANTATION CENTRE

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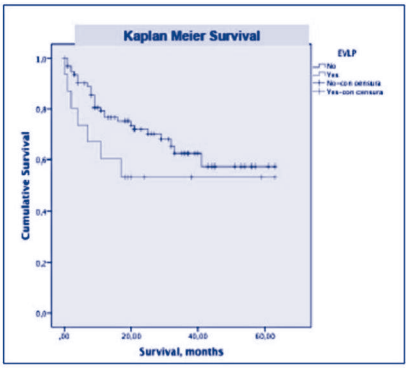
Purpose of study: Ex Vivo Lung Perfusion (EVLP) is a valuable tool for the reassessment of marginal lungs before transplantation and could increase the pool of available organs. The Ethics Committee of our hospital accepted EVLP program as a "rescue opportunity", starting from 2011. The aim of this study was to investigate the characteristics of the recipients of EVLP assessed grafts and their outcomes (early and late) in our hospital.

Statements of methods: A retrospective study was conducted including all lung transplant (LuTx) recipients from January 2011 to June 2016. Two groups of patients were identified based on their graft: EVLP assessed (Group A) or not (Group B). All data were statistically analyzed with SPSS version 22 for Macintosh. Bivariate analyses were conducted using Mann Whitney's U-test for continuous variables and chi-square or Fisher's exact tests for categorical variables. Survival rates were measured by the Kaplan Meier estimator and compared with the logrank test.

Summary of results: From January 2011 to June 2016, a total of 154 LuTx were performed; of those, 20 grafts underwent EVLP reconditioning. The two groups were similar in terms of recipient characteristics (demographics, indication, waiting list time) a part from LAS that was greater in EVLP group. Incidence of PGD3 and median and log-term outcomes were similar in both groups, in particular there was no difference in survivor rate (figure). EVLP group revealed mortality rate within the first 90 days greater than the control group.



Conclusions: In our series, EVLP grafts were given to more severe recipients at time of LuTx; this choice might have affected early perioperative results, with a higher mortality within the first 3 months after transplantation. However the incidence of PGD3 and other medium and long-term outcomes of EVLP were comparable to conventional transplantations; in particular, no difference was found between the two groups in terms of median survival. EVLP grafts are usually allocated to less compromised recipients; our data, instead, suggest that EVLP reconditioning may increase the number of available grafts, also for those patients whose conditions are too severe to wait for another donor.

ABSORBABLE STERNAL PINS FOR STERNAL CLOSURE FOLLOWING LUNG TRANSPLANTATION

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Background: Bilateral anterolateral thoracotomy associated to transverse sternotomy (Clamshell incision) is a commonly used surgical approach for bilateral lung transplantation, especially when extracorporeal support is needed. At the end of the procedure, surgical closure technique represents a major step as sternal repair may end with override, separation, or even sternal pseudarthrosis. The sternal defect will eventually hamper the functional outcome of lung transplantation

We present here a new technique for Clamshell closure using absorbable sternal pins for sternal stabilization and closure.

Methods: Since Jan 1st 2016, all patients undergoing bilateral lung transplantation with the need for Clamshell incision were included. At the time of sternal closure, two absorbable poly-L-lactide pins were inserted in the sternal medulla to ensure latero-lateral and antero-posterior stabilization. The bilateral thoracotomy and sternotomy were then closed using the usual technique with intercostal and sternal crossed sutures. Patients were observed for chest wall stability during the postoperative curse.

Results: From Jan 1st 2016 to April 30st 2018, 108 patients underwent lung transplantation at our institution. Amongst them, 30 (28%) patients had a clamshell approach either because of narrow chest or severe pleural adherences (n=12), or because of need for extracorporeal support (n=13). In 25 patients, sternal pins were used for sternal closure. Two patients deceased during the surgical procedure of transplantation. Five patients could not receive sternal pins for logistical reasons. The latter patients all presented with sternal separation during the postoperative curse and were stabilized using sternal pins for the second surgical closure. Postoperative curse was then uneventful. We observed no migration of the pins, neither sternal infection following the use of the sternal pins.

Conclusion: Using poly-L-lactide absorbable pins for sternal stabilization in sternal clamshell closure is a safe and reproducible technique. We could not evidence any adverse effect using this device. We had no sternal complications after using this device for primary clamshell closure. On the opposite, when the device was not available, patients experienced sternal separation and override with pain and respiratory distress. Using the pins for secondary closure demonstrated safe sternal healing.

LUNG TRANSPLANTATION FOR PULMONARY HYPERTENSION PRESENTING WITH GIANT ANEURYSM OF THE PULMONARY TRUNK

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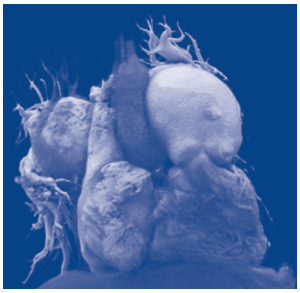
Background: Lung transplantation for idiopathic pulmonary arterial hypertension (IPAH) is associated with an increased perioperative mortality, however, mastering the challenging postoperative period, results in excellent long-term survival. In rare cases, the surgical treatment of IPAH patients is further complicated by severe aneurysmatic dilatation of the pulmonary trunk and the main pulmonary arteries. This requires a special approach with important differences to standard techniques of lung transplantation.

Methods: We performed a retrospective analysis of IPAH patients with a severe aneurysm of the pulmonary artery receiving lung transplantation between 1996 and 2018. A review of charts and institutional database was conducted and pre- and intraoperative data as well as patient outcome was analyzed.

Results:Out of 124 IPAH patients transplanted in the study period, six patients presented with pulmonary artery aneurysm. Pulmonary trunk diameters ranged from 52 to 80mm (68.8 mean), however, the pulmonary annulus was not significantly dilated and the pulmonary valve was competent in all patients. Mean mPAP levels were 68±26mmHg, while mean pulmonary vascular resistance was 10.5±1.6 WU. None of these patients required ECLS bridging to transplantation. In all patients the pulmonary trunk was replaced utilizing cardiopulmonary bypass (mean bypass time 233±57min). As the main surgical challenge are extensive mediastinal collaterals, patients required a mean of 9.3±8 erythrocyte concentrates and 11.5±7 units of fresh frozen plasma intraoperatively. Postoperative ICU stay was prolonged with a median of 20±16 days. One of the six patients died due to sepsis on POD 13. One patient required re-transplantation 3.3 years after the first transplantation for an early BOS. Long-term survival time was excellent with 83.3% at 1 year and 55.6% at 10 years and did not significantly differ from long-term outcome of non-aneurysmatic IPAH patients (1 year: 80.4%, 10 year: 70.0%, log rank: p=0.664)

Conclusion: Patients with giant pulmonary aneurysm are eligible for double lung transplantation and do not require a heart-lung transplantation. However, a special surgical management, which can only be provided by centers experienced in transplantation for IPAH, is required.



Computed tomography 3d reconstruction: Patient AF

COST-EFFECTIVENESS OF LUNG TRANSPLANT FOR END-STAGE CYSTIC FIBROSIS: EVIDENCE FROM A FRENCH OBSERVATIONAL STUDY

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Context

Our objective is to assess cost-effectiveness of lung transplant compared to medical palliative care for patients with end-stage cystic fibrosis, in so far as the opportunity and efficiency of lung transplant might still be debated in some contexts/countries. No such estimation has been conducted earlier in France.

Data & Methods

The study relies on a comparison between empirical observations for transplanted patients and theoretical assumptions to approximate the "non-transplanted" situation.
For transplanted patients, survival and quality of life data arise from a follow-up of end-stage CF patients at Hospital Foch who underwent lung transplant between 2005 and 2015. Average health costs are estimated on a sub-sample of this cohort.
For the comparison group ("non-transplanted" situation), quality of life and health costs are extrapolated from measures of the Foch cohort performed prior to lung transplant. Estimates of survival without transplant is based on evidence from literature.

Results

Over a 10 years period, total gain in quality-adjusted survival of lung transplant equals 4.2 years and incremental cost-effectiveness ratio is 30,000 Euros. Results prove to be robust to sampling errors (probabilistic sensitivity analysis) and are mainly sensitive to assumptions on values of health care costs (±50%) and on survival without transplant (±30%).

Conclusion

In addition to being highly effective on long-term survival, lung transplant can be considered as cost-effective if compared to common acceptance thresholds for social appraisal of health-technologies.
Main limitations stem from the use of theoretical assumptions for patients who do not receive transplant. Improvements are intended to better estimate survival for non-transplanted patients, using LAS prediction model instead of (controversial) evidence from literature.

DEVELOPMENT AND VALIDATION OF AN INSTRUMENT TO MEASURE KNOWLEDGE IN TRANSPLANT RECIPIENTS

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Background

Non adherence is a well-known barrier in the transplant population. Knowledge is a crucial patient-related factor that enables patients to adequately follow health regulations after solid organ transplantation. Educational interventions are systematically applied by nurses to ensure that patients achieve the necessary knowledge about organ transplantation and to prevent patients to become non adherent, when ready for discharge. Although knowledge is an important factor, there is currently no validated instrument available that evaluates patients' knowledge about organ transplantation in an objective way. This leads to knowledge deficits, which may lead to poor patient outcomes.

Purpose of the study

Development of a validated instrument to measure knowledge after a solid organ transplantation. This instrument was also developed to improve patients' discharge management.

Methods

University Hospital, tertiary referral center, biggest transplant center in Benelux.
Phased approach: first generating a potential pool of items from scientific literature (only four studies met inclusion criteria), current practice and the vision of transplant-professionals. Next, design of a multiple choice question-based instrument. Finally, validation by determining the reading level by using the Flesch Reading Ease Score and the content validity through expert rounds and cognitive debriefings.

Results

The validation procedure was obtained by two rounds of expert consults and cognitive debriefings, resulting in an instrument of 29 questions with an Scale item-Content Validity Index (S-CVI) of 0.94, which indicates an excellent content validity. Also the theoretical saturation was reached after 11 cognitive debriefings. Readability scored 71.3, determined by the Flesch Reading Ease Score, which indicates an acceptable reading level.

Conclusion

A Dutch instrument to measure patients' knowledge about organ transplantation was developed, consisting of 29 multiple choice questions with an excellent content validity and acceptable reading level. This instrument may allow to objectively assess transplant recipients' knowledge, so that educational interventions can be adapted and applied. However, further detailing of the validity and assessment of the reliability is necessary.

OUTCOME AFTER LUNG TRANSPLANTATION USING REPEATEDLY DECLINED MARGINAL DONOR LUNGS

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Background

Despite the implementation of extended donor criteria, acceptance rates of marginal donor lungs still vary between transplant centers. One reason for this is insufficient data on parameters, which constitute a truly unacceptable donor lung. This leads to a substantial number of lungs being rejected and a significant reduction of the donor pool.

Methods

We analysed 749 patients who received double lung transplantation between January 2010 and June 2017 in our institution. A total of 124 patients were transplanted with donors previously rejected by two or more transplant centers based on concerns about the organ quality (group I). A control group consisted of 625 patients who received lungs with none or only one previous rejection for quality reason (group II). Short- and long-term outcomes between the two groups were compared.

Results

Pre- and intraoperative factors of both groups were comparable. Organ offers in group I had been turned down between 2 and 12 times (median 3; IQR: 2-5). Donor parameters such as age, last pO2, last pCO2, duration of intubation and smoking status did not differ between the two groups. However, there was a significantly higher number of donors with radiological infiltrations (p=0.002), signs of lung contusion (p=0.001) as well as abnormal findings in bronchoscopy (p<0.001) in group I. Despite this, PGD 3 rates were comparable at all time points (t0: 13.2% vs 18.1%, p=0.318; t24: 2.5% vs 2.2%, p=0.402; t48: 1.7% vs 3.2%, p=0.765; t72: 0.8% vs 2.7%, p=0.432). Mean length of ventilation (119 vs 118 hours, p=0.958), ICU time (16 vs 17days, p=0.647) und total length of stay (32 vs 33 days, p=0.729) were also similar. Long-term survival (5 years: 72.6% vs 75.8%, log rank: p=0.970) as well as freedom from CLAD (5 years: 80.7% vs 83.9%, log rank: p=0.279) were comparable in both groups.

Conclusion

A high percentage of donor lungs previously rejected for quality reasons by other transplant centers can be safely utilized without a negative effect on short- and long-term outcome.

RIGHT SINGLE LUNG TRANSPLANTATION FOR EMPHYSEMA HAS BETTER SURVIVAL THAN LEFT SINGLE TRANSPLANT: A SINGLE CENTER EXPERIENCE

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Objective: Single (S) and double (D) lung transplantation (lung-Tx) are accepted treatment for end-stage emphysema. However, literature has revealed conflicting long-term outcomes of S versus D lung-Tx in emphysema. We investigated our long-term results after the introduction of the Lung Allocation Score (LAS) and explored differences among D, left single (LS) and right single (RS) lung-Tx recipients.

Methods: Retrospective analysis of 127 patients with emphysema who underwent lung-Tx after LAS inception: 67 received D, 60 S (27 RS and 33 LS). Survival, chronic lung allograft dysfunction (CLAD) development, and broncho-alveolar infection rates were assessed. Non-adjusted Kaplan-Meyer analysis, and adjusted stratified Cox survival models are reported. Mann Whitney test were performed.

Results: No survival differences at 5 and 10 years were found in S vs D (p=0.59 and p=0.56 respectively). The analysis of RS and LS cohorts showed a greater survival for RS recipients both at 5 and 10 years (p=0.02 and p=0.03, respectively). No significant differences were found between either S lung-Tx procedure versus D. The Table shows the adjusted survival. No differences were found for freedom from CLAD between RS and LS. LS lung-Tx had a greater bronch o-alveolar bacterial/fungal infection rate/year (median 1.81, 25th-75th percentile range 0.56-3.48) compared to RS (median 0.51; range 0.26-1.17), (p=0.01).

Discussion: Our experience following LAS inception showed that RS lung-Tx for end stage emphysema had better long-term outcomes than LS: greater 5 and 10-year survival along with lower airway infection rate. We speculate RS lung-Tx have lower infection rate being less likely compressed from contralateral native lung hyperinflation. These observations, if confirmed in a larger cohort may support the allocation of single as opposed to double lung-Tx in emphysema recipients for better utilization of scarce lung donor organs.

Adjusted Survival: Right Single vrs Left Single			
	HR	95% CI	p-value
Right	**3.1**	**1.12 - 8.5**	**0.030**
Age	1.0	0.96 - 1.1	0.362
Gender Mismatch	1.9	0.66 - 5.4	0.235
CMV Mismatch	2.4	0.74 - 7.45	0.145
LAS	0.99	0.95 - 1.03	0.654
HR: Hazard ratio; CI: Confidence Interval			

CENTRAL VERSUS PERIPHERAL CANNULATION OF EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT DURING DOUBLE LUNG TRANSPLANT FOR PULMONARY HYPERTENSION

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Objectives

Extracorporeal membrane oxygenation (ECMO) has become the standard of cardiopulmonary support during a sequential double lung transplant for pulmonary hypertension. Whether central or peripheral cannulation is the best strategy for these patients remains unknown. Our goal was to determine which is the best strategy by comparing 2 populations of patients.

Methods

We performed a single-centre retrospective study based on an institutional prospective lung transplant database.

Results

Between January 2011 and November 2016, 103 patients underwent double lung transplant for pulmonary hypertension. We compared 54 patients who had central ECMO (cECMO group) to 49 patients who had peripheral ECMO (pECMO group). The pECMO group had significantly more bridged patients who received emergency transplants (31% vs 6%, P = 0.001). The incidence of Grade 3 primary graft dysfunction requiring ECMO (14% vs 11%, P = not significant) and of in-hospital mortality (11% vs 14%, P = not significant) was similar between the groups. Groin infections (16% vs 4%, P = 0.031), deep vein thrombosis (27% vs 11%, P = 0.044) and lower limb ischaemia (12% vs 2%, P = 0.031) occurred significantly more often in the pECMO group. The number of chest reopenings for bleeding or infection was similar between the groups. The 3-month, 1-year and 5-year survival rates did not differ between the groups (P = 0.94).

Conclusions

Central or peripheral ECMO produced similar results during double lung transplant for pulmonary hypertension in terms of in-hospital deaths and long-term survival rates. Central ECMO provided satisfactory results without major bleeding provided the patient was weaned from ECMO at the end of the procedure. Despite the rate of groin and lower limb complications, peripheral cannulation remained the preferred solution to bridge the patient to transplant or for postoperative support.

BETTER PULMONARY FUNCTION IN UPPER LOBE THAN IN LOWER LOBE IN A PORCINE DCD DONOR LUNG MODEL USING CELLULAR EX VIVO LUNG PERFUSION

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Objectives

The utilization rate of donor lungs in the United States is only 15-20%. The major reason for this low rate of utilization is low PaO_2/FiO_2 (P/F) ratio. During donor management aspiration, pulmonary edema and atelectasis frequently occur on the dorsal side of the lower lobe in the supine position. Our hypothesis is that even if whole marginal donor lungs are judged to be non-suitable for transplantation, the upper lobes could still be suitable for transplantation. Some reports have supported that bilateral upper lobar transplantation could be considered as a valid option to solve the donor pool shortage in selected cases. The aim of this study is to compare lung function between the upper and lower lobes in marginal porcine donor lungs in cellular ex vivo lung perfusion (EVLP).

Methods

Following 2 hours of warm ischemia and 5 hours of cold storage, double lungs (n = 5) were perfused for 2 hours in cellular EVLP. Transplant suitability was evaluated by assessment of physiological parameters (airway parameters, vascular parameters, and blood gas analysis) as well as visual findings. The difference in lung function between upper and lower lobes was assessed by differential blood gas analysis and pathological and cytokine analysis in the lung tissue of each lobe.

Results

All five EVLP cases were judged as non-suitable for transplantation. P/F ratio was 273.8 ± 71.9 mmHg, peak inspiratory pressure was 18.4 ± 5.9 cmH2O, pulmonary vascular resistance was 526.9 ± 97.7 dyne·s/cm5, and all cases showed significant pulmonary edema in the lower lobes. On the contrary, P/F ratio in the pulmonary vein (PV) of the upper lobe was significantly higher than that in the lower lobe PV (427.6 ± 109.5 vs. 100.2 ± 67.0 mmHg, $p = 0.005$), significantly lower shunt fraction (24.5 ± 11.8 vs. 78.8 ± 27.7 %, $p = 0.004$) and significantly lower A-a gradient (238.8 ± 108.6 vs. 566.9 ± 68.3 mmHg, $p < 0.001$). The upper lobe was also associated with lower wet/dry ratio (5.5 ± 0.1 vs. 6.1 ± 1.3), better acute lung injury (ALI) grade [the number of ALI grade < 1, 5 (100%) vs. 3 (60%)], lower level of IL-1beta and IL-8 (IL-1beta, 4.0 ± 3.7 vs. 9.4 ± 4.8 pg/ml; IL-8, 0.4 ± 0.2 vs. 0.5 ± 0.1 pg/ml) and higher IL-10 (0.012 ± 0.003 vs. 0.007 ± 0.003 pg/ml).

Conclusions

Our results showed that the pulmonary function of the upper lobes was better than that of the lower lobes. These results suggest that it might be feasible to use these upper lobes in lung transplantation in small-size patients, especially pediatric recipients.

ITALIAN URGENT LIST TRANSPLANT PROGRAM: MONOCENTRIC EXPERIENCE

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Objective: Mortality in the waiting list for lung transplant is still very high and, at present state, there are no long-term support devices as a bridge to transplantation.
In 2010 Italian National Transplant Centre (CNT) established a dedicated graft allocation strategy, called Italian Urgent List Transplant Program (IULT), for rapidly deteriorating patients awaiting transplant. Conforming to this program, patients with respiratory failure on mechanical ventilation or extracorporeal membrane oxygenation (ECMO) may be included in this urgent list.
This review presents the early results in our Centre.

Methods: We retrospectively studied 180 patients who underwent lung transplantation from May 2004 to May 2017 to evaluate the impact of the IULT program.
We compared pre-operative status, peri-operative management, surgical procedure, mechanical ventilation, need for intra-operative and post-operative ECMO support, post-operative care, early and long-term outcome and survival in the two different groups (IULT vs NON-IULT).

Results: We performed 180 lung transplants, 156 on standard list and 24 on urgent list.
Underlying diseases were pulmonary fibrosis (44,9% vs 20,8%), cystic fibrosis (36,5% vs 70,8%), COPD (9% vs 4,2%), miscellaneous (7,1% vs 0%) and re-transplant (2,6% vs 4,2%).
Median age of the recipients at the time of transplantation was 45,8 vs 33 years.
Median standard transplant waiting list time was 221 vs 99,8 days.
Median waiting list time after being placed in the national urgent list was 6,33 days.
Median pre-operative FEV1 was 41,4% vs 29,3%.
Both groups were homogeneous about donor characteristics and surgical technique.
Post-operative ECMO was necessary in 20 vs 23 cases and in IULT list we highlighted a greater proportion of peri-operative complications (PGD, bleeding, duration of mechanical ventilation).
Postoperative hospital stay was 33 vs 68,79 days.
Median FEV1 one year after transplant was similar in both groups.
As well long-term mortality rates and survival distributions presented similar results in the two groups.
From the analysis of the results, despite the greater number of early intra-operative and post-operative complications (need for surgical revisions, prolonged mechanical ventilation, extracorporeal support, longer ICU stay and hospitalization), lung transplants performed in urgent list showed similar survival rates, percentages of chronic rejection and infectious complications in the first year, compared to standard list.

Conclusion: The IULT program allowed lung transplantation in prioritized patients with acceptable mortality and morbidity rates, without negative effects on the mid-long terms outcomes compared to non-urgent patients.
Further studies are needed to validate our results.

EX VIVO LUNG PERFUSION IS RELEVANT TO BYPASS ADVERSE LOGISTICS

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Background: The ex vivo lung perfusion technique is now a validated tool for lung preservation and/or lung reconditioning increasing the donor pool and the number of lung transplantations performed yearly. But performing lung transplantation also relies on available trained surgeons and ready operative room which may not always be the case facing daily tight logistics. In this setting, another advantage of ex vivo lung perfusion will be its ability to bypass adverse logistics. We present a case series to illustrate how ex vivo lung perfusion may be used to increase the efficiency of daily organization.

Methods: From May 2017 to July 2017, each time a standard lung graft was accepted in a time schedule that would hamper the regular operative schedule, we decided for prolonged ex vivo lung preservation. Lung criteria acceptance would not differ from standard conditions. Lung grafts were harvested and put on the OCS lung device for lung preservation. A lung function assessment was performed before leaving the retrieval hospital and the normothermic preservation was started for the journey back to our institution. The complete operative schedule was performed without any cancellation starting on a regular basis of 8 AM in the morning. The recipient was then transferred to the operative room, and the lung graft was assessed on the OCS lung device. Vascular and airway resistances were checked as well as the effluent blood gas for PAFiO2 to authorize general anesthesia and starting lung transplantation.

Results: Five patients underwent bilateral lung transplantation according to the method and schedule described above. Three patients had emphysema, one had cystic fibrosis and one had fibrosis with ECMO as bridge to transplantation with super emergency priority. Duration from aortic cross clamp in the donor to last graft unclamping ranged from 404 to 757 minutes. All grafts presented with a final assessment blood gas PaFiO2 superior to 300, decreasing vascular and airway resistances. One patient with emphysema developed PDG grade 3 with need for ECMO in the postoperative curse but was eventually weaned and extubated at day 4. The patient with fibrosis and ECMO as a bridge to transplantation was weaned from ECMO at the end of transplantation and extubated at day 2. All three other patients were extubated within 24 hours postoperatively.

Conclusion: Prolonging normothermic lung preservation demonstrated to be safe and reproducible with no negative consequences on the lung graft quality. Bilateral lung transplantation was performed on daytime avoiding any obstacle to performing lung transplantation or to perform the regular operative schedule. The high costs of ex vivo perfusion may be counterbalanced by the advantage of increasing the donor pool and the number of lung transplantations without negative consequences on the routine surgical activity.

CATEGORY III DONATION AFTER CIRCULATORY DEATH (DCD) LUNG DONORS FOR PEDIATRIC LUNG TRANSPLANTATION: INCREASING THE LUNG DONOR POOL WITH EXCELLENT OUTCOMES.

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Purpose

Access to timely suitably sized matched quality organs remains a challenge for LTx, particularly for pediatric lung transplantation (pLTx). DCD lungs are additionally providing organs for adult LTx (aLTx), however the utility and outcomes of DCD pLTx are rarely reported.

Methods

This report describes our centers controlled DCD and pLTx activity (<age 18 yrs) and outcomes since commencing use of DCD donors for LTx in 2006. The first pediatric DCD donor was used for aLTx in 2007 and the first DCD pLTx was done in 2012. Ex-vivo Lung Perfusion (EVLP) has not been utilized at our center to date.

Results

40 pLTx have been performed since 2006, 9 utilizing DCD and 31 donation after brain death (DBD) donors. 21 pLTX have been done since 2012; 9 DCD LTx included 4 pediatric DCD donors (mean age 8yrs), 2 adult cutdown bilobar and 3 adult BLTx DCD donors (mean age 43yrs) with a mean wait-list (W/L) time of 78 days, median 37d. The other 12 pLTx utilized DBD donors- 7 pediatric (mean age 9yrs), 2 adult bilobar cut down and 3 BLTx DBD (mean age 44yrs) with a mean W/L time of 142d, median 66d. The 9 pLTx recipients of DCD lungs had a median age 15 years with cystic fibrosis (n=5), pulmonary hypertension (n=3, with 1 on ECMO) and obliterative bronchiolitis (OB n=1). 100% survived 1yr, and 7/9 DCD pLTx are alive at a mean of 1140d, median of 1316d with 1 death at 531d from CLAD, 1 death from renal failure at 1813d. There have been 2 W/L pediatric deaths since 2006; 1 at 182d (a sensitized potential re-LTx age 16yrs) and 1 at 66d (OB due to GVHD age 8yrs).
Since 2006, 77 pediatric donors have been used for LTx. 15 of these were DCD donors (median age 16yrs), 11/15 have been used for aLTx, 6 since 2012. The 11 adult recipients LTx indications included COPD (n=5), cystic fibrosis/bronchiectasis (n=4), reLTx and ILD (n=1 each), with a mean age of 46 yrs and W/L time of 230d, median 97d. 10/11 aLTx are alive at a mean 2264d, median 1992d with 1 death at 2444d from CLAD.

Conclusion

Controlled DCD provide a significant and quality donor lung pool to increase LTx opportunities for pediatric patients (and adults) with terminal lung disease. With lives at stake, and an appropriate legal/organizational framework, all LTx centers should consider and embrace DCD for both pediatric and adult recipients.

CMV HYPERIMMUNE GLOBULINS AS SALVAGE THERAPY IN PATIENTS WITH CMV INFECTION FOLLOWING LUNG TRANSPLANTATION: THE FRENCH MULTICENTRIC EXPERIENCE

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Rationale: CMV infection remains a critical challenge in lung-transplanted patient. The main factors of treatment failure are antiviral resistance and intolerance. The latest international guidelines on CMV management in solid organ transplantation do not clearly state the place of CMV hyperimmune globulins (CMV-Ig) as a therapeutic option. Therefore, we aim to describe CMV-Ig current use (indications, efficacy and safety) in France in LT.

Method: We performed a retrospective survey within the 5 largest French centers: whole of the 22 lung transplanted patients who received CMV-Ig for CMV infections were recruited.

Results: 14 (63%) patients were female, and 17 (77%) were D+R- for CMV.
CMV-Ig was used in two major indications: first as a rescue therapy for clinical failure and/or CMV resistance of usual antiviral drugs concerning 10 patients (45% of the cases), second as an alternative therapy because of serious antiviral drug adverse effect for 11 patients (50%). One patient (5%) combined both indications.
14 patients received CMV-Ig in combination with antiviral drugs (63%) and 8 patients as a monotherapy.
With a median follow up of 225 days, we report that 14 patients (60%) did not experience CMV relapse while under anti CMV Ig. 9 of these 14 patients were treated with a combination of CMV Ig and antiviral drug.
With an efficacy defined as clinical improvement and significant decrease of the CMV threshold, CMV-Ig was successful for 5/10 patients (50%) treated for antiviral clinical failure and/or resistance, and 7/11 patients (63%) treated for antiviral serious adverse effect.
Only 2/12 (16%) patients experienced CMV relapse after discontinuation of CMV-Ig.
The only reported adverse event was a significant pruritus following the day of the first infusion.

Conclusion: These multicentric retrospective study describe the current clinical practice of anti CMV Ig in France: as a rescue therapy or as an alternative therapeutic needed for intolerance to effective antiviral drugs. CMV Ig used in these indications is associated with success in at least one of two cases and seems to be safe.
Further prospective controlled studies are needed to validate the use of anti CMV Ig in that clinical context.

ISAVUCONAZOLE FOR THE TREATMENT OF FUNGAL INFECTIONS IN LUNG TRANSPLANT RECIPIENTS: CASE SERIES FROM A SINGLE CENTRE

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Purpose of the study: Fungal infections are an important cause of morbidity and mortality after lung transplantation. Prolonged treatments with antifungals are hindered by intolerances and toxicities and by clinically significant drug-drug interactions that impact the management of the immunosuppression. Isavuconazole is a second-generation triazole with a broad spectrum of activity. It has shown comparable efficacy and improved tolerability and potential for drug-drug interaction compared to other azoles in clinical trials.
There is limited experience in treating fungal infection treatment with isavuconazole in lung transplant recipients.
We aim to describe our experience with isavuconazole dosing in lung transplant recipients.

Methods: Demographic, clinical and Therapeutic Drug Monitoring (TDM) data was collected for all lung transplant patients on isavuconazole between October 2016 and April 2018. They were commenced on the standard dose of 200 mg every 8 hours for the first six doses, then 200 mg once daily. Trough levels of isavuconazole were initially taken weekly till therapeutic (level >1ng/mL) then monthly, doses were adjusted accordingly.

Results:Five patients were taking voriconazole or posaconazole previously, 4 discontinued them due to adverse effects and 1 due to a breakthrough infection. None experienced side effects on isavuconazole. The mean time to reach the therapeutic level was 8.78 (SD +/- 6.32) days. Four patients required dose adjustment secondary to levels, 1 due to confirmed elevated minimum inhibitory concentration of the pathogen. All our patients needed a smaller immunosuppressant dose adjustment on isavuconazole compared to voriconazole and posaconazole.

Patient	Transplant	Sex	Lung disease	Time after Transplant (months)	Indication for isavuconazole	Time to Therapeutic level (days)	Dose to reach Therapeutic level (mg)	Treatment length (months)
1	BSSLTx	M	CF	19	*Aspergillus*	11	200	18
2	BSSLTx	F	CF	8	*Fusarium*	6	200*	15
3	RSLTx	M	COPD	71	Unidentified fungi	6	100	11
4	BSSLTx	M	IPF	50	*Penicillium*	21	200	9
5	BSSLTx	F	CF	143	*Aspergillus*	5	300	7
6	HLTx	M	CF	340	Aspergilloma	2	200	5
7	BSSLTx	F	COPD	92	*Penicillium*	5	200	0
8	BSSLTx	M	COPD	38	*Aspergillus*	17	100	5
9	BSSLTx	F	CF	0	Prophylaxis	6	200**	1

BSSLTx: bilateral sequential single lung transplant; RSLTx: right single lung transplant; HLTx: heart and lung transplant; CF: Cystic Fibrosis; IPF: Idiopathic Pulmonary Fibrosis.
*Subsequently increased to 400mg due to raised MIC
** intravenous

Conclusion: Our early experience suggests that isavuconazole is a well-tolerated treatment option for fungal infections post-lung transplant with a reduced drug-drug interaction impact on immunosuppressants compared to voriconazole and posaconazole. Due to interpatient variability TDM is a useful tool to guide dosing.

INFLUENCE OF PLASMAPHERESIS ON HEMOSTASIS AND HEMORRHAGE INTRAOPERATIVELY IN PULMONARY TRANSPLANTATION

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Introduction: The major long-term complication of patients after lung transplantation is graft rejection. This rejection is currently prevented by drug immunosuppression possibly accompanied by plasmapheresis, usually realized in postoperative. In our team, we perform pre-operative plasmapheresis for selected patients at high-risk of rejection. This technique has the disadvantage of partially eliminating hemostatic factors, which would therefore increase intraoperative bleeding. The aim of this study was to evaluate the relationship between the preoperative plasmapheresis and the risk of intraoperative hemorrhage.

Material and method: We performed a retrospective observational study of all bilateral lung transplantations at the Foch Hospital from January 2012 to December 2016, excluding those on bridge-to-transplantation, under cardiopulmonary bypass, and multiple-organ transplantation. We compared two groups depending on preoperative plasmapheresis requirement. The primary endpoint was the quantification of intraoperative bleeding. The secondary endpoints further examine the relationships between plasmapheresis and biological tests of hemostasis in whole blood.

Results: The estimated bleeding between the preoperative plasmapheresis group and the control group was similar with 1200mL vs 1100mL, respectively (p = 0.496). The administration of blood products was also similar between the two groups (5 red blood cells concentrate (3-6.25) vs 4 (3-7) p = 0.456). The whole blood hemostasis mesurement by thromboelastogram (table 2) was identical despite a decrease in fibrinogen (2.7g / L ± 0.80 vs 3.9g / L ± 1.2 (p <0.0001) and platelets at the end of plasmapheresis (267G / L ± 126 vs 315G / L ± 134 p = 0.021).

Table 1: Demographic data

	Plasmapheresis (85 patients)	No plasmapheresis (202 patients)	Total	P-value
Age (mean)	40,7 ± 13	41,3 ± 13	41,1	0.640
Sexe ratio (male %)	60	47,5	100	0.042
BMI	21 ± 4	20 ± 4	21	0.105
Preoperative pulmonary hypertension en %	46	39	41	0.315
Diabetes en %	31	32	32	0.904
Oto score (mean)	6 [4-7]	6 [4-8]	6	0.312
P/F ratio	362 [306 - 401]	358 [300 - 438]	361	0.209
Ex vivo (%)	16	13	14	0.479

Conclusion: Our study does not detect an increased risk of haemorrhage when preoperative plasmapheresis is performed prior to bipulmonary transplantation. It is now important to evaluate the benefit of plasmapheresis on the risk of acute rejection and the prognosis of these patients in the medium and long term.

Table 2: Thromboelastography test

	Before plasmapheresis	After plasmapheresis	P-value
R	4.2 [3.4-5.2]	3.4 [2.9-3.9]	0.331
AM	69 [65-73]	70 [62-73]	0.111
Ly	0.4 [0.0-2.0]	0.7 [0.03-3.47]	0.124

CYSTIC FIBROSIS-RELATED DIABETES BEFORE LUNG TRANSPLANTATION IMPACTS SURVIVAL BUT NOT LONG TERM RENAL FUNCTION

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Introduction. Lung transplanted CF patients differ from other LT patients because of their younger age, better survival after LT, and specific associated comorbidities related to CF. The objective was to describe the prevalence of CFRD before and after LT; and to analyse survival and renal function after LT according to CFRD status before LT.

Methods. CF patients treated in the Lyon CF reference centre and transplanted at the Lyon University Hospital (France) between 2004 and 2014 were retrospectively included. Genotype, pancreatic status, age at LT and survival were recorded. The criteria were recorded three months before LT, six months after LT, and each year of follow-up until December 2016: glucose tolerance status (CFRD or others), daily insulin dose requirement; renal function, defined by the estimated glomerular filtration rate (GFR); and daily glucocorticoid (GC) dose. Analysis for repeated measures data was conducted by using linear mixed-effect regression models.

Results. 63 adult CF patients were transplanted. 32 (53.3%) patients were delF508 homozygous. All were pancreatic insufficient, and 42 (70%) had CFRD before LT. The mean ± SD calculated GFR before LT was 109 ± 47 ml/min/1.73m^2, and did not differ according to CFRD status. The mean ± SD age at LT was 27.6 ± 8.4 year. The median (IQR) time of follow-up was 5.6 (3.8-8.2) years and 12 (20%) patients died in the follow-up: three patients died in the three post-operative months, seven patients in the five years following LT and the last two at 6 and 8 years after the LT. The prevalence of CFRD was 68% (41/60) and 54% (20/37) at two and five years after LT. For the 27 patients who had persistent insulin-treated CFRD, insulin requirement decreased with a slope of -2.1 ± 2.9 IU/day per year ($p<0.01$) and was correlated to the daily GC dose (+0.4 IU/day for one additional GC milligram, $p=0.012$). Seven (11%) patients who had insulin-treated CFRD before LT get free from diabetes after LT with at a median (IQR) time of two (1-4) years. After LT, the GFR decreased with a slope of -5.3 ± 5.3 ml/min/1.73m^2 per year ($p<0.001$) and was not correlated to CFRD status before LT, or cumulative dose of aminoglycoside. The Kaplan-Meier survival of patients with CFRD before LT was poorest compared to those without ($p=0.03$). In the univariate Cox model, the survival was not correlated to the GFR before LT, to the sex, to the age at LT, or to the CF.

Conclusions. CFRD before LT was associated with a poor survival after LT in CF patients, which should conduct to a better management of diabetes control. Some patients with pre-LT CFRD get free of diabetes after LT. CFRD is not associated with renal insufficiency after LT.

DEVELOPMENT OF A CUMULATIVE DEFICIT FRAILTY INDEX FOR CYSTIC FIBROSIS LUNG TRANSPLANT CANDIDATES TO PREDICT POST-TRANSPLANT SURVIVAL

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Introduction: Improvement of cystic fibrosis (CF) life expectancy and advances in lung transplantation (LTx) have resulted in more medically complex patients to be considered for this procedure. Frailty is a measure of biological age and physiologic reserve. It increases with age but it can be observed in younger subjects with advanced disease. The aim of this study was to develop a CF-specific cumulative deficit frailty index (CFFI) using elements of routine CF care and LTx candidacy evaluation, and also to assess whether CFFI can allow patient risk stratification for post-LTx mortality.

Methods: Adult CF patients listed in the Toronto LTx program between 2005 and 2015 were eligible for inclusion in the study. Multi-organ transplantation and retransplantation at study entry were exclusion criteria. We collected variables covering deficits relevant to comorbidities, nutritional and functional status, treatment, social support and laboratory results. Deficits directly associated with the lung and expected to be restored by LTx were used for the creation of a lung index, variables associated with patients' lifestyle and social circumstances were used for the creation of the lifestyle/social vulnerability index (LSVI), whereas all other parameters were used for the CFFI. The selection of variables and the development of the indices was in accordance with the previously published standard procedure (Searl et al. BMC Geriatr; 2008:8:24). Cox proportional hazards models - adjusted for age, gender, and time on the waitlist - were used to assess associations of the 3 indices with post-LTx mortality.

Results: Among 192 patients eligible for inclusion, the CFFI was possible to calculate for 187 patients (55.6% male, median age at LTx 30 years) whereas calculation was not possible only for 5 patients, due to missing data. Ninety-five deficits were used for the 3 indices: 18 for the lung index, 10 for the LSVI and 67 for the CFFI. The median (range) was 0.42 (0.18-0.66) for the lung index, 0.28 (0-0.9) for the LSVI and 0.23 (0.09-0.56) for the CFFI. Males had a worse LSVI (p=0.059) and women had a worse CFFI (p=0.0037). In the Cox proportional hazards models, CFFI and LSVI were associated with post-LTx mortality (multivariate HR 1.06, 95% CI 1.03-1.10 and HR 1.02, 95% CI 1.01-1.04 respectively) but not the lung index (HR 0.98, 95% CI 0.95-1.00). The CFFI had a dose-response association with post-transplant mortality (for each increase of the CFFI by 0.01 point, the post-LTx mortality increased by 6%).

Conclusions: The creation of the CFFI was feasible using data from routine clinical care. Although successful transplantation may restore lung-specific deficits, extrapulmonary deficits increase the risk of adverse outcomes after LTx. Capturing frailty through the CFFI can allow patient risk-stratification for post-LTx mortality.

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PREVALENCE AND PROGNOSIS OF CORONARY ARTERY DISEASE IN HIGH RISK PATIENTS REFERRED FOR LUNG TRANSPLANTATION

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Background

Identification of different comorbidities during lung transplant assessment is mandatory to exclude or enlist patients. Pre-existing severe Coronary Artery Disease (CAD) in high risk candidates could be considered a contraindication for lung transplant; and should be detected to evaluate possible treatment options.

Objective

To determine the prevalence and management of CAD in a cohort of End Stage Lung Disease (ESLD) patients referred for lung transplantation.

Population and Method

A retrospective and descriptive analysis of the records of all patients referred and assessed for lung transplantation between January 2000 and June 2017 at a single institution was performed. All patients >45 years old with systematic coronary angiography were included in the present analysis. The prevalence and anatomical characteristics of CAD requiring any treatment (medical, endovascular intervention or CABG surgery) was identified. Demographic characteristics (CAD related risk factors, gender, age and ESLD aetiology) were described. Mortality on waiting list and access to lung transplantation was analyzed.

Results

Over 1003 ESLD patients referred for lung transplantation assessment, 646 (64%) patients >45 years old underwent systematic coronary angiography and were included for the analysis. Previously unknown CAD was identified in 148 patients (22%): male 124 (84%), mean age 58 y-o (45-69), smoking history 127 (86%) with a mean of 55 pack/year. Aetiology of ESLD: IPF 71 (48%); COPD 55 (37%); Combined Pulmonary Fibrosis and Emphysema Syndrome 18 (12%) and Bronchiectasis non CF 3 (2%). Functional Class (NYHA) III and IV at referral time was 90 (62%) and 58 (38%). Medical treatment was prescribed in 93 patients (62%), PTCA and DES delivery in 56 patients (38%) and CABG surgery was indicated in 3 patients (2%). Four patients with severe LV dysfunction were excluded for listing. Lung transplantation was performed in 18 patients (12%) while 98 patients (65%) died on the waiting list, 4 of them related to CAD.

Conclusion

Systematic use of coronary angiography during pre transplant assessment of ESLD allows identifying and treating 22% of patients with prevalent unknown CAD. Mortality on waiting list related coronary events was extremely low. At our center, the presence of treatable CAD doesn't preclude listing patients for lung transplantation.

PATIENTS OUTCOME ACCORDING TO THE INDUCTION THERAPY FOR RENAL TRANSPLANTATION IN PATIENTS WITH HISTORY OF PREVIOUS CARDIAC OR PULMONARY TRANSPLANTATION

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Introduction: Because of the improvement of survival after cardiac and pulmonary transplantations late onset complications such as end stage renal disease are more frequent. Studies have demonstrated the superiority of renal transplantation (RT) compared to dialysis in this population but there is less information regarding the impact of immunosuppressive treatment, especially the induction therapy (IT). The aim of this study was to compare the patient outcome after RT according to the use of polyclonal anti-thymocyte globulins (ATG) vs basiliximab as IT.

Methods: We conducted a retrospective, multicenter, observational study. We included all cardiac and pulmonary recipients (CR and PR) in larger Paris transplanted between 1985 and 2009 and who underwent RT between 1993 and 2015. We used the random forest model (RFM) to evaluate the predictive variables for patient death.

Results: The population included 57 patients (37 CR and 20 PR). The mean age at RT was 44 years. ATG used was 65%, significantly less in PR compared to CR (40% vs 78.4% respectively, p=0.008). Median follow-up time after RT was 60 months (range 0.25-216). Patient death was significantly higher in the ATG group vs basiliximab (30% vs. 5% respectively, p=0.04). Using RFM, the most predictive variables for patient death were patient age, type of IT and type of thoracic transplantation (cardiac or pulmonary). There was no significant difference regarding patient survival according to the IT group. However, during the follow-up after RT, patient survival were significantly higher in PR compared to CR (at 3, 7 and 15 years respectively 93.8% vs 89.2%, 93.8% vs 85.9% and 93.8% vs 19.3% (p=0.04). According to the IT groups, we found no difference regarding the incidence of heart, lung and renal acute rejection, infections or neoplastic complications.

Conclusion: Our study showed a poorer outcome regarding patient's death in the ATG group compared to the basiliximab group used for IT in RT in patients with history of prior cardiac or pulmonary transplantation. This suggest the need to be cautious in the IT choice for RT in this population. The use of ATG should be restricted for RT at high immunological risk.

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Astellas s'engage à transformer les innovations scientifiques en solutions médicales porteuses de valeur et d'espoir pour les patients dans le monde entier.

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- **TRAITEMENT** du rejet de l'allogreffe résistant à un traitement par d'autres médicaments immunosuppresseurs

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Pour plus d'informations sur ce médicament, consultez la base de données publiques des médicaments : http://www.base-donnees-publique.medicaments.gouv.fr ou le site internet de l'ANSM (Agence Nationale de Sécurité du Médicament) : http://ansm.sante.fr

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