8th International Congress on

LUNG TRANSPLANTATION

Paris, september 11-12, 2008

Union Internationale des Chemins de Fer
16, rue Jean Rey, Paris XV

Program & Abstracts

8th International Congress on

LUNG TRANSPLANTATION

Paris, september 11-12, 2008

under the Patronage of

Fondation Franco-Américaine du Maréchal Foch

Société de Chirurgie Thoracique et Cardiovasculaire
de Langue Française

Contents

Welcome Address

Dear Colleagues,

The 8th edition of the International Congress on Lung Transplantation is headed by our two presidents:
Walter KLEPETKO from Vienna and Shaf KESHAVJEE from Toronto, eminent leaders of the two bestknown teams in the field of lung transplantation.

The scientific program includes in addition to classic topics, new subjects as lung regeneration and artificial lungs.

Our hope is that the numerous lectures and debates will be fruitful and have a positive impact for the future activity of each participant.

Bien amicalement.

Docteur Alain BISSON

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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 or 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.

General Information

Administrative Secretariat

Office hours :
Thursday, September 14 7:30 a.m. - 6:30 p.m.
Friday, September 15 7:30 a.m. - 4:30 p.m.

After the Congress :

VBCE - Lung Transplantation
43, rue de l'Abbé Groult
75015 Paris
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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 pre-registered participants is included in the documentation issued upon arrival. Participants who register on site should apply directly to the registration desk.

Technical Exhibition

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

Social Program

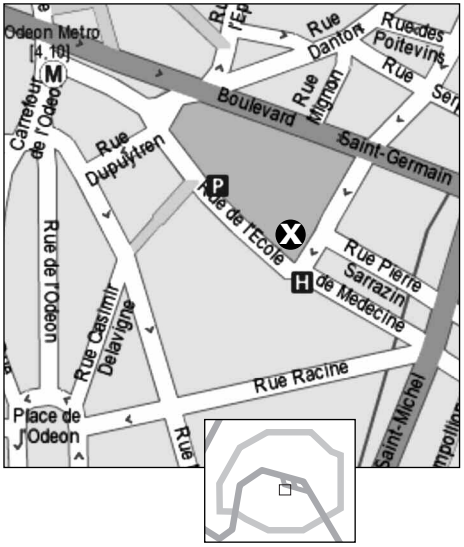
Thursday, September 11

DINNER IN THE
"Musée d'Histoire de la Médecine"
Université Paris V René Descartes
12 rue de l'École de Médecine - 75006 PARIS

8:00 p.m.

Price per person: 100 € (upon availability)

Discover and enjoy a private dinner in the prestigious Museum of the Medical Faculty in the heart of Paris.



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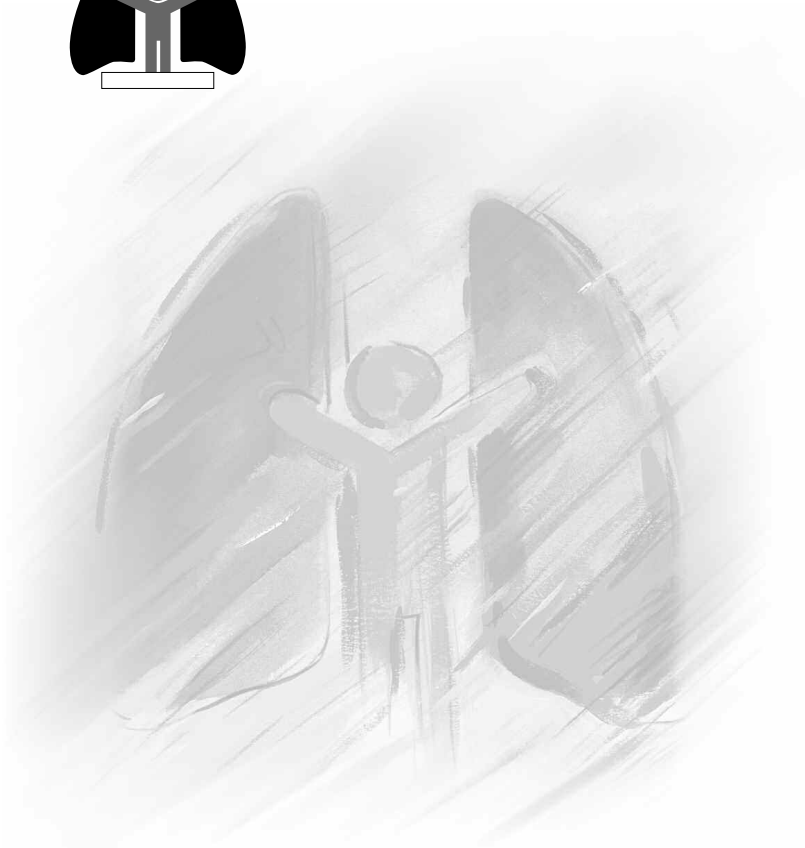

Scientific Program

Notes

Thursday 11 September

	Room Louis Armand	Room List and Stephenson
8:30	Opening Opening lecture p 12	
9:15		
10:20	Lung procurement p 13	Malignancies post lung transplantation p 14
12:30		
14:00	Acute rejection: What's new? p 15	Hot topics in infectious diseases p 16
16:20		Free communications p 17
18:00		

Friday 12 September

	Room Louis Armand	Room List and Stephenson
8:00	Chronic rejection p 19	Cystic fibrosis and lung transplantation p 21
10:20		Free communications p 22
12:30		
14:00	Artificial lung p 23	Lung regeneration p 24
16:00		

8:30 → 8:45 **Room Louis Armand**

Opening

A. BISSON (France)
President of the Organizing Committee

S. KESHAVJEE (Canada) **& W. KLEPETKO** (Austria)
Presidents of the Congress

8:45 → 9:15 **Room Louis Armand**

Opening lecture

Lung Transplantation: 25 years later!
S. Keshavjee (Toronto, Canada)

9:15 → 12:30 **Room Louis Armand**

Lung procurement

Chairpersons: S. Keshavjee (Toronto, Canada),
W. Klepetko (Vienna, Austria)

9:20 **New US Allocation System. Benefits and pitfalls**
T. Egan (Chapel Hill, USA)

9:40 **Critical analysis of lung procurement criteria from brain death donors**
H. Mal (Paris, France)

10:00 Break

10:30 **Technics of lung procurement**
M. de Perrot (Toronto, Canada)

10:40 **In recipient reconditioning of unsuitable donor lungs with ECMO: Experimental results**
G. Lang (Vienna, Austria)

11:00 **Ex vivo reconditioning**
- **Ex-vivo evaluation -** D. Van Raemdonck (Leuven, Belgium)
- **Ex-vivo lung repair -** S. Keshavjee (Toronto, Canada)

11:40 **Non Heart-beating donors**
- **Ex-vivo perfusion of lungs from non-heart-beating donors: Practical obstacles and opportunities -** T. Egan (Chapel Hill, USA)
- **Clinical experience -** A. Varela (Madrid, Spain)

12:20 **Living donor lobar double lung transplantation: A viable option for the lung transplant recipient of small body size** **01**
J.C. Mullen, P.S. Lo, K. Stewart, A. Valji, E. Bedard, D.C. Lien, J. Weinkauf, D. Stollery, K. Jackson (Edmonton, Canada)

10:20 → 12:30 **Room List**

Malignancies post Lung transplantation

Chairpersons: F. Parquin (Suresnes, France),
E.A.M. Verschuuren (Groeningen, The Netherlands)

10:20 **Incidence of cancers after lung Transplantation**
C. Cantrelle (ABM, France)

10:40 **Bronchogenic cancer after lung transplantation**
A.M. Hamid (Clamart, France)

11:00 **Lung Transplantation for known or unexpectedly detected bronchial cancer**
A. Hoda (Vienna, Austria)

11:20 **Cutaneous neoplasm: use of anti mTORs**
C. Lebbé (Paris, France)

11:40 **Metastatic skin cancer in lung transplant patient: The challenge of immune suppression** **02**
H. Khurana, G. Soo Hoo, G. Chaux (Los Angeles, USA)

11:55 **Predicting value of EBV replication**
E.A.M. Verschuuren (Groeningen, The Netherlands)

12:15 **Treatment of PTLD**
S. Choquet (Paris, France)

14:00 → 18:00 **Room Louis Armand**

Acute rejection: What's new?

Chairpersons: P. Corris (Newcastle, UK),
T. Egan (Chapel Hill, USA)

14:00 **Acute lung rejection: The 2007 ISHLT classification. New patterns and questions**
S. Stewart (Cambridge, UK)

14:20 **Surrogate markers to transbronchial biopsies**
T. Kotsimbos (Sydney, Australia)

14:40 **Molecular phenotyping of lung rejection: The near future?**
M. Hertz (Minneapolis, USA)

15:00 **HLA-G expression in bronchial epithelial cells is associated to a non-rejector status in lung transplant recipients** **O3**
O. Brugiere

15:15 **Minimal acute rejection (A1) to be treated?**
L. Singer (Toronto, Canada)

15:35 **Chronic infections and the lung allograft. What are the key questions?**
T. Kotsimbos (Sydney, Australia)

15:55 Break

16:20 **Acute Humoral rejection**
C. Knoop (Brussels, Belgium)

16:40 **Therapy of humoral rejection: What lessons from renal transplantation experience?**
D. Glotz (Paris, France)

17:00 **Cytochrome P450 3A polymorphisms: Therapeutic implications for immunosuppressive management**
E. Thervet (Paris, France)

14:00 → 16:00 **Room List**

Hot topics in infectious diseases

Chairpersons: M. Estenne (Brussels, Belgium),
A. Boehler (Zurich, Switzerland)

14:00 **Which surrogate markers for an adequate anti CMV protection**
B. Autran (Paris, France)

14:20 **A prophylaxis-free strategy for the prevention of CMV infection after lung transplantation: Early results** **04**
S. Soresi, A. Bertani, P.Vitulo, P.Grossi, L.Conti, G. D'Ancona, M. Parrinello, A. Arcadipane, B.Gridelli (Palermo, Italy)

14:30 **Role of bacteria (Pseudomonas infection) in chronic lung rejection**
A. Fisher (Newcastle, UK)

14:50 **Non-tuberculosis mycobacteria in heart and lung transplantation: A 10-year retrospective study in a UK transplant center** **05**
D.J. Dhasmana, N. Roy, K. Thaning, A. Hall, M. Burke, M. Hodson, M. Carby

15:05 **Papilloma Virus infections. Cidofovir treatment**
C. Knoop (Brussels, Belgium)

15:25 **Successful lung transplantation in an HIV and HBV positive patient with cystic fibrosis** **06**
A. Bertani, P. Vitulo, P. Grossi, G. D'Ancona, A. Arcadipane, S. Soresi, B. Gridelli

15:40 **Organ transplantation in HIV infected recipients**
D. Samuel (Villejuif, France)

16:20 → 18:00 **Room List**

Free communications

Chairpersons: B. Philippe (Suresnes, France),
P. Jaksch (Vienna, Austria)

16:20 **Selection of patients for lung and cardiopulmonary transplantation: identification of exclusion criteria** **07**
J.M. Ossés, R. Ahumada, G. Wagner, R. Majo, S. Moscoloni, M. Marquez, L. Martinez, J. Cáneva, A. Bertolotti, R.R. Favaloro (Buenos Aires, Argentina)

16:35 **Prevalence and control of cardiovascular risk factors in lung transplant recipients** **08**
J.C. Johnston, R.D. Levy, J. Yee, N. Partovi, J. Kerr, J.M. Wilson (Vancouver, Canada)

16:50 **17 years experiences with lung transplantation in Norway** **09**
O.R. Geiran, Ø. Bjørtuft, H. Lindberg, E. Seem, A.E. Fiane, S. Birkeland, M.B. Lund, T. Leivestad, Rikshospitalet (Oslo, Norway)

17:05 **Should the choice between single lung transplant vs. both lung transplant be influenced by the expected survival benefit?** **010**
J.M.A. Smits, A.O. Rahmel, G. (Leiden, the Netherlands)

17:20 **Survival after repeat lung transplantation** **011**
J.C. Mullen, P.S. Lo, D. Modry, K. Stewart, D. Lien, J. Weinkauf (Edmonton, Canada)

17:35 **Serum tarc levels post lung transplantation as a predictor for the bronchiolitis obliterans syndrome** **012**
E.A. van de Graaf, A.W.M. Paantjens, J.M. Kwakkel-van-Erp, W.G.J. van Ginkel, D.A. van Kessel, J.M.M. van den Bosch, H.G. Otten (Utrecht, The Netherlands)

17:50 **Comorbidities and health-related quality of life after lung transplantation** **013**
H.M. Hoy, I. Feurer, J. Loyd, A. Milstone, E. Lambright, C.W. Pinson (Nashville, USA)

18:05 **Employment status after lung transplantation in a developing country** **014**
L. Martínez, F. Márquez, S. Moscoloni, J. Osses, A. Bertolotti-Favaloro (Buenos Aires- Argentina)

Notes

8:00 → 12:30 **Room Louis Armand**

Chronic rejection

Chairpersons: C. Pison (Grenoble, France),
M. Hertz, (Minneapolis, USA)

8:00 **Mechanisms of Fibrosis in chronic rejection**
M. Hertz (Minneapolis, USA)

8:20 **The killer cell immunoglobulin-like receptor haplotype A predisposes to the bronchiolitis obliterans syndrome after lung transplantation** **O15**
H.G. Otten, J.M. Kwakkel-van-Erp, A.W.M. Paantjens, G.D. Nossent, W.G.J. van Ginkel, J. Schellekens, D.A. van Kessel, J.M.M. van den Bosch, E.A. van de Graaf (Utrecht, The Netherlands)

8:35 **Extensive and advanced Fibrosis may not be irreversible: Lessons from hepatic cirrhosis**
A. Mallat (Créteil, France)

8:55 **Local Humoral allogenic response in chronic rejection**
O. Thaunat (Lyon, France)

9:15 **Epithelial to mesenchymal transition: Concept and implications for organ transplantation**
P. Corris (Newcastle, UK)

9:35 **Biomarkers of operational tolerance**
J. Ashton-Chess (Nantes, France)

9:55 Break

10:20 **Chronic rejection: "Possible prophylaxis or treatment options"**
H. Reichenspurner (Hamburg, Germany)

10:40 **The link between Primary Graft Dysfunction and BOS/chronic graft dysfunction**
A. Boehler (Zurich, Switzerland)

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11:00 **GERD: What to do with?**
C. Pison (Grenoble, France)

11:20 **Azithromycin. Mechanisms of action and long term results**
G.M. Verleden (Ieuven, Belgium)

11:40 **Photopheresis: A possible tool for treatment of BOS**
P. Jaksch (Vienna, Austria)

8:00 → 10:00 **Room List**

Cystic fibrosis and lung transplantation

Chairpersons: L. Singer (Toronto, Canada),
C. Knoop (Brussels, Belgium)

8:00 **Lung transplantation for B. Cepacia colonized patients: Is it fair?**
L. Singer (Toronto, Canada)

8:20 **Atypical mycobacteria: Management for transplantation**
P. Corris (Newcastle, UK)

8:40 **Urgent lung transplantation in cystic fibrosis patients**
V. Boussaud (Paris, France)

9:00 **Advance in lung transplantation for cystic fibrosis and survival improvement** **016**
P. Mordant, P. Bonnette, P. Puyo, E. Sage, M. Stern, M. Fischler, A. Chapelier (Suresnes, France)

9:15 **Lung transplantation and pregnancy**
D. Hubert (Paris, France)

9:35 **Psychological and behavioural aspects after thoracic organ transplantation**
F. Dobbels (Leuven, Belgium)

10:20 → 12:30 **Room List**

Free communications

Chairpersons: F. Parquin (Suresnes, France),
E.A.M. Verschuuren (Groeningen, The Netherlands)

10:20 **RAGE, a marker of alveolar epithelial typeI cell injury, predicts impaired alveolar fluid clearance in isolated perfused human lungs** **017**
R. Briot, J.A. Frank, T. Uchida, M. Matthay
(Grenoble, France ; San Francisco, USA ; Tokyo, Japan)

10:35 **Novel superiority of subzero non-freezing preservation of rat lung with supercooling technology in ex vivo model and lung transplantation model** **018**
T. Okamoto, X. Zhao, T. Nakamura, J. Zhang, A. Aoyama, N. Satoda, A. Takahashi, F. Chen, T. Fujinaga, H. Hamakawa, T. Shoji, H. Sakai, T. Bando, H. Date (Kyoto, Japan)

10:50 **Ex vivo evaluation of non-heart-beating donor lungs in larger-size pigs** **019**
T. Okamoto, F. Chen, J. Zhang, X. Zhao, N. Satoda, A. Takahashi, T. Fujinaga, T. Shoji, H. Sakai, T. Bando, H. Date (Kyoto, Japan)

11:05 **Experimental donor lungs from donation after cardiac death in various settings** **020**
T. Yamada, F. Chen, J. Zhang, T. Okamoto, T. Fujinaga, H. Morikawa, N. Satoda, A. Takahashi, T. Shoji, H. Sakai, T. Bando, H. Date (Kyoto, Japan)

11:20 **Off-pump single lung transplantation in COPD: intraoperative prediction of post-transplant ventilation improvement** **021**
C.B. Gómez, A.M. Bertolotti, D.O. Absi, J.M. Osses, J.O. Caneva, J. Negroni, R.R. Favaloro (Buenos Aires, Argentina)

11:35 **The impact of limited anterior thoracotomy incisions in lung transplantation surgery** **022**
H.B. Bittner, S. Lehmann, C. Binner, F.W. Mohr (Leipzig, Germany)

11:50 **Double lung transplantation in a cystic fibrosis patient with donor lungs procured from a brain dead heart transplant recipient donor** **023**
F.R. Klein, A. Bertolotti, J.M. Osses, A. Cicolini, J. Caneva, R. Ahumada, D. Absi, R.R. Favaloro (Buenos Aires. Argentina)

14:00 → 16:00 **Room Louis Armand**

Artificial Lung

Chairpersons: A. Chapelier (Suresnes, France),
W. Klepetko (Vienna, Austria)

14:00 **Novalung experience**
M. Struber (Hanover, Germany)

14:25 **ECMO experience for bridge to TX**
G. Lang (Vienna, Austria)

14:50 **Lung transplantation for ARDS after prolonged ECMO support** **O24**
A. Bertani, P. Vitulo, S. Soresi, A. Arcadipane, G. Burgio, M. Pilato, B. Gridelli (Palermo, Italy)

15:05 **ECMO replacing intraoperative cardiopulmonary bypass**
W. Klepetko (Vienna, Austria)

15:30 **Bridge to recovery**
E. Sage (Suresnes, France)

14:00 → 16:00 **Room List**

Lung Regeneration

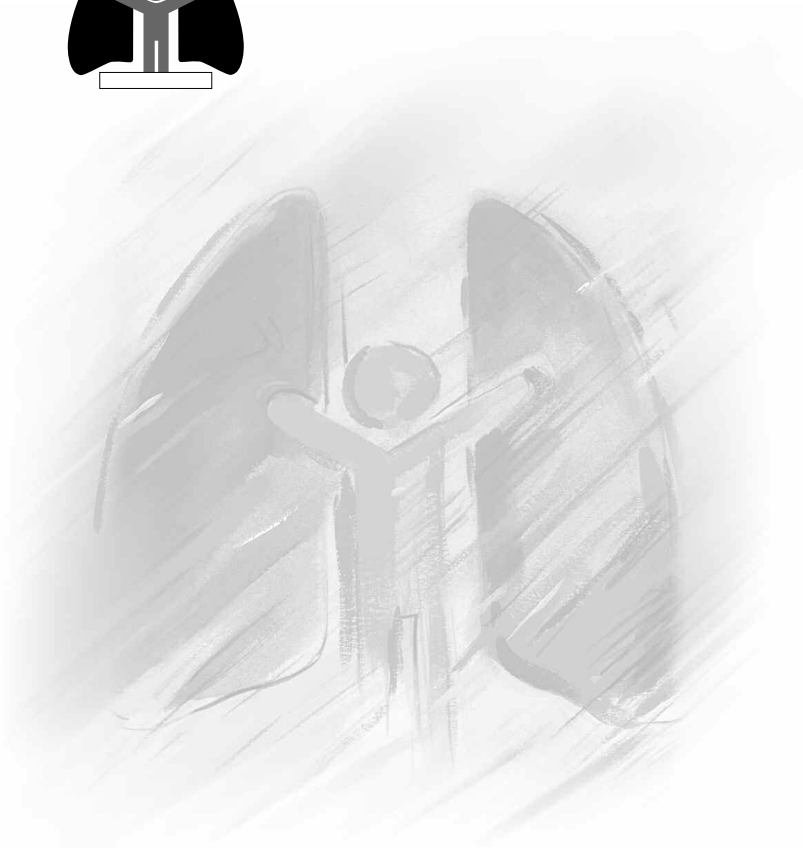
Chairpersons: T. Waddell (Toronto, Canada),
P. Birembaut (Reims, France)

14:00 **Prospects for bone-marrow derived cell therapy**
T.K. Waddell (Toronto, Canada)

14:30 **Epithelial regeneration from ES cell**
A.E. Bishop (London,UK)

15:00 **Repair and regeneration of the lung: Local progenitors**
P. Birembaut (Reims, France)

15:30 **Circulating fibrocytes in pulmonary fibrosis and bronchiolitis obliterans**
R.M. Strieter (Charlottesville, USA)



Abstracts

LIVING DONOR LOBAR DOUBLE LUNG TRANSPLANTATION: A VIABLE OPTION FOR THE LUNG TRANSPLANT RECIPIENT OF SMALL BODY SIZE

JC Mullen, MD[1]; PS Lo, BSc[1]; K Stewart, MD[1]; A Valji, MD[2]; E Bedard, MD[2]; DC Lien, MD[3]; J Weinkauf, MD[3]; D Stollery, MD[4], K Jackson, RN[3]

1 Department of Surgery, University of Alberta, Edmonton, Alberta, Canada
2 Department of Surgery, Royal Alexandra Hospital, Edmonton, Alberta, Canada
3 Department of Medicine, University of Alberta, Edmonton, Alberta, Canada
4 Department of Medicine, Royal Alexandra Hospital, Edmonton, Alberta, Canada

Background: Bilateral living donor lobar double lung transplantation (LDLLT) was introduced as an alternative method of lung transplantation for patients who were thought to be too critical to wait for cadaveric lungs. Right and left lower lobes from two healthy donors are implanted in the recipient in place of the whole right and left lungs, respectively. Because only two lobes are transplanted, the procedure may be particularly applicable to patients on the waiting list with small body size, who may face very long waits due to the scarcity of suitably sized small lungs.

Purpose: To review the donor and recipient characteristics of six patients we have performed this procedure for, as well as their post-operative outcomes.

Methods: All LDLLT conducted at the University of Alberta Hospital were retrospectively reviewed.

Results: Six LDLLT have been performed from February 2001 to March 2008.

Table 1: Donor and Recipient Characteristics

	1	2	3	4	5	6
Date of Operation	Feb 2001	Oct 2004	Nov 2004	Apr 2005	Sep 2006	Mar 2008
Recipient Age	22	20	22	51	25	17
Gender	F	F	F	F	F	F
Height (cm)	162	161	160	150	158	155
Weight (kg)	40	46	47	61	41	42
Diagnosis	CF	CF	CF	IPF	CF	CF
Donor #1 age/gender	46 M	51 M	48 F	30 M	33 M	24 M
Donor #2 age/gender	26 M	46 M	44 F	27 M	51 M	28 M
Donor #1 Relationship	Father	Father	Mother	Son	Cousin	Cousin
Donor #2 Relationship	Friend	Uncle	Aunt	Son	Uncle	Cousin
Complications	None	GF, ReTx, Aspergillosis	None	None	None	None
Survival	Y	3 months	30 months	Y	Y	Y

CF: Cystic Fibrosis, IPF: Idiopathic Pulmonary Fibrosis, GF: Graft Failure, ReTx: Retransplantation

Conclusions: Living donor lobar double lung transplantation is a viable option for small recipients. Living donor lobar double lung transplantation is logistically and surgically challenging, requiring an experienced multi-disciplinary team approach. Our initial experience with a 1-year 80% survival rate warrants continued expansion of its use.

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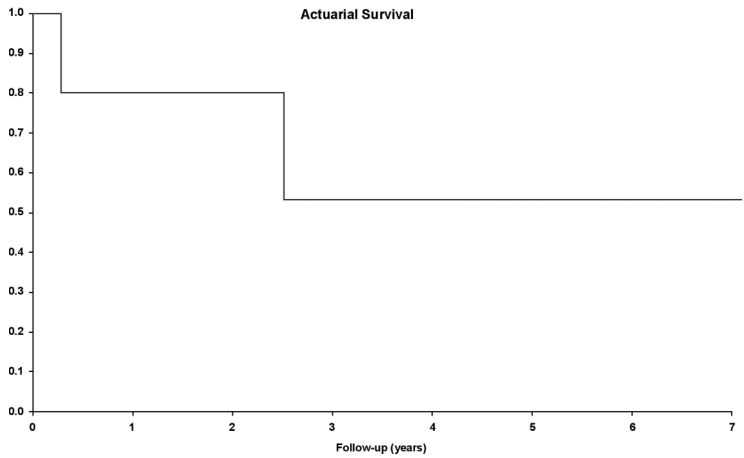

Figure 1: Actuarial survival curve by Kaplan-Meier analysis of living donor lobar double lung transplantation. One-year survival was 80%.

METASTATIC SKIN CANCER IN LUNG TRANSPLANT PATIENT: THE CHALLENGE OF IMMUNE SUPPRESSION

Hargobind Khurana, MD, Guy Soo hoo, M.D., George Chaux, M.D.
Cedars Sinai Medical Center, Los Angeles, Ca, USA. hskhurana@yahoo.com

Case report: 60 yr old male with idiopathic pulmonary fibrosis (IPF) received a right single lung transplant 5 years ago. He is admitted for a cold cyanotic left index finger. He had mild cough and exertional dyspnea for two weeks. He was on immune suppressant medications along with prophylaxis for pneumocystis, aspergillus and CMV. The patient had a recent history of cutaneous squamous cell cancer (SCC) involving the right cheek and neck which was excised. Good healing wound was observed. Initial labs were unremarkable. Chest X-ray showed a prominent right hilum and features of IPF in the native lung. A duplex study revealed a 10 cm clot in the left ulnar artery. Patient was admitted for thrombolysis and was found to have in addition a near occlusion of left subclavian artery. During his hospital stay, the patient developed worsening infiltrates in the transplant lung, requiring mechanical ventilation. CT chest showed marked hilar and mediastinal lymphadenopathy with diffuse parenchymal infiltrates. Patient was placed on empiric antibiotics, bactrim and ganciclovir. Bronchoalveolar lavage showed evidence of atypical cells. All cultures were negative. He became hypotensive and developed worsening pulmonary infiltrates and gas exchange. The patient demised despite all active measures. At autopsy, widespread metastases to cervical and mediastinal lymph nodes, pleura, lungs, pericardium and heart were found. The arterial clots in the left upper extremity showed evidence of tumor cells.

Conclusion: Cutaneous SCC's are more aggressive in transplant patients as evidenced by an increased risk of local recurrence, metastases and mortality. Treatment includes surgical excision and radiation therapy. They may also benefit from reduction in immune suppression.

HLA-G EXPRESSION IN BRONCHIAL EPITHELIAL CELLS IS ASSOCIATED TO A NON-REJECTOR STATUS IN LUNG TRANSPLANT RECIPIENTS

O. Brugière

Rationale: Human leukocyte antigen-G (HLA-G), a non-classical MHC-I protein with restricted tissue expression, plays an essential role in immune tolerance and has been negatively associated with acute and chronic rejection following solid-organ transplantations as heart or liver-kidney transplantation. Up to now, no data exist in lung transplantation.

Objectives: We assessed pulmonary tissue expression of HLA-G in a cross sectional study of lung transplant recipients.

Methods: Retrospective analysis of 48 lung transplant performed 1995-2005 who underwent 56 transbronchial biopsies (TBBx). Patients were classified into 4 groups according to the clinical status at the date of TBBx: (1) stable patients; (2) acute rejection; (3) unstable chronic rejection (bronchiolitis obliterans syndrome); (4) viral infection.

Results: A marked expression of HLA-G in bronchial epithelial cells was frequently observed in stable recipients [n = 17/26 (63%)] and in patients ongoing viral infection [n = 4/7; 62%), and never observed in recipients with acute rejection (n = 12) or with unstable bronchiolitis obliterans syndrome (n = 6). Furthermore, looking at the outcome of graft function into the stable patients group, we observed a lower incidence of resistant acute rejection episodes in HLA-G positive patients, and a trend towards lower prevalence of bronchiolitis obliterans syndrome.

Conclusion: These data suggest that the expression of HLA-G in bronchial epithelial cells of lung transplant recipients is associated with a non-rejector status.

A PROPHYLAXIS-FREE STRATEGY FOR THE PREVENTION OF CMV INFECTION AFTER LUNG TRANSPLANTATION: EARLY RESULTS

S. Soresi, A. Bertani, P. Vitulo, P. Grossi, L. Conti, G. D'Ancona, M. Parrinello, A. Arcadipane, B. Gridelli
Ismett – UPMC, Palermo, Italy

Introduction: Cytomegalovirus (CMV) infection remains an important cause of morbidity and mortality after lung transplantation (LTX). The incidence of CMV infection and disease is higher in LTX recipients than in other solid organ transplant patients, (54% to 92% in patients without CMV prophylaxis).
CMV infection has been associated with acute and chronic allograft rejection, which remains a major limiting factor to the long term success of lung-transplantation. A number of centers have reported on the efficacy of ganciclovir-containing prophylactic regimens in LTX recipients. However, the optimal prophylactic strategy against CMV remains controversial; the optimal regimen and duration of therapy remain unclear.

Materials and methods: We report the results of our CMV prophylaxis strategy in patients who underwent LTX between June 2005 and April 2008. During this time course we performed 41 LTX in 39 patients. The most prevalent indication was IPF. The mean recipient age was 40 years (range 3-63). The immunosuppressive regimen included basiliximab, tacrolimus, low dose steroids and mycophenolate mofetil (in selected cases). None of the patients received a prophylactic treatment for CMV, irrespective of the serological status. Blood viral DNA replication was assessed weekly for the first 3 months following LTX and monthly thereafter, or according to clinical indication. All patients displaying a positive DNAemia underwent repeated weekly follow-ups until negativization. Patients with a DNAemia × 100.000 copies or with clinical evidence of disease (histologically confirmed) were treated with i.v. gancyclovir (5 mg/kg/day bid) or with p.o.valgancyclovir (900 mg po bid). The treatment was continued until 2 negative DNAemia samples were obtained.

Results: After a mean follow-up time of 15 months (range 1-35), eight out of 39 patients (20.5%) received a treatment for CMV activation/disease. 1/8 patients (2.6% of all LTX) had evidence of CMV pneumonia. 3/39 patients had a serology mismatch (donor positive/recipient negative) but none of them developed any viral replication. All but one treated patients were responsive to either gancyclovir or valgancyclovir and fully recovered with negativization of the DNAemia. One patient required long-term treatment with Foscarnet because of gangyclovir resistance, and was eventually able to be cleared from viral replication. We did not observe major complications derived from the liberal use of all antiviral drugs.

Conclusions: In our initial lung transplant experience we adopted a CMV prevention strategy consisting in a strict follow-up of viral replication without any prophylaxis. This strategy was shared with other organ transplant programs at our Institution. The preliminary results showed an acceptable rate of viral activation and disease. Serological mismatch did not impact on the development of a positive DNAemia. All patients were able to fully recover after treatment. A longer follow-up will warrant further validation.

NON-TUBERCULOUS MYCOBACTERIA IN HEART AND LUNG TRANSPLANTATION: A 10-YEAR RETROSPECTIVE STUDY IN A UK TRANSPLANT CENTRE

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Aims: Non-Tuberculous Mycobacteria (NTM) are environmental organisms found in soil and water systems and their significance in heart and lung transplantation remains unclear. Chemotherapy is complicated by drug-toxicity and significant drug-interactions. Few large scale cohorts exist that explore this subject, and moreover, describe their associations with rejection, morbidity and mortality. We report clinical and microbiological data from our transplant cohort at Harefield Hospital, UK, over a 10-year period, a cohort that consisted of 928 lung and/or heart transplant recipients and one of the largest series studied to date.

Methods: Case notes for all NTM culture-positive cases identified between July 1st 1993 and June 30th 2003 through hospital microbiological and clinical databases were recalled from hospital medical records and archive-systems, with follow-up extended to September 2007. An 'isolate-event' was that clinical presentation associated with a positive NTM isolate. Bronchiolitis Obliterans Syndrome (BOS) was diagnosed from one or more of spirometry data (FEV1 <80% baseline), DTPA (diethylenetriaminepenta-acetic acid) imaging, high-resolution CT imaging and histology.

Results: A total of 104 isolates of Mycobacteria were obtained: 97 NTM (from 84 patients), 7 Mycobacteria *tuberculosis*. NTM was isolated in 9% of all transplants, but when heart-only transplants were excluded, NTM made up 21% of all remaining lung-related transplants, with no difference in single-lung versus double-lung operations. 73% of the NTM species were made up of *xenopi, chelonae or gordonae*, the majority isolated only once (74%). Co-pathogens were most commonly aspergillus and pseudomonas. BOS was demonstrated in 51 patients, absent in 18 patients and showed no relationship to NTM-isolates. However, when 'early NTM-isolates' (<3 months post-transplant) were excluded, 57% of NTM-isolates were found in the context of established BOS, while only 33% preceded it. Whilst overall NTM-transplant mean survival was 6 years, later NTM-isolation (>3 months post-transplant) correlated with higher mortality *beyond* isolation and lower mean post-isolate survival: 2.4 years for late NTM-culture vs. 4.8 years for early culture. In 6 patients, anti-mycobacterial therapy was initiated for a range of 3 weeks – 6 months, complicated by drug toxicity, morbidity or death. This latter group's post-isolate median survival was 9 months, and all patients had demonstrated BOS in the preceding 2 years.

Conclusions: 21% of our UK lung-transplant cohort demonstrated NTM-isolates, a proportion much greater than might be perceived. The majority of isolates are made up by *xenopi, chelonae and gordonae* species. Whilst the majority of patients did not require specific treatment, those few that did tolerated treatment poorly, incompletely and demonstrated a median survival of just 9 months, equivalent to the recommended duration of therapy. The data suggests that NTM-isolation may be a bystander-effect, a marker of poor prognosis and a product of advanced lung rejection, and that in only exceptional cases should be treated.

SUCCESSFUL LUNG TRANSPLANTATION IN AN HIV AND HBV POSITIVE PATIENT WITH CYSTIC FIBROSIS

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Objectives: HIV infection is still a contraindication to lung transplantation (LTX) in most institutions, despite the promising results of liver and kidney transplantation in HIV+ individuals.

Methods: We present the report of LTX in a 45 yr old man with end-stage respiratory failure secondary to cystic fibrosis and HIV/HBV coinfection, who underwent a double LTX at our Institution. The decision to proceed with LTX was based on: 1)a completely controlled and asymptomatic HIV infection fulfilling the criteria for transplantation in HIV+ individuals 2)a completely normal liver function and histopathology, an HDV negative status, and a powerful anti-HBV coverage included in his highly active antiretroviral therapy. 3)approval and support from the IRB and Italian Health Ministry.

Results: The operation was uneventful and the postoperative course was unremarkable. The patient was discharged in POD 28 and is alive and well at a 12 months follow up. His HBV and HIV viral load, as well as CMV, EBV, and HHV were kept under strict surveillance and have always been undetectable. His CD4+ cell count, was back to normal levels in 2 weeks. The antiretroviral therapy was withheld for 3 days after LTX and then restarted given the excellent clinical course. Immunosuppression was based on Basiliximab induction, Tacrolimus and steroids, and was influenced by the interactions between CNIs and antiretroviral agents. The follow-up biopsies at 15, 60 and 90 days showed no signs of rejection.

Conclusions: LTX in an HIV+ individual was successful in the short term. A dedicated and very strict follow-up is mandatory for infectious and immunological monitoring. HIV+ individuals can be considered for LTX provided that a thorough and case to case evaluation is performed.

SELECTION OF PATIENTS FOR LUNG AND CARDIOPULMONARY TRANSPLANTATION: IDENTIFICATION OF EXCLUSION CRITERIA

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Introduction: In the selection process of patients for lung and cardiopulmonary transplantation risks and benefits must be evaluated in order to optimize the results of the procedure; that is identifying the best surgical technique considering the patients` clinical status, and at the same time the contraindications for transplantation.

Objective: To identify the exclusion criteria for lung (TxL) and cardiopulmonary transplantation (Tx CP) for patients with advanced lung or cardiopulmonary diseases.

Materials and Methods: A retrospective analysis was conducted based on the evaluation data of potential candidates for lung transplantation admitted to our institution during the period between January 2000 and august 2007.
The evaluation included: complete chemistry analysis, X ray studies, lung and cardiac function at rest and during exercise, infection and tumor screening, psychological - social and nutritional status.

Results: 354 patients were evaluated, 266 (75.1%) of which were selected for TxL and 88 (24.9%) for TxCP. The indications for TxL were: Emphysema 95 patients (35.7%), Cryptogenic fibrosing alveolitis 89 (33.5%), Bronchiectasis 29 (10.9%), Cystic fibrosis 29 (10.9%), Occupational diseases 7 (2.6%), others 17 (6.4%).
For TxCP , the indications were: Primary pulmonary hypertension 45 patients (51.1%), Congenital heart diseases 23 (26.1%), Heart and Lung disease 3 (3.4%), Pulmonary vascular and parenchymal lung diseases 17 (19.4%), 60 (17%) patients evaluated were not accepted for lung and cardiopulmonary transplantation due to contraindications: 20 (33.3%) due to psychological and social conditions, 5 (8.3%) due to active tumors, 12 (20%) due to the possibility of improving with medical treatment, 5 (8.3%) due to active infection, 7 (11.6%) due to active smoking, 11 (18.5%) due to other causes.

Conclusions: In our experience, the percentage of patients excluded for lung and cardiopulmonary transplantation during the evaluation is consistent with the data available in international bibliography. The psychological and social conditions were the most frequent causes of exclusion.

PREVALENCE AND CONTROL OF CARDIOVASCULAR RISK FACTORS IN LUNG TRANSPLANT RECIPIENTS

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Purpose of Study: Recent data from the Registry of the International Society for Heart and Lung Transplantation shows a high prevalence of cardiac risk factors in lung and heart-lung transplant recipients. We sought to describe our experience with the prevalence and control of certain modifiable cardiovascular risk factors, including obesity, diabetes, hypertension, and hyperlipidemia.

Methods: The clinical characteristics of all active lung transplant recipients in our clinic were analyzed in a retrospectively descriptive study. Obesity was defined as a Body Mass Index greater than 30 on the most recent measurement. Diabetes control was defined as a hemoglobin A1C value of less than 7.0. Hypertension was defined as the presence of anti-hypertensive medication, or a blood pressure greater than 130/80 in a diabetic or 140/90 in a non-diabetic patient on their most recent blood pressure. Uncontrolled hypertension was defined as the presence of anti-hypertensive medication with a blood pressure greater than 130/80 in a diabetic or 140/90 in a non-diabetic patient on their most recent blood pressure. Hyperlipidemia was defined as the presence of antilipid medication or by lipid values meeting the recommended treatment criteria of the Canadian Cardiovascular Society.

Results: There were 75 patients reviewed with a mean age of 46 years and mean transplant duration of 67 months. Of these patients, 8% were classified as obese. The prevalence of diabetes was 27%. Of the diabetic patients, 40% did not meet criteria for adequate blood glucose control. Sixty-one percent of patients met the criteria for hypertension, with only 52% of the hypertensive patients receiving anti-hypertensive medication. Of the patients receiving anti-hypertensive medication, 46% had uncontrolled hypertension. Forty-two percent of the patients were classified as hyperlipidemic, with 52% of hyperlipidemic patients on antilipid medication. Of the patients receiving antilipid medication, 35% remained hyperlipidemic.

Conclusions: With improvement of survival statistics in lung and heart-lung transplant recipients, the influence of cardiovascular mortality on this population will likely increase.Despite this, the recognition and appropriate treatment of modifiable cardiovascular risk factors such as obesity, uncontrolled diabetes, hypertension, and hyperlipidemia in our transplant population is inadequate. The treatment of cardiovascular risk factors needs to be more aggressive to maintain adequate control.

17 YEARS EXPERIENCES WITH LUNG TRANSPLANTATION IN NORWAY

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From March 1990 – 2007 lung transplantation (Tx) on ECC have been offered patients with end-stage pulmonary disease (RF). 231 Tx were performed in 226 pts., 10-64 years of age. Aetiology (Dx) of RF was COPD 48%, α1-AT def. 16.5%, pulmonary fibrosis 11%, CF 5%) and miscellaneous causes (12%).

Since 1998 bilateral procedures were more preferred, particularly when severe pulmonary hyperinflation and hypertension was present. Pneumoplegia am Papworth, and later Perfadex solution, was used. Aprotinin was administrated on indication. Rejection surveillance was based on clinical information and a biopsy protocol. Since 2001 more aggressive endobronchial diagnostic and therapeutic measures were also applied postoperatively. Follow-up is complete.

87 single TX and 144 bilateral Tx were performed (mean waiting time 400 days), mean ischemic time distant/local donors was 236/127 min. 30d mortality was 7.1 % - one, five, ten, fifteen years patient survival were 80.8- 60.1- 37.4-18.9% irrespective Dx, age, time period and procedure performed. Since 2000, one and five year survival was 87 resp.70.7%. Main causes of death were OB, infection, primary graft failure.

Conclusion: The palliation of end-stage pulmonary disease has gradually improved. Bilateral transplant, Perfadex preservation and more aggressive postoperative treatment is related to improved results approaching patient survival of other solid organ transplants.

SHOULD THE CHOICE BETWEEN SINGLE LUNG TRANSPLANT VS. BOTH LUNG TRANSPLANT BE INFLUENCED BY THE EXPECTED SURVIVAL BENEFIT?

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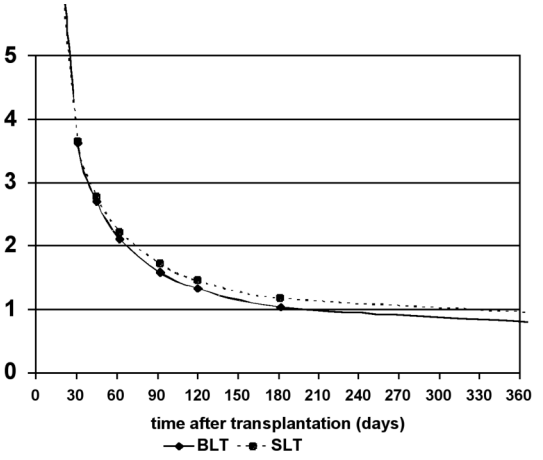
1- On behalf of the Eurotransplant Thoracic Advisory Committee, Innsbruck, Austria

Aim: To investigate whether the use of 2 organs is justified in terms of survival benefit.

Patient and methods: All consecutive adult patients listed for their first lung transplant in ET between Jan 1 2000 and Dec 31, 2003, N=1856. Patients were followed up from wait listing till either death on the waiting list or death post-transplant occurred. By use of a non-proportional hazards model it was tested whether transplantation modified the life expectancy of the patient.

Results: 928 Patients were transplanted with both lung transplant (BLT), while 332 received a single lung transplant (SLT) and 596 patients were either still on the waiting list (N=121), were de-listed without receiving a transplant (N=83) or had died while waiting for an organ to come available (N=392). The relative risk of death after BLT and SLT occurred after 210 days and 330 days, respectively.(see figure). Multivariate modeling further showed that the type of transplantation (BLT vs. SLT) is - independent from underlying primary disease - associated with post-transplant outcome.

Conclusion: Lung transplantation using either single or both lungs confers a survival benefit. Mortality risk reduction associated with transplantation occurs 1,5 times earlier for BLT compared to SLT.



SURVIVAL AFTER REPEAT LUNG TRANSPLANTATION

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Purpose: An increasing number of lung retransplantions are being performed because of acute or chronic graft failure. Due to the constant shortage of donor organs and the previously known worse results with retransplantation, some centres have been reluctant to offer this. Because therapies utilized have continued to improve in all aspects of transplantation, we re-examined our experience with repeat lung transplantation.

Methods: We retrospectively reviewed all 344 lung and heart-lung transplants performed at the University of Alberta Hospital between December 1989 and August 2007. Pre- and post-transplant characteristics were studied. Survival analysis was performed using Kaplan-Meier method.

Results: Repeat transplantation was performed in 6 patients (1.7%). Three patients had single lung retransplantation after initial double lung. Double lung was performed after previous double lung in one patient. Heart-lung retransplantation was performed after single lung in one patient, and after double lung in another patient. Two patients requiring acute retransplantation (<1 month since initial) survived more than 30 days but less than one year. Time from primary to repeat transplantation averaged 188 days (range 5-569 days).

Table 1: Characteristics of Primary and Repeat transplantations

	Primary (n=338)	Repeat (n=6)	p Value
Pediatric/Adult	5 / 333	0 / 6	0.764
Single/Double/Heart-Lung	81 / 235 / 22	3 / 1 / 2	0.006
Recipient Age: Range:	48 ± 13 (5 - 68 years)	38 ± 14 (19 - 53 years)	0.095
Gender (F/M)	41% / 59%	33% / 67%	0.701
Donor Age	38 ± 16	42 ± 8	0.630
Donor Ischemic Time (minutes)	334 ± 132	339 ± 111	0.172
ICU length of stay (days)	11 ± 13	11 ± 8	0.991
30 Day Survival	95%	100%	0.582
1 Year Survival	81%	33%	0.003

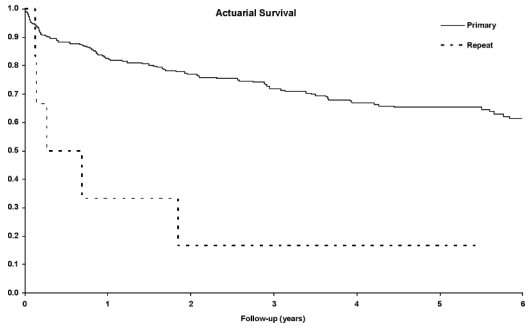

Figure 1: Actuarial survival curve of primary and repeat lung transplantations. One-year survival was 81% primary transplantation and 33% repeat transplantation (p = 0.003).

Conclusions: Repeat transplantation had significantly poorer survival than primary transplants (33% vs 81%, respectively, p=0.003). Retransplantation should continue to be applied only in carefully selected individuals.

SERUM TARC LEVELS POST LUNG TRANSPLANTATION AS A PREDICTOR FOR THE BRONCHIOLITIS OBLITERANS SYNDROME

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Introduction: Pre transplantation sCD30, which is produced by activated Th2 cells, was shown to be related to the development of the bronchiolitis obliterans syndrome (BOS). The aim of this study was to investigate the relation between the development of BOS and the Th2 chemoattractant thymus and activation regulated chemokine (TARC/CCL17).

Methods: In 54 patients (M/F=27/27, mean age 50 years (range 17-64), follow up range 4-75 months) we measured serum TARC levels prior to transplantation. Furthermore, sera were analyzed taken at months 1, 2 and 3 after LTx from 45 patients. In addition, longitudinal measurements (range 9-17 measurements) were performed in sera taken over a period of 2 years post transplantation in a group of 14 patients consisting of 7 patients developing BOS, who were matched for age, gender, primary disease and follow up time to 7 BOS-free patients. As control, sera taken at different time points from 8 healthy (M/F=5/3, mean age 35 years (range 26-46)) individuals were analyzed.

Results: Median serum TARC levels post transplantation of the patients who developed BOS (median 130, range 114-573 pg/ml) were lower than those of the matched BOS-free patients (median 642, range 243-1202 pg/ml, p=0.05, WSR). A receiver operating characteristics analysis (AUC 0.76) together with a Kaplan Meier analysis showed that serum TARC levels in the first months post transplantation can predict the development of BOS within 5 years post transplantation if a cut off value of 325 pg/ml is used (p=0.03, LR). In contrast, pretransplant serum TARC levels (range 121-1679 pg/ml) were not significantly different between patients eventually developing BOS, patients that remained BOS-free or healthy controls. TARC production itself appeared not to be affected by lung transplantation or the immunosuppressive regimen employed as serum TARC levels taken prior vs. 1 month post transplantation did not differ. The median TARC level (range 205-1832 pg/ml) in healthy controls was found to be similar to that in patients after transplantation. Analysis of patient sera during/preceding the onset of BOS, or CMV and EBV reactivation showed no relation with the course of serum TARC levels post transplantation.

Conclusion: The data indicate that serum TARC levels pre transplantation do not predict the development of BOS post transplantation. However, measurement of the serum TARC levels over the first months directly post transplantation can provide us with a tool to identify the group at risk of developing BOS within the first five years post transplantation.

COMORBIDITIES AND HEALTH-RELATED QUALITY OF LIFE AFTER LUNG TRANSPLANTATION

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Purpose: This dissertation examines the impact of comorbidities (osteopenia/osteoporosis, diabetes, overweight status/obesity) prior to lung transplantation and their effect on health-related quality of life (HRQOL) after lung transplantation. Lung transplantation has moved from a rare, life saving procedure to a life enhancing option for patients with end stage lung disease. Pre-existing comorbidities may be worsened after lung transplantation and may impact post-transplant health-related quality of life (HRQOL). Yet, the effects of existing comorbidities pre-transplant on post-transplant HRQOL is not known.

Methods: 92 lung transplant recipients completed the Medical Outcomes Study 36-item Short Form Health Survey (SF-36) version 1 HRQOL instrument at various times after transplant. The clinical data were extracted from their medical record corresponding to the survey time frame. Blockwise multiple regression was used to test the incremental independent effects of the pre-transplant comorbidities on post-transplant HRQOL. Block one covariates included time post transplant, evidence of chronic rejection, and underlying disease. The second block consisted of the comorbidities osteopenia/osteoporosis, diabetes, and body mass index (BMI). Outcome variables included the physical and mental component summary scores and the subscales of the Medical Outcomes Study 36-item Short Form Health Survey (SF-36) version 1.

Results: After controlling for the block one covariates ($p<0.05$), pre-transplant BMI had a significant negative effect (β = -.285, $p = 0.007$) on the physical function aspect of HRQOL after lung transplantation. Moreover, overweight status (BMI ≥25) and obesity (≥ 30) both exerted independent negative effects ($p \leq 0.05$) on the physical function scale of the SF-36. The pre-transplant comorbidity measures did not significantly affect post-transplant SF-36 physical and mental component summary scores.

Conclusion: Re-evaluation of elevated BMI as a relative risk for reduced physical functioning quality of life after lung transplantation should be considered based on this study. The negative effect of elevated BMI is present for both overweight and obese patients. Overweight status should be carefully considered when evaluating patients prior to listing and while on the waiting list for lung transplant. Future researchers may want to consider domain-specific predictor and outcome variables when studying HRQOL in the lung transplant population.

EMPLOYMENT STATUS AFTER LUNG TRANSPLANTATION IN A DEVELOPING COUNTRY

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Introduction: Transplantation is an experience of disruptive character that hits in the patient's psyches and environment (family and work). The transplant allows recipients to eliminate the physical barrier for the performance of multiple labour activities, but in certain social contexts with high rates of unemployment it operates like a variable of exclusion in front of the employment selection. The dependency of the patient to its health insurance also conditions its insertion in the labour world through informal works, which assure to him to continue with the clinical follow-up in their centre of transplant.

Objective: To analyze changes of the recipients' pre and post lung transplantation employment status, and to evaluate if the impact of the transplant conditions the working bonds of the patient.

Material and Methods: Between 06/1994 and 10/2006, 123 lung and heart lung transplantation were performed at a single institution in Argentina. For the present analysis, 79 adult patients (age > 18 years) with a 6 month conditional survival were included. Mean age was 38 years, and 31 (39%) were female.

Results:

PRE-TRASPLANT	POST-TRASPLANT
51(64%) retired, not working	30/51 (38%) illegal (informal) work 21/51 (26.5%) not working
15 (19%) unemployed	11/15 (14%) 6 illegal (informal) work /5 formal work 4/15 (4.5%) not working
3 (3.8%) formal work	3 (3.8%) formal work
3 (3.8%) studing	3 (3.8%) studing
7 (9.4%) domestic labour (Housewives)	7 (9.4%) domestic labour (Housewives)

Pre transplant only 3.8% (n=3) of the patients on the waiting list were working. This percentage reached to 55.8% (n=44) in the post-transplant follow-up. All three patients working pretransplant were formal work (100%) while only 8/44 (18%) had a formal work.

Conclusions: Although the increase number of patients who got up themselves into the labour market, the majority of them did it in informal conditions. Ignorance on the part of the employers, the little employ supply and the fear of the patients to lose their health insurance operates like important variables in the employment insertion of the patient. The task of education and information at communitarian level is essential to improve this situation

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THE KILLER CELL IMMUNOGLOBULIN-LIKE RECEPTOR HAPLOTYPE A PREDISPOSES TO THE BRONCHIOLITIS OBLITERANS SYNDROME AFTER LUNG TRANSPLANTATION

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Introduction: The Bronchiolitis Obliterans Syndrome (BOS) occurring after lung transplantation is caused by chronic allograft rejection. This syndrome is the main limiting factor for long term survival and respiratory viral infections are associated with an increased incidence of BOS. Natural Killer cells play an important role in the defense against viral infections and their activation is largely controlled by activating and inhibitory Killer Immunoglobulin-like receptors (KIRs). In previous reports on haematopoietic stem cell transplantation, significant associations were found between KIR genes and clinical key-parameters including chronic graft-versus-host-disease and CMV reactivation. The pupose of the current study was to determine whether the patients' KIRs influence the development of BOS and CMV infection after lung transplantation.

Methods: The KIR gene contents were determined in 48 patients who received a lung transplant, and HLA-Cw and –Bw4 typing was performed on their respective donors. From the 48 patients analyzed, 7 developed BOS and in 16 recipients CMV reactivation occurred.

Results: No correlation was found between KIR gene content and CMV reactivation. Analysis shows that 58% of the patients received a lung transplant without the HLA-ligand for inhibitory KIRs, but this was not associated with the development of BOS nor with CMV reactivation. However, 5 out of 19 patients homozygous for the KIR haplotype A developed BOS, compared to 2 out of 27 patients with KIR haplotype AB or B ($p=0.03$). Furthermore, in none of the patients with BOS the activating KIR 2DS5 could be found whereas it was present in 35% of patients without BOS ($p=0.04$).

Conclusions: These data indicate that inhibitory KIRs play an important role in the development of BOS but not in the control of CMV reactivation after lung transplantation.

ADVANCE IN LUNG TRANSPLANTATION FOR CYSTIC FIBROSIS AND SURVIVAL IMPROVEMENT

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Objective: To study advance in the management of lung transplanted patients for cystic fibrosis in our center and its incidence on survival.

Method: A retrospective study has been done, including 100 patients who underwent lung transplantation for cystic fibrosis between 1/1/1990, and 1/15/ 2007. There were 78 sequential double lung transplantations and 22 bilateral pulmonary lobe transplantations. CBP was used in 14 cases, mostly for lobar transplantations. Patients have been classified in two groups of 50 patients each, according to the date of transplantation: group I, before september 2003 and group II, from september 2003 to january 2007.

Results: Recipients characteristics were similar in both groups. In group II, donors were older (40 vs 33 years, p=0,013), with lower PaO2/FiO2 ratios (372 vs 427 mm Hg, p=0,022).
35 patients had the benefit of a thoracic epidural analgesia in group II against 13 patients in group I (p<0,001). A bilateral anterior thoracotomy with sternal preservation was more frequently used in group II (n=42 vs n=9, p<0,001). A lobar transplantation was performed in 7 cases in group I, and in 15 cases in group II. The overall actuarial 5yr survival rate is 50% in this series. The survival rates are 73%, 60%, and 43%, respectively at 1, 2, and 5yrs in group I; they are 88%, 78%, and 69% respectively at 1, 2, and 3yrs in group II, with no statistically significant difference.

Conclusion: Acceptance of older donors with lower PaO2/FiO2 ratios and techniques of pulmonary lobe transplantations allowed increasing lung transplantations for cystic fibrosis. Concomitantly, in our experience, the extensive use of thoracic epidural analgesia and of limited thoracic incisions have contributed to the improvement of 1 and 2yr survival rates.
Keywords: Lung transplantation. Cystic fibrosis. Survival.

RAGE, A MARKER OF ALVEOLAR EPITHELIAL TYPE I CELL INJURY, PREDICTS IMPAIRED ALVEOLAR FLUID CLEARANCE IN ISOLATED PERFUSED HUMAN LUNGS

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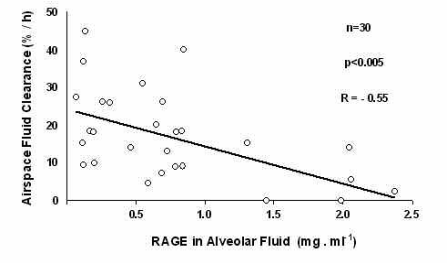
Purpose of the study: As established by recent studies : 1) the receptor for advanced glycation end-products (RAGE) can be used as a marker of epithelial type I cell injury (*AJRCCM 173:1008-15, 2006*) ; 2) type I cells play an important role in alveolar fluid clearance (AFC) (*PNAS 103:4964-9, 2006*). The purpose of this study was to test if elevated levels of RAGE would identify lungs with impaired AFC in an isolated perfused human lung preparation using lungs rejected for transplantation (*Am J Physiol Lung Cell Mol. Physiol 2007; 293:L52-59*).

Methods: Human lungs (n=30) were received 18 +/- 12h after procurement. The bronchus of a single lung was cannulated and a continuous positive airway pressure of 10 cm H2O was applied. The pulmonary artery was cannulated and perfused at a constant pressure of 12-15 mmHg. AFC was measured with sequential concentrations of protein in the distal air spaces by standard methods. RAGE levels were measured in the alveolar fluid and the perfusate.

Results: The rate of AFC was inversely correlated with RAGE levels both in alveolar fluid ($p < 0.005$; see Figure) and in the perfusate ($p < 0.05$). A concentration of RAGE above 0.7 mg.ml-1 in the alveolar compartment predicted, with a positive predictive value of 69%, an AFC < 14%, previously defined as impaired clearance.



Conclusions: RAGE may be a useful biological marker of alveolar epithelial injury and barrier dysfunction in the human lung.

NOVEL SUPERIORITY OF SUBZERO NON-FREEZING PRESERVATION OF RAT LUNG WITH SUPPERCOOLING TECHNOLOGY IN EX VIVO MODEL AND LUNG TRANSPLANTATION MODEL

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Purpose: A lower temperature has been thought desirable for organ preservation because of the lower rate of metabolism. However, its benefits are still poorly understood. Supercooling is a nonfreezing state of liquid below the freezing point and the new development of a refrigerator for supercooling has now made it possible to preserve organs at subzero temperatures in a non-frozen state without cryoprotectants. We hypothesized that supercooling would reduce metabolism of organ grafts and lung preserved in supercooling would have better physiological function than in the clinically standard storage at 4°C.

Methods and Materials: We investigated pulmonary functions not only in ex vivo rat lung perfusion model but also in rat left lung orthotopic transplantation model. In ex vivo model, in which lungs were preserved for 17 hr and subsequently reperfused for 60 min, physiological parameters, ATP level, and pathological findings were assessed. All animals were divided into three groups; fresh, 4°C, and supercoolng (-2°C) groups (each, n=7). In rat lung transplantation model, lungs were preserved at 4 or -2°C for 24 hrs and PaO_2 in left PV and pathological findings were evaluated on POD 7.

Results: Ex vivo model showed that the supercooling group significantly attenuated ischemia-reperfusion injury with a decrease in pulmonary artery pressure (p<0.02) and weight gain (p<0.001) and an increase in tidal volume (p = 0.001) and arterial oxygen tension (p<0.001) in comparison to the 4°C group. In the supercooling group, most of these parameters were equivalent to the fresh with less damage to the endothelial cells and higher levels of ATP than the 4°C. Rat lung transplantation revealed that both groups survived on POD 7 but the pathological finding in the supercooling group was normal lung architectures while severe fibrosis were observed in the 4°C group.

Conclusions: Supercooling demonstrated the superiority in hypothermic preservation of rat lungs to the standard storage of 4°C both in an ex vivo model and lung transplantation model. There is a possibility of clinical application of this supercooling technology.

EX VIVO EVALUATION OF NON-HEART-BEATING DONOR LUNGS IN LARGER-SIZE PIGS

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Purpose: Since the first introduction of pig lung ex vivo evaluation system by Steen et al, many groups have begun the animal ex vivo system using pigs and dogs. Out of all reports, the maximum weight of pigs was 60 kg and the total flow of perfusion was 4.0 L/min. On the other hand, there will be a wide variety of body weight of patients from children to adults in a clinical situation. We investigated ex vivo evaluation of larger-size pig lungs under higher total flow of perfusion simulating non-heart-beating donor of large-size adults.

Methods: Heart-lung blocks (n=5) were obtained in a local slaughter house just 10 min after the death of pigs (average weight: 115 kg). The pulmonary artery was immediately flushed with cold Perfadex and the lungs were carried to Kyoto University in an ice box. After 6 hr of cold ischemia, lungs were perfused in ex vivo evaluation system, which consisted of a hard-shell reservoir, a centrifugal pump, an artificial lung, and leukocyte/arterial filter. The perfusate was concentrated red blood cells of the same pig and the STEEN solution. The flow was gradually increased according to the rise of the temperature of the perfusate as long as the PA pressure was less than 20 mmHg. The gas to the artificial lung was changed to N_2+CO_2 and the ventilation was started after the temperature reached to 32°C. The final flow was aimed to be 5.0 L/min and the perfusion was continued for 2 hr. Physiological data such as PaO_2, the pulmonary artery pressure, and the shunt fraction, were measured.

Results: In all 5 cases, the perfusion was stably sustained for more than 2 hr. The final flow was 4.9 ± 0.1 L/min, the pulmonary artery pressure was 14.8 ± 1.7 mmHg, and the PaO_2/FIO_2 was 517.8 ± 17.9 mmHg (69.0 ± 2.4 kPa). The shunt fraction was 20.5 ± 4.0 %.

Conclusions: We have successfully established the ex vivo lung evaluation system using larger-size pig lungs from a slaughter house. The total flow of 5.0 L/min may be possible for large-size donor lungs.

EXPERIMENTAL DONOR LUNGS FROM DONATION AFTER CARDIAC DEATH IN VARIOUS SETTINGS

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Background: To resolve the shortage of donors for lung transplantation, lung transplantation from donation after cardiac death (DCD) donors has been investigated. Considering various situations such as controlled DCD or uncontrolled DCD, methods for cardiac arrest have become an essential problem in an experiment of DCD donor lungs.

Material and Methods: Male Lewis rats weighing 320-400g were used in this study. Animals were randomly allocated to 4 groups (n=5 each): Sham, Ventricular fibrillation (VF), KCl, and Asphyxia groups. After one hour of postmortem interval from cardiac arrest, the pulmonary artery was cannulated directly. All study lungs were flushed with 50mL of trypan blue solution (0.2mM, 4°C) through the main pulmonary artery at a pressure of 20cmH2O. Lungs were flushed with trypan blue solution without the induction of cardiac arrest (Sham group), and 60minutes after cardiac arrest induced by fibrillator (VF group), KCl injection (KCl group), and ventilator switch-off (Asphyxia group), respectively. The time requiring 50mL of flush was measured on each animal and histological findings of the flushed lungs were also analyzed.

Results: Cardiac arrest was successfully induced in all groups. Flush of trypan blue solution was completely accomplished in all lungs. Flush time was 91 ± 31 seconds, 112 ± 15 seconds, 243 ± 10 seconds, and 205 ± 9 seconds in the Sham, VF, KCl, and Asphyxia groups, respectively. Flush time was significantly longer in KCl group than that in Asphyxia group ($P < 0.05$), in Asphyxia group than in VF group ($P < 0.05$) and in VF group than in Sham group ($P < 0.05$). Macroscopic findings of lungs in Sham and VF groups showed homogeneous stain by trypan blue, while those in KCl and Asphyxia groups were apparently inhomogeneous. Histological findings also revealed that lungs in the KCl and Asphyxia groups significantly showed more remains of blood in the pulmonary vessels than those in VF and Sham groups.

Conclusions: We found that there was a significant difference in the flushing of the DCD donor lungs among the various settings. Our data suggested that the difference between VF and Asphyxia groups would explain the difference among uncontrolled and controlled DCD donors. Further investigation with ex vivo rat lung perfusion system is to be done in order to perform functional evaluation of such DCD donor lungs.

OFF-PUMP SINGLE LUNG TRANSPLANTATION IN COPD: INTRAOPERATIVE PREDICTION OF POST-TRASPLANT VENTILATION IMPROVEMENT

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Introduction: Patients with diagnosis of advanced chronic obstructive pulmonary disease (COPD) who undergo off-pump single lung transplantation (SLT) are at high risk of suffering volume or pressure related damage of the native lung during selective ventilation. Permissive hypercapnia (PaCO2 between 50 and 100 mmHg, and pH × 7.20) is a preventive alternative in selective lung ventilation, although it leads to transient alveolar hypoventilation.

Objectives: The aim was to identify intraoperative predictors in arterial blood gases (ABG) samples of post-transplant alveolar ventilation improvement in single lung transplant (SLT) COPD recipients.

Material and Methods: Between June/1994 and September/2007, 118 lung transplants were performed at a single institution. Of this, 44 COPD patients who received off-pump SLT were included in the present study. Mean age of the 44 patients was 54±5 years of which 5.6% were male. All patients were in NYHA FC IV The ventilatory modality during the anaesthetic procedure was controlled volume with permissive hypercapnia. ABG samples were obtained after anaesthetic induction (baseline) and at the end of the procedure (final). Variables were compared using a paired t test.

Results: Basal and Final measurements of ABG (mean ± SD) are compared in the following table:

	Baseline	Final	*p* value
$PaCO_2$ (mmHg)	**61 ± 10.8**	**51 ± 10**	**<0.001**
pH	**7.33 ± 0.06**	**7.35 ± 0.07**	**>0.05**
HCO_3 (mM)	**30.4 ± 5.9**	**28.0 ± 4.5**	**<0.001**
PaO_2 (mmHg)	**377 ± 137**	**387 ± 158.5**	**>0.05**
BE (mM)	**5.38 ± 4.4**	**2.28 ± 4.26**	**<0.001**

A linear correlation was found between baseline pH and $\Delta PaCO_2$ ($PaCO_2$ basal – $PaCO_2$ final), with the following linear adjust: $\Delta PaCO_2$ = 144.8 . pH baseline – 1070.7 ($p < 0.001$; $r^2 = 0.78$). In a multivariate linear regression model, baseline pH was an independent predictor of $\Delta PaCO_2$ ($p< 0.001$) r2= 0.50.

Conclusions: $PaCO_2$, HCO_3 and base excess (BE) were immediately improved by the procedure. A linear correlation was identified between baseline pH and $\Delta PaCO_2$. Pre transplant pH was an independent predictor of post-transplant alveolar ventilation improvement in this study.

THE IMPACT OF LIMITED ANTERIOR THORACOTOMY INCISIONS IN LUNG TRANSPLANTATION SURGERY

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Objective: Predisposing factors for wound complications following lung transplantation (LTX) are sudden increases in intrathoracic pressure, rib or cartilage fractures, intercostal muscle weakness, surgical trauma, and in particular chronic immunosuppression therapy and steroid abuse. Muscle sparing limited anterior thoracotomies without transsection of the sternum may lead to decreasing the sequelae of wound complications.

Methods: We used the single institution based transplant data bank, phone questionnaire, ambulatory care unit follow-up data in order to investigate the incidence of wound healing complications following muscle and sternum sparing and mammary artery protecting limited access small submammary anterior thoracotomy incisions (AT) for lung transplantation surgery. Intra-op cryo-ablation of the thoracotomy wound corresponding intercostal nerves and sympathetic ganglia ws performed surgically for pain control. In the need for cardiopulmonary bypass (CPB) the femoral v/a were canulated. Statistical analysis: ANOVA, t-tests, chi2 ($p<0.05=^{*}$).

Results: Following exclusion of 5 clamshell operations for LTX combined with cardiac surgery 71 recipients (65 % male), age 19-68, mean 54 ±8 years underwent 64 AT and 42 post.lat. thoracotomies (PT) for IPF (48%), obstructive disease (40%), CF (5%), and PAH (7%). AT ranged from 5.5 cm to 26 cm (mean 20.3 ±4.8) and PT from 12 cm to 25 cm (mean 19.8 ±2.4) and was not significant different (p=0.37). Ischemic time for single lung (322 ±59min), sequential bilat. (399 ±135 min) was significantly longer compared to ISHLT-reporting. Warm ischemic times ranged from 30 to 92 min (mean 56 ±11). Four patients required re-thoracotomy for bleeding/hematoma formation. CPB/intra-op ECMO was used in 40% (femoral a.v. cannulation). Superficial wound infection and subsequent drainage/care was needed in 2 PT incisions. Re-operation for lung herniation using patch repair technique for thoracic wall stabilization was required in 2 AT (3%) and 3 PT (7%).

Conclusions: Sternum sparing and mammary artery protecting limited access small submammary anterior thoracotomy incisions for lung transplantation surgery are feasible and do not lead to a high incidence of wound complications and lung hernias. There 0% severe wound infection. In the event of CPB supported lung transplantation femoral vessel cannulation is required, which allows undisturbed operative situs and exposure.

DOUBLE LUNG TANSPLANTATION IN A CYSTIC FIBROSIS PATIENT WITH DONOR LUNGS PROCURED FROM A BRAIN DEAD HEART TRANSPLANT RECIPIENT DONOR

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Introduction: Even though previous transplantation has not been an established exclusion criteria for cadaveric donors, references in the medical literature regarding this possibility have been almost inexistent.

Case Report: A 23 year-old female patient (p.) with a diagnosis of cystic fibrosis (CF) received a double lung transplant from a brain dead heart transplant recipient. The patient had a BMI of 15.6 kg/m^2 ,was in class III NYHA functional status and under continuous ambulatory oxygen therapy. She had pancreatic involvement and under supplemental pancreatic enzymes on a regular basis. The patient had long standing bacterial colonization with Pseudomona Aeuruginosa (only sensitive to Piperacillin-Tazobactam, Aztreonam and Meropenem) and Methicillin Sensitive Staphylococcus Aureus. CMV status was +.
The donor, who was 27 years old, died because of subarachnoid hemorrage with a massive intraventricular bleeding (Hunt-Hess and Fisher's scales V and IV respectively) received a heart transplant 7 years before because of a post myocarditis dilated cardiomyopathy. He carried a diagnosis of hypogonadotrophic hypogonadism for which he received supplemental hormonal therapy. Immunosupression was obtained through Sirolimus 2 mg/day, Mycophenolate Mofetil 1 g bid and Prednisone 6 mg. Serological status was CMV +. Brain death was certified 12 hours post admission. The donor was hemodinamically stable under a Norepinephrine infusion of 0.15 micrograms/kg/min with mechanical ventilation delivered through the controlled volume mode with a TV of 8.6 ml/kg and a FiO2 of 0.5. Maximal Airway and Plateau Pressures were 22 and 17 cm. H20 respectively. The PaFiO2 was 490.
A sequential double lung transplantation was performed at the same center. Ischemic time was 210 and 285 minutes for the left and right lungs respectively.
The double lung transplantation patient had an uneventful postoperative course being discharged from the hospital after a 22 days stay.
Through the multiorganic procurement procedure one renal, one reno-pancreatic and one orthotopic liver transplantation were performed in three different local transplantation centers. The rest of the transplants also had normal postoperative courses and were discharged from the hospital. References were obtained from the public organ sharing agency.

Discussion: References in the medical literature regarding the possibility of brain dead transplanted patients as suitable organ donors have been almost inexistent. The frequent infections arising from immunosupression and the rest of noninfectious potential complications may explain the reluctance to consider them as a potential source of organ donation.

Conclusion: Further studies and follow up are warranted to study the suitability of brain dead transplanted patients as potential organ donors and the immunological considerations that might arise from it.

LUNG TRANSPLANTATION FOR ARDS AFTER PROLONGED ECMO SUPPORT

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Objectives: Acute Respiratory Distress Syndrome (ARDS) is a debated indication for lung transplantation (LTX), particularly after ECMO support is instituted. We present the case report of a double LTX for ARDS performed after 3 weeks of veno-venous ECMO support.

Methods: A 22 year patient was transferred to our institution with ARDS secondary to aspiration pneumonia, after 13 days of ventilatory support. Despite aggressive antibiotic therapy and steroids the gas exchanges and airspace disease progressively worsened. 24 hours after admission the patient was placed on veno-venous ECMO through a percutaneous femoro-jugular approach. All circuits were completely heparin coated, which allowed to keep anticoagulation within low ranges (ACT=150). The hemodynamics and metabolic status and the gas exchanges were optimized and a protective ventilatory strategy instituted.

Results: The patient was placed on the LTX waiting list and, 21 days after ECMO placement, a set of lungs became available from a 35 year old donor. A sequential double LTX was performed after switching to veno-arterial peripheral ECMO. The immediate function of the graft was excellent and the patient was weaned off extracorporeal support. The postoperative recovery was uneventful. The pt. was discharged from the hospital on POD number 31 in excellent clinical conditions and is alive and well at a a follow up of 8 months.

Conclusions: A few reports of LTX for ARDS are available. Most centers don't consider performing LTX after ECMO support. The local allocation system allowed us to list this patient with realistic chances of LTX. A low anticoagulation allowed to reduce the risk of prolonged ECMO-related complications. In selected cases, LTX can be a therapeutic option for ARSD after prolonged ECMO support.

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