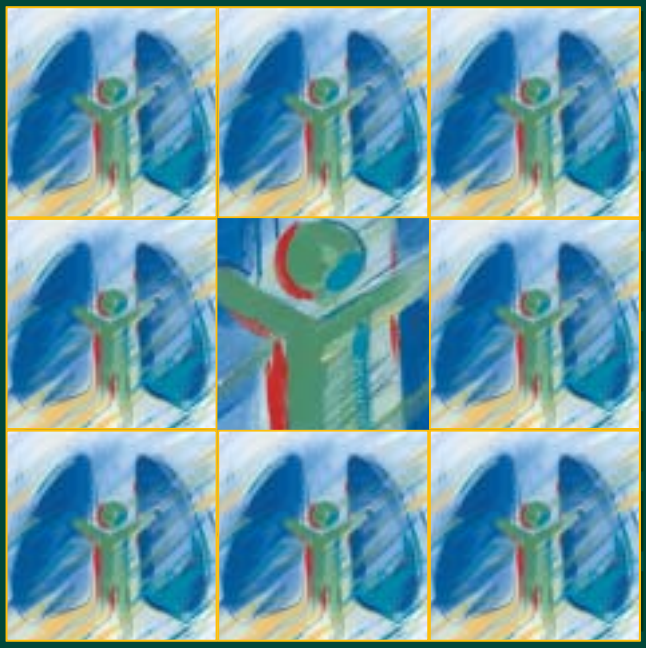
6th International Congress on

LUNG TRANSPLANTATION

PARIS, September 16-17, 2004



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

PROGRAM & ABSTRACTS

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6th International Congress on

LUNG TRANSPLANTATION

PARIS, September 16-17, 2004

under the Patronage of

Fondation Maréchal Foch

Société Française de Chirurgie Thoracique et Cardiovasculaire

Welcome Address

Dear Colleagues,

I am honoured to welcome you in Paris for the sixth occasion to the International Congress on Lung Transplantation.

This year again the scientific program is dealing with the major issues of lung transplantation such as Lung Procurement, Ischemia and Preservation, Immuno-suppressive Therapies, Pulmonary Hypertension etc. This meeting will provide the ideal setting for discussion and a forum for exchanges between the world's most eminent specialists and all those involved in the fields of Lung Transplantation.

You will have the opportunity of visiting or re-visiting Paris, one of the world's most beautiful city.

On behalf of the Organizing Committee, it gives us very great pleasure to welcome you.

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SCIENTIFIC INFORMATION

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.

If you are presenting a poster

Mounting
Thursday 16 September
7.30 a.m. - 8.30 a.m.

Dismantling
Friday 17 September
4.00 p.m. - 4.30 p.m.

The number of your poster board correponds to the one indicated in this program.
Hanging fixtures can be obtained from the hostesses at the Welcome Desk during the allocated mounting schedule.

GENERAL INFORMATION

Administrative Secretariat

Office hours :

Thursday 16 September	7:30 a.m. - 6:30 p.m.
Friday 17 September	7:30 a.m. - 4:30 p.m.

After the Congress :

VBCE - Lung Transplantation
43, rue de l'Abbé Groult
75015 Paris
Tel: +33 (0) 1 45 33 60 46
Fax: +33 (0) 1 45 33 57 15
e-mail : v.buffet@vbce-fr.com

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.

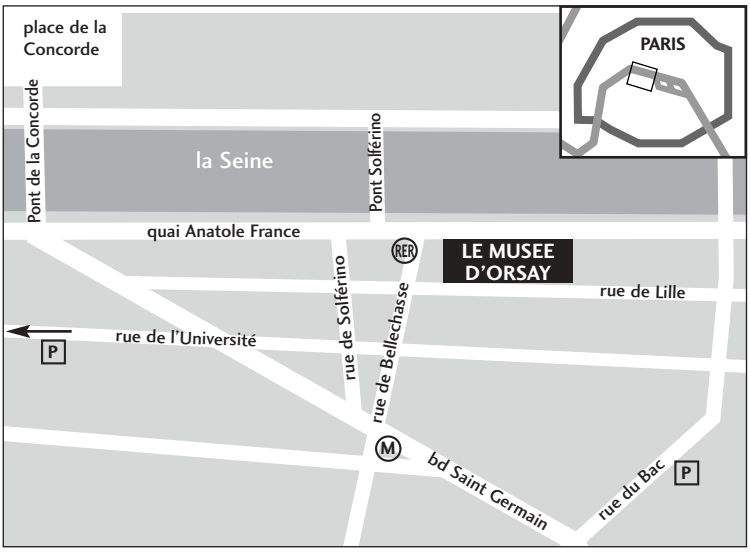
SOCIAL PROGRAM

Thursday, September 16

DINNER AT "LE MUSÉE D'ORSAY"

19:15

Price per person : 120 €
(upon availability)



Ⓜ *Métro: Solférino station (line n° 13)*
RER: Musée d'Orsay station (line C)

P *Parking*
Rue du Bac
Esplanade des Invalides

ACKNOWLEDGEMENTS

The Organizing Committee wishes to extend its thanks and appreciation to the following sponsors for their contribution :

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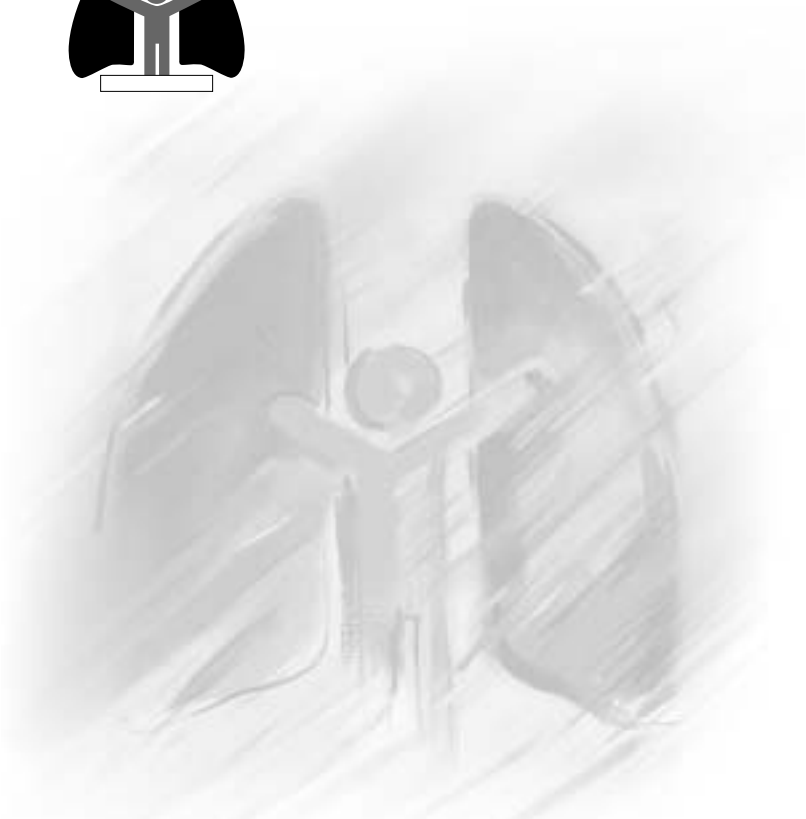

SCIENTIFIC PROGRAM

Thursday 16 September

	Espace Louis Armand	Salle List and Stephenson
8:30 8:45	Opening	
10:00	Immunosuppression : New Clinical trials p 13	
	Break	
10:30 12:30	Immunosuppression : New Clinical trials p 13	Free Communications p 14
14:00 16:00	Marginal donors p 15	Long term care Issues p 16
	Break	
16:30 18:00	Alternative therapies p 17	LT in emergent countries p 18

Friday 17 September

	Espace Louis Armand	Salle List and Stephenson
8:00 10:00	Allocation/distribution p 19	Ischemia/reperfusion Injury p 20
	Break	
10:30 12:40	Non-Heart Beating Donors p 21	Diagnosis-dependant benefits p 22
14:00 16:00	Bronchiolitis Obliterans Syndrome p 23	Free Communications p 24
16:30 18:00	Bronchiolitis Obliterans Syndrome p 23	

8:30 → 8:45 Espace Louis Armand

Opening

Alain BISSON
President of the Organizing Committee

Carine CAMBY
President of the *Etablissement Français des Greffes*

Thomas EGAN & Herman REICHENSPURNER
Presidents of the Congress

8:45 → 12:30 **Espace Louis Armand**

Immunosuppression : New Clinical trials

Chairpersons: **T.M. EGAN** (USA), **H. REICHENSPURNER** (Germany)

8:45	**Overview on clinical trials** H. Reichenspurner (Germany)	**L1**
9:15	**Induction therapy** R.D. Davis (USA)	**L2**
9:45	**Pharmacodynamic monitoring of the conversion of drug therapy in human heart and lung transplanted recipients** A. Rahmel, J. Garbade, M. Richter, H.B. Bittner, S. Dhein, F.W. Mohr, J.F. Gummert	**O1**
10:00	BREAK	
10:30	**Everolimus in Lung Transplantation** G. Snell (Australia)	**L3**
11:00	**Sirolimus in Lung Transplantation** S.M. Bhorade (USA)	**L4**
11:30	**Anti-inflammatory agents Azithromycin** J.B. Orens (USA)	**L5**
12:00	**New challenges in Lung Transplantation: Discontinuing corticosteroids or anticalcineurins?** P. Corris (UK)	**L6**

10:30 → 12:15 Salle List & Stephenson

Free Communications

Chairpersons: **J. NIEDERMEYER** (Germany), **B. PHILIPPE** (France)

10:30 **The Copenhagen National Lung Transplant Group: Survival after single lung, double lung and heart-lung transplantation performed in 1992-2003, a study comprising 362 patients**
C. Burton, N. Milman, J. Carlsen, H. Arendrup, K. Eliasen, C. Andersen, M. Iversen **O2**

10:45 **The development and analysis of a screening tool to assess the psychosocial functioning of lung transplant assessment patients**
A. McDermott, C. Hallas, M. Carby **O3**

11:00 **Patient self-report vs. toxicology to confirm abstinence from tobacco products alcohol or illicit drugs**
I. Nizami, K. Perry, C. Elkins, J. Chaffin, P. Kanaly, D. Nelson, W. Paris **O4**

11:15 **Lack of clinical and functional predictors of mortality in interstitial lung disease waiting for lung transplantation. Possible role of delayed referral**
J. Cáneva, A.M. Bertolotti, F.R. Klein, J. Ossés, R.R. Favaloro **O5**

11:30 **Assessment of pharmacodynamics of cyclosporin plus mycophenolate mofetil at C0h / C2h in human transplanted recipients**
A. Rahmel, J. Garbade, M. Richter, H.B. Bittner, S. Dhein, F.W. Mohr, J.F. Gummert. **O6**

11:45 **Multiple lower respiratory tract infections (LRTI) adversely affect mortality among lung transplant recipients who receive Total Lymphoid Irradiation (TLI) for chronic rejection**
A. Barlow, M. Khan, S. Stinchcombe, M. Carby **O7**

12:00 **Systemic fungal infections after lung transplantation**
F. Klein, H. Solar Muñiz, J. Díaz, A.M. Bertolotti, C.B. Nagel, R.R. Favaloro **O8**

14:00 → 16:05 Espace Louis Armand

Marginal donors

Chairpersons: **H. MAL (France), G. SNELL (Australia)**

14:00	**Donor management recommandations** I. Vinatier (France)	**L7**
14:20	**Ex vivo resuscitation of human lungs declined for transplantation** D. Van Raemdonck (Belgium)	**L8**
14:40	**The use of high-dose Narcan to minimize the effect of neurogenic pulmonary edema and improve pulmonary function of the organ donor** M. Thibault (USA)	**O9**
14:55	**The hemodynamically instable lung donor: A case for non-Heart Beating Donation** G. Lang (Hungary)	**O10**
15:10	**Liberation of donor criteria: clinical results** G. Snell (Australia)	**L9**
15:30	**A Donor History of Smoking Affects Early But Not Late Outcome from Lung Transplantation** T. Oto, A.P. Griffiths, B. Levvey, D.V. Pilcher, H. Whitford, T.C. Kotsimbos, M. Rabinov, D.S. Esmore, T.J. Williams, G.I. Snell	**O11**
15:45	**Strategies to increase limited donor resources** M. De Perrot (Canada)	**L10**

14:00 → 16:00 **Salle List & Stephenson**

Long term care Issues

Chairpersons: **S.M. BHORADE** (USA), **Ph. LOIRAT** (France)

14:00	**Quality of Life** P. Loirat (France)	**L11**
14:30	**Renal Insufficiency** J. Niedermeyer (Germany)	**L12**
15:00	**Malignancies** S.M. Bhorade (USA)	**L13**
15:30	**Pregnancy** C. Knoop (Belgium)	**L14**

16:30 → 18:10 Espace Louis Armand

Alternative therapies

Chairpersons: **J.F. MORNEX** (France), **M. HUMBERT** (France)

16:30 **PPH: Vasodilator therapy and consequences on lung transplant referral**
M. Humbert (France) **L15**

16:55 **Obstructive Pulmonary Arterial Hypertension**
P. Dartevelle (France) **L16**

17:20 **Lung Volume Reduction Surgery in Emphysema: Results and Long term perspective**
W. Weder (Switzerland) **L17**

17:45 **Lung Volume Reduction in Emphysema: Endobronchial techniques**
M. Noppen (Belgium) **L18**

16:30 → 18:00 Salle List & Stephenson

LT in emergent countries

Chairpersons: **S.A. ALY** (Egypt), **A. BISSON** (F)

16:30 **Lung transplantation in emerging countries. Current problems, future perspectives in Egypt**
S.A. Aly (Egypt) **L19**

Pulmonary transplantation management in Romania
T. Horvat, M. Grigoroiu, M. Davidescu, Cl. Nistor, C. Savu, C. Petreanu (Romania) **L20**

Results of two years of lung harvesting in Hungary ; an example for international cooperation in transplantation in Middle-Europe
G. Lang (Hungary) **O12**

Analysis of complications of lung transplantation in Korea (Single institute experience)
H.C. Paik (Korea) **O13**

An example of North South cooperation in transplantation
A. Dunbavand (EFG, France) **L21**

From end-stage organ disease to transplantation: ISMETT perspective in Mediterranean emerging countries
B. Gridelli (Italy) **L22**

8:00 → 10:00 Espace Louis Armand

Allocation/distribution

Chairpersons: **T.M. EGAN** (USA), **G. SNELL** (Australia)

8:00	**The US model** T.M. Egan (USA)	**L23**
8:30	**The Eurotransplant model** J. Smits (The Netherlands)	**L24**
9:00	**The French Model (EfG)** M. Stern (France)	**L25**
9:30	**General discussion**	

8:00 → 10:00 Salle List & Stephenson

Ischemia/reperfusion Injury

Chairpersons: **D. VAN RAEMDONCK** (Belgium), **M. DE PERROT** (Canada)

8:00 **Primary graft failure after Lung Transplantation**
J. Christie (USA) **L26**

8:30 **Recipient T-cell lymphocyte in ischemia reperfusion injury**
M. De Perrot (Canada) **L27**

9:00 **Evaluation of reperfusion injury**
F. Wagner (Germany) **L28**

9:30 **Inhalative Donor Pretreatment Using The Aerosolized Prostacyclin Analogue Iloprost Optimizes Postischemic Function of Lung Allografts**
T. Wittwer, U. Franke, T. Sandhaus, A. Schuette, S. Richter, T. Mueller, H. Schubert, M. Ochs, N. Dreyer, J. Richter, Th. Wahlers **O14**

9:45 **Impact of Retrograde Graft Preservation in Perfadex-based Experimental Lung Transplantation**
T. Wittwer, U. Franke, A. Fehrenbach, D. Meyer, T. Sandhaus, F. Pfeifer, N. Dreyer, T. Mueller, H. Schubert, J. Richter, Th. Wahlers **O15**

10:30 → 12:40 Espace Louis Armand

Non-Heart Beating Donors

Chairpersons: **T.M. EGAN** (USA), **A. VARELA** (Spain)

10:30 **Preservation in NHBD**
D. Van Raemdonck (Belgium) **L29**

11:00 **Ischemia- reperfusion in NHBD**
T.M. Egan (USA) **L30**

11:30 **Out-hospital NHBD**
A. Varela (Spain) **L31**

12:00 **Clinical lung transplantation with NHBD**
P. Gámez, M. Córdoba, J. Calatayud, F. Hernando, A. Gómez **O16**

12:15 **NHBD Perspectives in a near future : Global discussion**

10:30 → 12:40 Salle List & Stephenson

Diagnosis-dependant benefits

Chairpersons: **P. CORRIS** (UK), **C. PISON** (France)

10:30 **Emphysema**
H. Mal (France) **L32**

10:55 **Cystic Fibrosis**
J. Niedermeyer (Germany) **L33**

11:20 **PPH**
P. Dartevelle, A. Chapelier (France) **L34**

11:45 **Improved Survival after Lung Transplantation for Pulmonary Hypertension: Right Ventricular Ejection Fraction and Selection of Surgical Procedure**
R. Daly (USA) **O17**

12:00 **Pulmonary Fibrosis**
C. Pison (France) **L35**

12:25 **Lung transplantation for end-stage lung disease (ESLD): Patient selection, outcome and survival on the waiting list**
A.M. Bertolotti, J. Cáneva, F.R. Klein, J. Ossés, R.R. Favaloro **O18**

14:00 → 17:30 Espace Louis Armand

Bronchiolitis Obliterans Syndrome

Chairpersons: **M. ESTENNE** (Belgium), **H. REICHENSPURNER** (Germany)

14:00 **Definitions and limitations**
J.B. Orens (USA) **L36**

14:30 **Predictive values and Substitute markers**
M. Estenne (Belgium) **L37**

15:00 **GERD as Risk factors**
R.D. Davis (USA) **L38**

15:30 **Medical therapy**
P. Corris (UK) **L39**

16:00 BREAK

16:30 **Total Lymphoid Irradiation reduces the rate of FEV1 decline in lung transplant patients with chronic rejection but not all patients experience the same degree of benefit**
A. Barlow, M. Khan, S. Stinchcombe, M. Carby (UK) **O19**

16:45 **Reduction of chronic vascular rejection by mycophenolate mofetil (MMF) after late treatment of acute pulmonary rejection in an allogenic rat lung transplant model**
T. Pühler, S.W. Hirt, E. Lesser, M. Frahm, C. Hass, M. Ernst, R. Pühler, J. Cremer, H.U. Wottge **O20**

17:00 **Retransplantation**
O. Brugière (France) **L40**

14:00 → 15:30 Salle List & Stephenson

Free Communications

Chairpersons: **F. WAGNER** (Germany), **P. BONNETTE** (France)

14:00 **Ex-vivo evaluation of non-acceptable donor lungs**
P. Wierup, F. Nilsson, L. Pierre, H. Scherstén, M. Silverborn, T. Sjöberg, S. Steen **O21**

14:15 **High Prevalence of Pulmonary Arterial Thrombi in Donor Lungs Rejected for Transplantation: Implications for Lung Dysfunction in Donor Lungs and Lung Recipients**
L.B. Ware, X. Fang, W.D. Babcock, K. Jones, M.A. Matthay **O22**

14:30 **Clinical applications of ET-Kyoto solution for lung transplantation in Kyoto University hospital**
T. Fujinaga **O23**

14:45 **Presensitization accelerates chronic allograft rejection in heterotopic rat tracheal allograft model**
T. Okumoto, Y. Sano, M. Yamane, M. Aoe, H. Date, N. Shimizu **O24**

15:00 **Modifications of mitochondrial respiration from lung recipients' skeletal muscle : effects of rehabilitation**
K. Guerrero, B. Wuyam, L. Kay, J.C. Borel, R. Hacini, O. Chavanon, B. Aguilaniu, P. Mezin, V. Saks, C. Pison **O25**

15:15 **Single Lung transplantation in end-stage lung disease (ESLD) with secondary pulmonary hypertension (SPH): A survival assessment**
A.M. Bertolotti, F.R. Klein, C. Gómez, J. Cáneva, J. Ossés, R.R. Favaloro **O26**

Posters

EXHIBITORS LIST

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ABSTRACTS

Pharmacodynamic monitoring of the conversion of drug therapy in human heart and lung transplanted recipients

Axel Rahmel, Jens Garbade, Markus Richter, Hartmuth B. Bittner, Stefan Dhein, Friederich W. Mohr, Jan F. Gummert

Aims: In the current clinic practice therapeutic drug monitoring (TDM) in heart and lung transplanted (HTx, LTx) recipients for cyclosporine (CsA), tacrolimus (TRL) and sirolimus (SRL) relies on the daily measurements of blood concentrations (pharmacokinetic, PK) to maintain drug concentrations within their respective target ranges. However, the unknown absolute drug bioavailability, the inter-individual variability regarding the biological drug effect and drug interactions (e.g. shared metabolism through the cytochrome P450) are limitations of TDM based on PK. In this study we investigated the conversion of drug therapy by assessing the pharmacodynamics (PD) of lymphocyte function in whole blood in HTx and LTx.

Methods: PD effects and PK in HTx and LTx recipients were assessed of two reasons: first, conversion of CsA to TRL in patients with gingival hypertrophy (Group I, 8 patients) and second, conversion of CsA to SRL in patients with severe renal dysfunction (Group II, 10 patients). 24 hours (Group I) or 28 hours (Group II) after the last CsA dose (75 or 100mg) patients were treated with a fixed dosing regime: Group I: 6mg/BID TRL on days-1 and –2; Group II: 6 mg/ QD SRL on day 1 and 2mg/QD SRL at days 2 and 3. Patients of both groups received mycophenolate mofetil/BID co-therapy (dose range of 500-2500mg/day). PK measurements of CsA, TRL were done by EMIT and for SRL by LC-MS/MS. PD effects of lymphocyte proliferation (PCNA) and activation (CD25, CD95, CD134, CD154) were analyzed by FACS.

Results: PKtrough- and PDtrough-values (%expression) on day-1 and -2 under TRL therapy (Group I) or on days-1to -3 under SRL therapy (Group II) were compared with PKtrough- and PDtrough-values under CsA therapy (day 0), e.g. for 2 patients of each group: Group I: patient AI: day 0: CsA:141 ng/ml; PCNA:8,4%; CD25:16%; day 1: TRL:7.2 ng/ml; PCNA:2,8%; CD25:11,9%; day 2: TRL:14.3 ng/ml; PCNA:2,1%; CD25:10,4%; patient BI: day 0: CsA:130 ng/ml; PCNA:11%; CD25:5,3%; day 1: TRL:4 ng/ml; PCNA:5,4%; CD25:8,4%; day 2: TRL:8 ng/ml; PCNA:5,1%; CD25:3,9%. Group II: patient AII: CsA:125 ng/ml; day 0: CD25: 7%, CD95: 15%; day 1: SRL 8.4 µg/L; CD25: 17%, CD95: 11%; day 2: SRL 15.7 µg/L, CD25: 11%, CD95: 14%, day 3: SRL 5.4 µg/L, CD25: 25%, CD95: 14%; Patient BII: CsA:118 ng/ml; day 0: CD25: 9%, CD95: 14%, day 1: SRL 4.3 µg/L, CD25: 6%, CD95: 4%; day 2: SRL 11 µg/L, CD25: 8%, CD95: 8%, day 3: SRL 5.4 µg/L, CD25: 8%, CD95: 5%.

Conclusions: For the first time, the switch to TRL or SRL from CsA therapy in HTx and LTx was assessed by monitoring the PD of lymphocyte functions. The results showed that PK monitoring does not always predict the immunosuppressive effect actually achieved. Furthermore, indicating that TDM by assessing the PD effects will enhance the value of PK monitoring to achieve the goal of individualized immunosuppression to avoid toxicity and to enhance efficacy.

The Copenhagen National Lung Transplant Group: Survival after single lung, double lung and heart-lung transplantation performed in 1992-2003, a study comprising 362 patients

C. Burton, N. Milman, J. Carlsen, H. Arendrup, K. Eliasen, C. Andersen, M. Iversen
Division of Lung Transplantation, Department of Medicine B, Department of Thoracic Surgery, Department of Thoracic Anaesthesiology, The Heart Center, Rigshospitalet, University of Copenhagen, Denmark

Objective: To review the 13-year clinical experience of a single centre's lung transplantation program. **Methods:** From January 1992 to December 2003, 369 lung transplant procedures have been performed on 362 patients. Single lung transplant was performed in 234 cases, double lung transplant in 113 cases (comprising en-bloc double lung transplantation in 44 cases and bilateral sequential lung transplantation in 69 cases), heart-lung transplantation in 21 cases, and lobe of lung transplantation in 1 case. Recipient diagnoses included COPD (n=175), alpha-1-antitrypsin (alpha1AT) deficiency (n=86), cystic fibrosis (n=36), pulmonary fibrosis (n=20), Eisenmenger syndrome and secondary pulmonary hypertension (n=24), primary pulmonary hypertension (n=8), sarcoidosis (n=7), silicosis (n=4), bronchiectasis (n=1), and graft versus host disease (n=1).
Results: The 30 day mortatily for the entire series was 6% (n=23). The one-, 3-, 5- and 10-year actuarial survival rates for the entire series was 81%, 68%, 63%, and 35%, respectively. There were no statistically significant differences in survival between type of transplant, or gender.

		Perioperative mortality		Survival			
	n	30 days (%)	90 days (%)	1 y (%)	3 y (%)	5 y (%)	10 y (%)
Organ							
SLT	228	7.0	8.8	81.7	67.6	60.3	37.2
DLT	112	3.6	10.8	79.7	69.9	66.1	34.8
Bloc	68	2.9	10.3	82.4	72.1	69.1	36.8
Sequential	44	4.6	11.7	75.1	67.4	57.7	
SLT & DLT	340	5.9	9.5	81.1	68.4	62.9	32.3
HLT	21	9.5	14.3	85.7	64.8	64.8	49.5
Total	***362***	***6.1***	***9.8***	***81.4***	***68.3***	***63.3***	***35.1***
Diagnosis							
COPD	175	6.3	9.2	78.5	64.7	57.0	30.8
α1AT deficiency	86	1.2	4.7	90.5	76.2	69.3	29.4
Cystic fibrosis	36	5.6	8.4	82.2	74.5	74.5	
Pulmonary fibrosis	20	20.0	5.0	65.0	58.5	58.5	58.5
Eisenmenger/SPH	24	12.5	20.8	70.6	59.7	59.7	53.8
PPH	8	12.5	25.0	75.0	56.3	56.3	

Conclusions: This centre has one-, 3-, and 5-year survival rates comparable to other, high volume centres. Good medium time survival is obtained by single and double lung transplantation but long term survival is limited by complications to treatment.

The development and analysis of a screening tool to assess the psychosocial functioning of lung transplant assessment patients
McDermott Anne, Hallas Claire, Carby Martin

Background: Depression and anxiety are commonly exhibited (between 20-35%) in patients with respiratory diseases. These emotions have been found to be predictive of poor post transplant quality of life (QoL), mental health and increased symptoms and are also related to increased post transplant mortality. As a consequence, it has been recommended by UK Transplant that individuals who are being assessed for transplantation should receive a psychosocial assessment. Careful assessment of psychosocial function and QoL in this population should indicate areas where effective treatment and intervention can be implemented.
Rationale for change: Until 2003, all patients who were admitted to hospital for transplant assessment underwent a routine psychosocial assessment. However, following an audit of 126 psychosocial assessments, of these 61% of patients did not require any intervention from a psychologist or social worker. Due to increased demand upon psychosocial services it was felt necessary to implement changes to the assessment process to enable greater patient prioritisation.
Design: As a result a thirteen-item psychosocial screening tool was developed. The content of items were based on risk factors and symptoms relevant to psychiatric and neurological history, current mood and avoidant coping strategies. Other items assessed any potential unmet needs related to social care. Senior nursing staff received training in the implementation, completion and scoring of the tool. In addition, patients completed the Hospital Anxiety and Depression Scale (HAD) to compare with the sensitivity of the screening tool. The nursing staff referred patients if they identified any pre-determined risk factors stated on the tool and/or if patients scored 11+ on the HAD scale.
Outcome: To date, forty-five patients have been assessed using the screening tools and of these 17 (38%) were referred to the psychologist. Ten of the referred patients (22%) were seen and the remainder were discussed. Seven patients (16%) were referred on both screening tools, eight patients (18%) on the psychosocial screening tool alone and two patients (4%) were referred on their HAD score alone. Outside of the referral form there have not been any further referrals from either the Consultant Physician or senior nursing staff.
Discussion: From the analyses, the new psychosocial screening tool has face validity being brief, acceptable to staff and patients and has identified additional appropriate candidates for referral that were not identified by the HAD scale. The results indicate that with training, nursing staff can effectively implement psychosocial assessments for transplant candidates. The implementation of this screening tool has also highlighted additional benefits to patient care and the assessment process. For example, it has normalised the psychological assessment of patients, has allowed greater prioritisation of psychology and social services and has subsequently streamlined the patient journey. It has also shown to be valuable to nursing staff as it informs knowledge and practice, provides a new perspective on total patient care and is a good example of professionals working together in partnership. There is clear evidence to suggest that a relationship exists between poor psychosocial functioning and post-transplant mortality and therefore it is imperative that all patients are psychosocially assessed in order to maximise long-term outcomes post-transplant.

Patient self-report vs. Toxicology to confirm abstinence from tobacco products alcohol or illicit drugs

Imran Nizami, MD, Karen Perry RN, Craig Elkins, MD, John Chaffin, MD, Paul Kanaly, MD, David Nelson, MD, Wayne Paris, MSW, PhD

There is little debate about the rationale for denying lung transplantation (TX) to patients who continue to use tobacco products or meet criteria for a DSM-IV diagnosis of substance abuse/dependence (SA/D). Published statistics from our program indicate there is an acceptably low risk of SA/D relapse (<10%), with statistically similar survival rates in recipients who remain abstinent from alcohol or drugs, complete recommended treatment programs, and participate in needed psychiatric treatment as compared to recipients with no history of SA/D. The purposes of this study were to compare the reliability of patient self-report versus urine toxicology (TOX) results to confirm continued abstinence from tobacco products, alcohol, or illicit drugs and the effect of treatment on SA/D relapse. Each prospective candidate was informed of our programs expectation of: (i) abstinence from all tobacco products; (ii) abstinence from any form of alcohol or illicit drugs for those who met the criteria for SA/D; (iii) that each was subject to random TOX measurements; (iv) that failure to provide a specimen for TOX would be considered as a positive result; and (v) a positive TOX and/or refusal to participate in recommended treatment was grounds for dismissal from TX consideration and/or would result in a delay in their candidacy. Of the most recent 25 lung TX candidates who were currently using, or had previously used tobacco products, or met criteria for a DSM-IV diagnosis of SA/D at the time of initial assessment: 84% (21/25) had or were using tobacco products; 28% (7/25) had used both tobacco products and/or met SA/D criteria, and 16% (4/25) met S A/D criteria. All prospective candidates with negative TOXs (12/12) accurately reported their abstinence from use of tobacco products or SA/D relapse and all with positive TOXs (13/13) also reported abstinence while they continued to use tobacco products or had suffered a SA/D relapse. Forty-eight% (12/25) had a documented period of abstinence from tobacco products or SA/D and were not referred for SA/D treatment. Twenty-eight% (7/25) had continued to use tobacco products and were required to have clean urine toxicology's for 6 months prior to listing. Twenty-four% (6/25) had an insufficient period of abstinence from SA/D or lacked insight about their disorder and were referred for treatment. All attended treatment as referred, presented with negative TOXs and were later listed for lung transplantation.

We conclude that: (i) patient self-reports of abstinence from tobacco products and SA/D are reliable only for those who are abstinent, (ii) random TOXs are the best way to confirm compliance with tobacco and SA/D policy because of the lack of credibility of patient self-reports for those who relapse or continues to use tobacco or other SA/D, and (iii) patients who participate in SA/D treatment are less likely to relapse.

Lack of clinical and functional predictors of mortality in interstitial lung disease waiting for lung transplantation

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Introduction: End stage lung disease in severe interstitial pulmonary fibrosis (IPF) is a disabling pulmonary condition with a high mortality in patients (pts) waiting for lung transplantation (LTx).
Objectives: To identify clinical or functional parameters that could discriminate mortality predictors in a IPF population placed in the LTx waiting list.
Methods: We assessed 63 consecutive adult pts with IPF referred and listed in the waiting list (WL) for LTx during a ten years´ period.. Clinical data at first assessment were compared between the non survivors (NSG) and those who finally received a LTx (LTG.) Five pts. were excluded from the waiting list and from this analysis, due to clinical improvement and consequent exclusion from the WL.
Results: The LTG included 18 pts (28.6%).Thirty two pts (50.7%) died while waiting for a LTx ; and 8 (12.6%) are still in the WL. Demographic characteristics between the three groupswere similar. No clinical or functional (FVC, DLCO, PaCO2, 6MWT) differences were found between the non surviving pts. and those in the LTG (NSG vs LTG: FVC =42±15% vs 47±12 % ; DLCO =28±17% vs 28±18 ;PaCO2 =42±8 mmHg vs 43±5 mmHg ; 6-minutes walk test [6MWT]=140±93 m vs 125±128 m). Patients in the NSG had a higher PAPs and PAPm (47±21 and 28±13 mmHg vs 35±12 and 20±7 mmHg; p= .04).The mean time in the WL to LTx was 10.2 months and The mean follow up time in the NSG was 9.8 months. A univariate Cox regression analysis of clinical and functional variables, failed to determine mortality predictors .
Conclusions: Although the lack of statistical significance, trends showed that pulmonary hemodinamics were worse in pts. dying on the waiting list and might have contributed to their poorer outcome. No statistical significant clinical mortality predictors were found. The difficulty to identify mortality predictors might represent a more severly ill population combined with a delayed referral for assesment and listing.
Funded by: Favaloro Foundation

Assessment of pharmacodynamics of cyclosporin plus mycophenolate mofetil at c0h / c2h in human transplanted recipients

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Aims: Pharmacokinetic (PK) parameters like C2h have improved efficacy of immunosuppressive therapy after heart and lung transplantation (HTx, LTx). However, drug interactions, toxicities and individual differences to drug effects still remain challenging. Therefore, this study was designed to assess pharmacodynamic (PD) effects of the combination cyclolsporin (CsA) plus mycophenolate mofetil (MMF) on lymphocyte functions in peripheral blood of stable HTx recipients using our established FACS assays. Methods: Blood from 30 HTx patients was drawn before (C0h) and 2h after dosing (C2h). CsA and mycophenolic acid (MPA) concentrations were measured by EMIT. FACS assessed expression of cytokine production (e.g. INF-g, IL-2, IL-4, TNF-a), lymphocyte proliferation (PCNA) and of T cell activation antigens (e.g. CD25, CD71, CD95, CD154).
Results: Evening doses of CsA (25/50/75 or 100mg) and MMF (250/500 or 1000mg) produced C0h-levels: CsA: 162±12ng/ml and MPA: 1.7±0.2mg/L. Morning doses of CsA (50/75 or 100mg) and MMF (250/500/1000 or 1500mg) produced C2h-levels: CsA: 589±56ng/ml and MPA: 7.4±1.3mg/L. PD effects at C0h / C2h (%expression±SEM, all $p<0,05$) were:. IL-2:18±3 / 10±2; TNF-a:12±2 / 7±1; PCNA:8±1 / 5±1; CD25:26±4 / 13±2; CD95:23±4 / 11±2). Correlations (r_) at time point C2h between inhibition of lymphocyte functions (PD) with drug concentrations (PK) and with drug doses were: CsA-PK:0,71-0,91; MMF-PK:0,55-0,76; CsA-dose:0,73-0,87, MMF-dose:0,61-0,80.
Conclusion: For the first time, the immunosuppressive effects of the combination CsA plus MMF were quantified in peripheral blood of human HTx recipients at different time points. The results indicate that TDM by assessing the PD effects on lymphocyte functions may enhance the value of PK monitoring. Future clinical trials in HTx and LTx recipients should be performed by both effect-controlled and concentration-controlled immunosuppressive therapy to constitute the rational of individualized immunosuppressive drug therapy.

Multiple Lower Respiratory Tract Infections (LRTI) adversely affect mortality among lung transplant recipients who receive Total Lymphoid Irradiation (TLI) for chronic rejection

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Introduction: Up to 80% of long term survivors of lung transplantation develop chronic rejection (CR). CR is a significant cause of morbidity and mortality. Treatments such as Total Lymphoid Irradiation (TLI) need to demonstrate reductions in FEV1 decline without causing any significant harm or death.

Methods: We undertook a retrospective case review of all the patients who had received TLI at the Harefield Transplant Unit between September 1994 and March 2004. All the patients received a total of 8Gy in 8 fractions over a 10-day period. 4 Gy to the mediastinal lymphatics and 4 Gy to the sub-diaphragmatic lymph node chains. Complications including post TLI infection, post-transplant lymphoproliferative disease, CMV reactivation and death were recorded. The patients were split into 4 sub-group pairs. The sub-group pairs were age over 35 vs. under 35 at the time of TLI; BOS stage 1 and 2 vs. BOS stage 3; One or more preceding infections (any confirmed LRTI in the 12 months preceding TLI) vs. No infections and CF plus bronchiectasis patients vs. all other indications. Kaplan Meyer plots were used to identify differences in survival between the sub-groups and Odds Ratios with 95% confidence intervals were used to compare differences in mortality between these groups.

Results: 38 patients were identified for the study (22 male; 16 female; aged 35±12.7). 10/38 had their diagnosis of CR based on spirometry alone. 9/38 had biopsy proven obliterative bronchiolitis and 28/38 had spirometric deterioration plus at least one other imaging modality to support the diagnosis of CR. Kaplan Meyer Survival curves for each sub-group pair were compared using either the Peto-Prentice Test or the Log Rank Test. The p values are as follows: Multiple infections vs. No infections ($p<0.01$). <35's vs. > 35's: ($p<0.115$). BOS stage 1+2 vs. BOS stage 3 (0.74). CF and bronchiectasis patients vs. all other indications ($p<0.15$). Post TLI mortality was compared using Odds Ratios with 95% confidence intervals (95% CI). The OR for No infections vs Multiple LRTI= 0.24 (0.06,0.98). The OR for age>35's vs. age<35's= 1.96 (0.5,7.4). The OR for vs. BOS stage 3 compared to BOS stage 1+2= 1.5 (0.40,5.7). The OR for CF/bronchiectasis patients vs. all other indications= 0.254 (0.059,1.097).

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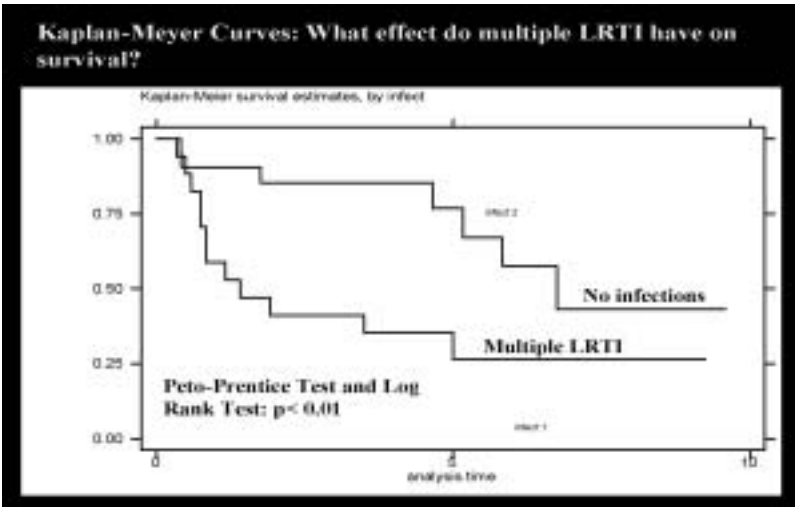

Mean survival post TLI was 24 months (4-81 months). A total of 21 patients died of which only 9 were within 12 months of their TLI. 29 patients survived at least 12 months beyond their TLI treatment. 2 patients had evidence of CMV disease within 12 months of TLI (CMV pneumonitis, CMV antigenaemia). Infection (19/38) and self-limiting bone-marrow dysfunction(4/38) was common. Isolated organisms included pyogenic bacteria, Pseudomonas aeruginosa and Aspergillus spp. One patient whose sputum had isolated Mycobacteria Kansasii before TLI therapy developed an upper lobe cavity. One patient had evidence of parvovirus infection in association with bone marrow suppression.

Conclusions: Whilst the original indication, age and BOS stage have no influence on post-TLI mortality, patients who experience multiple infections prior to TLI have a significantly greater risk of dying compared to those who are infection free. CMV reactivation affected the post TLI course for 2 patients, a complication which has not previously been reported. Self-limiting bone marrow suppression and infection were common attendants of TLI therapy. Mortality rates were comparable to those published in other case series.

Systemic fungal infections after lung transplantation

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Background: Immunosupression, use of effective broad spectrum antibacterial agents, multiple invasive procedures and permanent exposure of the transplanted lung to the external environment make LTx. patients (p.) particularly prone to invasive fungal infections which are reported to occurr in 10% to 35% of them.
Methods: Retrospective analysis of the clinical records. A total of 104 consecutive p. transplanted during a ten years´ period were analyzed with 47 (45.2%) Single Lung Transplantation (SLTx), 27 (25.96%) Double Lung Transplantation (DLTx) and 28 (28.84%) Heart and Lung Transplantations (H-LTx).
Results: A total of 11 documented fungal infections (DFI) were found (Four in DLTx, 2 in SLTx and 5 in H-LTx) . In two additional p., even though non-documented, a fungal infection was assumed (NDFI) and empirical antifungal therapy was started. Documented fungal infections occurred in 10.6% of the 104 p. Four (36%) of the DFI were due to Aspergillus spp (100 % respiratory infections), with 4/11 (36%) positive cultures for Candida spp (2 bloodborne infections, 2 respiratory infections). One p.(9%) developed Pneumocystis Carinii Pneumonia, Trichosporum Beigelli was found in one bronchopneumonia patient´s bronchoalveolar lavage (9%) and CSF cultures rendered Cryptococcus Neoformans in the remaining one (9%). Aspergillus infections appeared at 351 ± 295 days (42-590) post LTx with Candidiasis being diagnosed at 7.75 ± 6.25 days (5-14) post LTx. There were no significant differences in the type of transplant or the number and/or severity of acute cellular rejection episodes that would discriminate the p. later developing systemic mycoses.
Conclusions: In our study population, DFI occurred in 10.6% of the patients. Respiratory infections were the most frequent diagnosis (8/11; 72%). Aspergillus and Candida species were the most prevalent pathogens (36% and 36% respectively). Systemic Candidiasis infections were found earlier than Aspergillosis (7.75 ± 6.25 vs 351 ± 295 days post LTx).

		Seguimiento en años	EDAD	BMI	TPO_LISTA (días)
N	Valid	47	47	47	47
	Missing	0	0	0	0
Mean		1,851	51,13	24,135	386,87
Median		1,211	53,00	23,720	395,00
Std. Deviation		1,872	9,06	4,486	234,83
Minimum		,0	18	16,2	13
Maximum		6,4	66	38,7	1028

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	Masc	Total
	32	47
	68,1	100,0
	68,1	100,0
	100,0	

Statistics DLTransplantation

		FU_AÑOS	EDAD	TPO_LISTA	BMI
N	Valid	27	27	27	26
	Missing	0	0	0	1
Mean		1,797	28,22	765,07	20,596
Std. Deviation		2,195	12,47	538,35	4,727
Minimum		,0	10	2	14,9
Maximum		8,1	56	1926	32,4

Status en L de E

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Electivo	15	55,6	55,6	55,6
	Urgencia	6	22,2	22,2	77,8
	Emergencia	6	22,2	22,2	100,0
	Total	27	100,0	100,0	

SEXO

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Fem	10	37,0	37,0	37,0
	Masc	17	63,0	63,0	100,0
	Total	27	100,0	100,0	

Statistics HLTransplantation

		FU_AÑOS	EDAD	TLISTA	BMI
N	Valid	28	27	27	20
	Missing	0	1	1	8
Mean		2,745	33,52	643,19	21,0998885
Std. Deviation		3,602	10,98	583,62	3,2084386
Minimum		,0	14	1	15,85414
Maximum		13,7	54	2520	26,81359

SEXO

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Fem	16	57,1	57,1	57,1
	Masc	12	42,9	42,9	100,0
	Total	28	100,0	100,0	

Status en L de E

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Elect	19	67,9	67,9	67,9
	Urg	8	28,6	28,6	96,4
	Emerg	1	3,6	3,6	100,0
	Total	28	100,0	100,0	

The use of high-dose narcan to minimize the effect of neurogenic pulmonary edema and improve pulmonary function of the organ donor

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Pulmonary dysfunction after acute brain injury is a common, but poorly understood phenomenon. Causes of pulmonary dysfunction in the head-injured patient include pneumonia, aspiration, pulmonary embolus, and neurogenic pulmonary edema (NPE). Neurogenic pulmonary edema has been described in trauma patients as parenchymal edema, hemorrhage, and congestion without evidence of chest trauma in victims of isolated head injury. (1)

The etiology of NPE is unclear, however two theories predominate its cause. Blast theory states initial brain injury results in sympathetic discharge (catecholamine storm) leading to systemic hypertension, peripheral vasoconstriction, increased pulmonary artery pressure, and pulmonary microvascular constriction. The blast effect damages the pulmonary endothelium and a permeability defect persists even when pulmonary pressures return to normal. (2) The permeability theory states NPE is caused by a neurally induced increase in capillary permeability, suggesting that stimulation of sympathetic nerves in the lung could directly affect vascular permeability by altering the endothelial pores, thus allowing fluid to enter the interstitial space. (2)

Traditional medical management of NPE has been mainly supportive using positive end expiratory pressure (PEEP) and osmotic diuretics to maximize ventilation and increase vascular volume. Alpha-adrenergic blockers are an experimental treatment of NPE based on the theory that it counteracts the alpha-adrenergic effects of increased vascular resistance from the sypathetic discharge that follows CNS injury. The limiting factor is that the blockers must be given soon after CNS insult. Clinical trials demonstrating efficacy have not been conducted.

Peterson, et al showed that NPE could be prevented or reduced in sheep models with elevated intracranial pressure with the use of naloxone.(3) The following case presentation documents the use of naloxone in an organ donor; increasing a low PaO2, improving chest x-ray studies, clearing breath sounds, and eventual transplant of both lungs into 2 separate recipients.

Subsequent to this case, a standard protocol for potential lung donation was developed. This protocol includes the use of high dose naloxone to treat the effects of NPE. A 3-arm pilot study has been completed and data suggests improved pulmonary function resulting in increased rates of lung recovery and transplantation, approaching 30% of eligible donors.

Case Presentation

S.T. was a 43 year-old female, 81.5 kg, with no medical history who presented with to the emergency department with altered mental status, left-sided weakness, and hemianesthesia. CT scan of the head revealed 5 x 3 x 3 centimeter right basal ganglia hemorrhage with effaced right paramedian cephalic cistern and a 1cm right to left midline shift. Neurological status deteriorated to brain death within 12 hours of admission. The family gave consent for recovery of all life-saving organs for transplantation.

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Initial evaluation of lung function revealed right lower lobe atelectasis on settings of TV 900, Rate 10, PEEP +5. 100% FiO2 blood gas revealed: pH 7.648, pCO2 20.2, pO2 291, HCO3 22, saturation 100%. High frequency chest wall oscillation (HFCWO) was instituted every one hour, with turning side to side and suctioning every hour. Albuterol nebulizers were instituted every 4 hours.

Second chest x-ray 8 hours later revealed mild right lower lobe atelectasis with slight infiltrates. Bronchoscopy revealed no endobronchial lesions. On auscultation, rhonchi were noted bilaterally.

Four hours later, arterial blood gas on 100% oxygen revealed pH 7.631, pCO2 24.7, pO2 407, HCO3 26. Nebulizers, suctioning, and HFCWO were continued for the next 4 hours. Chest x-ray 4 hours later revealed worsening infiltrates. Arterial blood gas on 100% oxygen revealed pH 7.511, pCO2 23, pO2 419, HCO3 18. Auscultation continued to reveal rhonchi bilaterally.

The donor was given Narcan 10mg IV push, dosage chosen to combat effects of catecholamine storm from brain stem herniation. Arterial blood gas on 100% oxygen one hour later revealed pO2 569. Chest x-ray 2 hours later was clear. Ausculatation found clear lungs bilaterally. Intra-operative bronchoscopy also showed both lungs continued to remain clear. Both lungs were recovered and transplanted into 2 recipients. Both recipients continue to do well post-transplant.

A 3-arm internal pilot study by LifeQuest has been completed over the course of the past 18 months. The purpose of the study was to gather data and determine presence of a trend that may indicate further, more formalized study. One arm included the use of HFCWO and the use of Narcan 8mg. The second arm included the use of HFCWO without Narcan. The third arm included the use of Narcan only. Preliminary data suggests significant improvement in pulmonary function in the first and third study arm. In general, pO2 rises over 120 mmHg over the course of 12 hours in these arms versus a drop in pO2 of 90 mmHg over the same time frame in the second arm. Over the course of this pilot study, lung procurement at LifeQuest increased 50% in 2003 vs. 2002. By June 2004, lung procurement is already 66% of the 2003 total. During this time frame, the number of eligible donors remained essentially the same. LifeQuest has received University of Florida Institutional Review Board (IRB) Exemption for use of this drug in the brain dead population. LifeQuest will commence a multi-center OPO, randomized study to determine if the use of Narcan in the brain dead population improves pulmonary function and increases lung procurement and transplant. The study will begin in October 2004.

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The hemodinamically instable lung donor: a case for non-heart beating donation

Lang György

Objective: Initial experience with non-heart beating donation has demonstrated the feasibility of the method. The same principle could be applied for management of hemodynamically instable donors, who in the past were excluded from lung donation.

Methods: A 47 years old female donor was referred from a remote country hospital for multiple organ donations. Functional parameters of the lungs were excellent, with a PaO2 of 555 mmHg at FiO2=1,0 and a clear chest X-Ray. Prior to organ harvesting circulatory arrest occurred and the donor was resuscitated for 15 minutes, resulting in regain of a spontaneous heart activity. The local abdominal transplant team was informed and attempts to transfer the donor to the operating theatre were made. On the way to the OR the donor heart arrested again and resuscitation was restarted once more, however being ineffective this time. Since the lung harvesting team was not yet on the site the abdominal team was asked to heparinise the donor patient, to administrate steroids and to perform topical cooling of the lungs with cold saline solution. After 20 minutes of warm and 60 minutes of cold ischemia, the lung team arrived and harvesting of the lungs, after flushing with perfadex solution, was init!

iated. The lungs were procured and bilateral lobar transplantation was performed in a 28-year-old recipient suffering from CF.

Results: PaO2 sample, taken from the pulmonary vein prior to perfusion, was 445 mmHg, indicating excellent allograft function until cardiac arrest 80 minutes earlier. The cold ischemic time was 275 and 350 minutes for the right and left side, respectively. The allograft showed excellent oxygenation and the patient was weaned from the respirator within 7 days, and left the hospital after 22 days.

Conclusions: Evolving criteria for non-heart beating donation should be applied to hemodynamically instable or arresting donors with otherwise excellent lung quality.

A donor history of smoking affects early but not late outcome from lung transplantation

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Backgrounds: Liberalisation of tobacco exposure history as an exclusion to lung donation has recently occurred to increase donor organ availability. This study investigated the effect of donor smoking status and current and cumulative cigarette dose on early and late outcomes from lung transplantation.

Methods: From 1995 to 2002, 173 heart-lung and bilateral single lung transplant recipients were reviewed retrospectively. Seventy-seven of total 173 (45%) donors were ever-smokers and 64 of 77 were current smokers. These were divided into sub-groups by current number of cigarettes to investigate acute dose effects, and by pack-year to investigate cumulative dose effects. Risks of smoking were assessed by uni and multi-variate hazard regression model.

Results: Univariate analysis revealed that there were significant differences among both current and cumulative dose sub-groups in early post-operative variables, including PaO2/ FiO2 ratio, ventilation time, and ICU stay. Additionally these were dose dependent. There was no significant difference in 3-year survival between never and ever-smokers (73% versus 64%, p=0.27) and a rate of decline of survival was similar. There was a trend for the % of patients dying of BOS to be lower in the ever-smokers rather than never-smokers (6% versus 11%, respectively). Multivariate analysis revealed current and cumulative smoking as a risk factor for early but not late outcomes.

Conclusions: Donor smoking history had a significant effect on early outcomes from lung transplantation in a current and cumulative dose dependent fashion, however, no significant effect on late outcomes including BOS was seen.

Results of two years of lung harvesting in Hungary – an example for international cooperation in transplantation in Middle-Europe

Lang György

Background: There is no lung transplant program established in Hungary. Since 1995 29 Hungarian patients underwent lung transplantation in Vienna, Austria. After training for Hungarian surgeons in Vienna within a bilateral cooperation, lung harvesting was introduced in 2002 in Hungary.

Methods: Between 15/1/2002 and 31/12/2003 Hungarotransplant offered 164 potential lung donors to the Korányi National Institute for Pulmonology, Budapest, Hungary.

The offer was refused in 32 cases due to donor related anamnestic data, in 26 cases due to allograft pathology, respectively. In 14 cases the allograft was refused only after bronchoscopy and/or explantation. 43 donor lungs have been transplanted, 6 harvested lungs underwent only histopathology. In 57 cases the harvesting was turned down due to logistic reasons.

All operations were performed within multiorgan harvestings. Immediately before cross clamping the aorta 500μg epoprospenol (Flolan®) was administered intravenously for opening the pulmonary vascular bed. The lung was perfused anterogradly through the main pulmonary trunk whit a single flush of 6 liter 40C extracellular type low potassium dextran solution (Perfadex®), vented through the left auricle or the posterior midline of the left atrium. During the perfusion both thoraces were cooled topical by 0,9% saline ice slush. After back table separation the donor lungs was packed and transported whit topical cooling.

Results: From the 43 harvested lungs 41 bilateral and 3 single lung transplant procedures have been performed in Vienna. The average cold ischaemic time was 375 +/- 50 minutes (range: 230-560 min). 42 donor lungs showed excellent primary graft function. 1 allograft undervent down-sizing lobectomy, where the histology of the specimen showed multiple microembolisation, and signs of fibrosis and silicosis. In this case the cold ischaemic time was 560 min. The patient needed an ECMO bridge immediately postoperatively, and died after 4 weeks due to sepsis and rejection. After induction of lung harvesting in Hungary the average waiting time of Hungarian citizens decreased within one year from 14 +/- 8 weeks (range: 2-36 weeks) to 2,6 +/-1,3 weeks (range: 1-4 weeks). Unfortunately in 2002 3 Hungarian patients died on the waiting list, but their waiting time was 1, 1, and 7 days (!) respectively. In 2003 the waiting list mortality for Hungarian patients was 0%.

Conclusions: After introducing of lung harvesting both the waiting time and the waiting list mortality for Hungarian patients could be decreased. The potential lung donor pool of Hungary is in the range of 50/year, that means 5 / million people. Transparent legislative background and close, personal based inter-institutional cooperation is essential to establish both the training possibilities for a new transplant program and providing an additional organ supply for lung transplant centres accepting foreign citizens.

Analysis of complications of lung transplantation in Korea (Single institute experience)

Paik Hyo Chae

Purpose: Lung transplantation is a life-saving procedure for end stage lung disease, and the risk of infection and rejection is higher than other solid organ transplantations. The lung transplantation program in Korea started late in 1996, and total of nine lung transplantation has been performed in Korea. Complications of infection and rejection has been a key factor of long term survival, and the purpose of this study is to analyze factors limiting the long term survival.

Methods: Six lung transplantations and one heart-lung transplantation has been performed from July 1996 to December 2003. We retrospectively reviewed medical records and analyzed early and late complications.

Results: Total of 7 patients (5 male and 2 female) with mean age of 47 years old (range, 33-58) underwent lung or heart-lung transplantation. The most common indications of lung transplantation was emphysematous lung disease (57%: 4 of 7), and other indications were idiopathic pulmonary fibrosis (1 case), secondary pulmonary hypertension (Eisemmenger's syndrome) (2 cases), and bronchiectasis (1 case). Five patients underwent single lung transplantation, one patient underwent bilateral sequential single lung transplantation, and one patient underwent heart-lung transplantation. One surgical mortality occurred in a patient with bronchiectasis who succumbed to death on operation table due to bleeding. When excluding one case of surgical mortality, one year survival was 50 % (3 of 6), with mortality occurring on postoperative 76 days, 17 months, 15 months, 4 months, and 7 months. One patient who underwent bilateral lung transplantation is alive and have an active daily life. The major postoperative complications are: infection (aspergillosis, cytomegalovirus, and tuberculosis), post-transplantation lymphoproliferative disease, aspiration pneumonia, and gastric ulcer perforation. All patients had experienced one or more episodes of complications and only one survived.

Conclusion: We have experienced a small number of lung transplantation during the last eight years and a variety of complications have occurred. Early detection and proper management of these complications are utmost important for long term survival. However, further experience is necessary in order to lead them through the postoperative course, and based on our experience of morbidity and mortality, we hope to extend our recipient pool and transplantation activities in the future.

Inhalative donor pretreatment using the aerosolized prostacyclin analogue iloprost optimizes postischemic function of lung allografts

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Lung transplantation is an effective therapy in end-stage pulmonary disease, but its successful application is still limited by organ shortage and suboptimal preservation techniques. Therefore, optimal allograft protection is essential to reduce organ dysfunction especially in the early postoperative period. After intravenous prostanoids are routinely used to ameliorate reperfusion injury, latest evidence suggests similar efficacy of inhaled prostacyclin. Therefore, the impact of donor pretreatment using the stable prostacyclin-analogue Iloprost on postischemic allograft function was evaluated.

In group 1, five pig lungs, each, were retrogradely preserved with Perfadex solution (PER) and stored for 27 hours. In group 2, 100 μg of Iloprost were aerosolized over 30 minutes using a novel mobile ultrasonic nebulizer (Optineb®) prior to identical organ harvest (PER-ILO). Following left lung transplantation and contralateral lung exclusion, hemodynamics, pO2/FiO2 and dynamic compliance were monitored for 6 hours and compared to sham-operated controls. Pulmonary edema was determined by both standard stereological examination in terms of relative volume fractions and wet-to-dry weight ratio (W/D). Statistics comprised ANOVA analysis with repeated measures and Mann Whitney tests.

Dynamic compliance and PVR were significantly improved in Ilomedin-treated animals as compared to untreated organs ($p<0.05$), while oxygenation was not statistically different between groups. Wet-to-dry lung weight ratio revealed a significantly lower amount of total lung fluid in PER-ILO organs ($p=0.048$). Correspondingly, in stereological evaluation a trend toward reduced relative volume fractions of intraalveolar edema was noticed in PER-ILO Grafts.

Alveolar deposition of Iloprost in donor lungs prior to preservation ameliorates postischemic edema and significantly improves lung compliance and vascular resistance. This easily applicable innovative approach using a mobile ultrasonic nebulizer offers an important strategy for improvement of pulmonary preservation.

Impact of retrograde graft preservation in perfadex-based experimental lung transplantation

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Optimal preservation of postischemic organ function is a continuing challenge in clinical lung transplantation. Retrograde instillation of preservation solutions has theoretical advantages to achieve a homogeneous distribution in the lung due to perfusion of both the pulmonary and the bronchial circulation. So far, no systematic screening studies followed by in-vivo large animal reevaluation including stereological analysis of intrapulmonary edema exist concerning the influence of retrograde preservation on postischemic lung function after preservation with Perfadex solution.

For initial screening in an extracorporeal rat model 8 lungs, each, were preserved for 4 hours using antegrade or retrograde preservation with Perfadex (PERant / PERret). Respiratory and hemodynamic results after reperfusion were compared to low-potassium-Euro-Collins (LPEC). For systematic reevaluation, 5 pig lungs, each, were preserved correspondingly for 27 hours, and results were compared to sham-operated control lungs. In both models, edema formation was quantified stereologically. Statistics comprised different ANOVA models.

In both models, use of PERret resulted in significantly higher oxygenation capacity, lower inspiratory pressures and lower amount of intraalveolar edema as compared to PERant. Results of PERret were not different from sham controls in the in-vivo model; furthermore, a continous retrograde elimination of blood clots from pulmonary microcirculation was noticed.

Retrograde application of Perfadex results in significant functional and histological improvement as compared to antegrade perfusion. This innovative technique can be applied very easily in clinical practice and might be an ideal adjunct to further optimize the results after lung transplantation with LPD-based graft protection.

Clinical lung transplantation with NHBD

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Introduction: In November 2002 we started a lung transplantation program with NHBD. At the moment we have performed 7 lung transplantations.
Objetive: To present our experience and results in terms of morbidity, mortality and survival.
Method: All the donors were categorie II of the Maastrich classification, and multiorgan retrival were performed. Warm ischemic time was less than 120 minutes in all cases. Before retrival, lung preservation was based on topical cooling with Perfadex solution, and renal preservation was based on femoral ECMO and deep hypothermia. Functional lung evaluation was performed with 300ml of donor blood, and ABG’s was checked. Finally biphasic lung preservation with Perfadex was performed just before retrival.
Results: We have performed 6 bipulmonary and 1 unipulmonary transplantations. Extracorporeal circulation was needed in two bipulmonar transplants. Total ischemic time (from cardiac arrest to second lung reperfussion) ranged between 9 and 12 hours.
Early lung function was excellent in 6 patients, one recipient presented pulmonary aedema at the end of the procedure. The oxigenation index (PaO2/FiO2) at arrival to ICU was > 250 mmHg in all patients. Four patients were extubated in the first 72 hours. Five patients were discharged, and two patients died in hospital. Five recipients are currently alive and in an out patient regime.
Conclusion: Lung transplantation with NHBD is a reality. Our results in short and middle term have been excellent. Our initial experience is here reported and it’s hoped it will be of help for those involved in clinical lung transplantation programs worldwide.

Improved survival after lung transplantation for pulmonary hypertension: right ventricular ejection fraction and selection of surgical procedure

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Introduction: Average survival after lung transplantation (LT) for pulmonary hypertension (PH) is 67% in the United Network for Organ Sharing (UNOS) national U.S. database. Outcome may be improved by applying appropriate selection criteria. Patients with PH may eventually develop significant right ventricular (RV) failure. We have used RV ejection fraction (RVEF) and clinical evidence of RV failure to select the transplant procedure.

Methods: 18 patients with PH underwent LT between Dec 1997 and Feb 2003; 12 (67%) were female, mean age was 42.5 years (range 27 to 58 years). RVEF was measured by electron beam CT scanning every 6 months on the waiting list. Procedures were: single-LT (SLT) in 4 pts, double-LT (DLT) in 4 pts and heart-LT (HLT) in 10 pts. Inotropic support was necessary pre-transplant in 50% of patients in the HLT group. Mean RVEF was 53% for patients selected for SLT, 37.8% for DLT and 25.2% for HLT (SLT vs. HLT p=0.001; DLT vs. HLT p=0.04; SLT vs. DLT p=0.25).

Results: Survival at 1, 2 and 5 years, respectively was: 94%, 82% and 69% overall; 100%, 100% and 50% for SLT; 80%, 80% and 80% for DLT; and 100%, 80% and 80% for HLT.

Conclusions: We were able to obtain very good survival after LT for PH by limiting SLT to those patients with preserved RVEF and minimal symptoms of RV failure. Patients with advanced RV failure and PH had a good outcome with HLT. Quantitative assessment of RVEF was helpful in selection of the appropriate procedure.

Lung transplantation for end-stage lung disease (ESLD): patient selection, outcome and survival on the waiting list

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Background: A growing number of patients (pts.) with ESLD are referred for assessment to lung transplantation (LTx) programs. Survival rates on the waiting list (WL) depend on the balance of the possibilities of being transplanted (organs´ availability) and on the progression of the native lungs´ disease.

Objectives: Analyze the outcome and survival of pts. with ESLD evaluated for LTx.

Methods: Data from all the pts. with a diagnosis of ESLD referred to our program for pre-LTx assessment were analyzed retrospectively. Patients with a primary diagnosis of pulmonary vascular disease were excluded from this study.

Results: Two hundred fourty three pts. with a diagnosis of ESLD were evaluated (mean age 43±15 years [4-70] with a male/female ratio of 1.65). Baseline diagnosis were: bronchiectasis (BE) (n=34, 13.9%); cystic fibrosis (CF) (n=33, 13.5%); emphysema (Emph) (n=94, 38.5%); fibrosis (Fi) (n=74, 30.3%); lymphangioleimyomatosis (LL) (n=2, 0.8%), and others (n=7, 3%). From the 243 pts. evaluated, 164 (67.2%) were accepted and registered on the National LTx WL, while 39 (16%) were rejected on the basis of formal contraindications. Fifteen pts. (6.1%) died during the evaluation; 15 (6.1%) are still undergoing the assessment process, and the remaining 10 (4.1%) were lost to follow-up. Fifty five pts. (33.5%) originally listed in the WL received a LTx; 60 (36.5%) died, and 48 still remain on the WL. Table 1 shows the univariate analysis of pts on the WL.

Diagnosis	Enrolled	Transplanted	Deaths	On WL
All	164	55 (33.5%)	61 (37.1%)	48 (29.4%)
Emph	58	25 (43%)	14 (24%)	19 (33%)
Fi	54	13 (24%)	25 (46.3%)	16 (29.7%)
BE	24	7 (29%)	9 (37.5%)	8 (33.5%)
CF	25	9 (36%)	12 (48%)	4 (16%)
Other	3	1	1	1
P		.1	.06	.08

Mean follow-up time was 793±815 days (1-4574). The time on the WL (median, percentiles 25-75) for p. receiving LTx was 376 days (187-578). Overall survival on WL at 1, 2, and 5 years was 59±4%, 33.8±4% and 15±3.6% respectively. Two-year survival according to pathology was: Be 60.6±10%; Fi 31.2±6%; Emph 25.7±6%, and CF 21.2±9%.

Conclusion: In our study group, ESLD pts. were younger when compared to the data published by the ISHLT Registry. Only one third of those initially listed on the WL finally received a LTx. The number of pts. dying during the evaluation process and while on the WL outweighed the number of those who were finally transplanted. The mean survival rate of the p. on the WL was less than two years and varied according to the baseline diagnosis with CF showing the worst evolution. Due to our local conditions of organs´ availability, an earlier referral and placement of p with advanced lung disease in the WL might be reasonable in order to increase their possibilities of receiving a LTx.

Total lymphoid irradiation reduces the rate of FEV1 decline in lung transplant patients with chronic rejection but not all patients experience the same degree of benefit

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Introduction: Up to 80% of long term survivors of lung transplantation develop chronic rejection (CR). CR is a significant cause of morbidity and mortality. Data from small trials suggest that Total Lymphoid Irradiation (TLI) may be a useful treatment in slowing the rate of decline in FEV1 characteristic of CR. However it is not clear whether the original indication for the transplant, the patients' age, the stage of BOS at the time of treatment or the presence of infective episodes prior to TLI influences the degree of benefit derived from TLI treatment.

Methods: We undertook a retrospective case review of all the patients who had received TLI at our transplant unit over the last 10 years. All the patients received a total of 8Gy in 8 fractions over a 10-day period. 4 Gy to the mediastinal lymphatics and 4 Gy to the sub-diaphragmatic lymph node chains. The FEV1 results were analysed for the 3 months prior to TLI and then for a year following treatment. Subgroup analysis was performed with respect to: Age over 35 versus under 35 at the time of TLI; BOS stage 1 and 2 versus BOS stage 3; One or more infections in the preceding year versus no infections and bronchiectatic patients (including cystic fibrosis) vs. all other indications. Covariance Pattern Modelling was used for the inter-group comparisons as well as for the pre and post-TLI comparison.

Results: 38 patients were included in the study (22 male; 16 female; aged 35±12.7). 10/38 had their diagnosis of CR based on spirometry alone. 9/38 had biopsy proven obliterative bronchiolitis and 28/38 had spirometric deterioration plus CT appearances consistent with a diagnosis of CR. There was a mean delay from transplant to diagnosis of CR of 34±32 months. 21 of the 38 patients had died at the time of analysis. 9 of the deaths were within 12 months of receiving TLI. For the 3 months preceding TLI the average rate of fall in FEV1 in ml/month pre-TLI was 149 ml/month (range -6 to 573). The average rate of fall in FEV1 for the 12 months following TLI was 14 ml/month (range –9 to 155). For the group as a whole TLI lead to a significant reduction in FEV1 decline ($p<0.0001$). There was no significant difference in the FEV1 decay curves according to patient age ($p<0.75$); BOS stage 1 and 2 vs. BOS stage 3 ($p<0.079$) or the CF/bronchiectasis group vs. all other indications ($p<0.071$). Although TLI was effective at reducing the rate of decline in FEV1 for those patients with multiple infections ($p<0.0097$), the FEV1 decay curve for the infection group was significantly steeper when compared to the FEV1 decline in patients who were infection free ($p<0.0001$).

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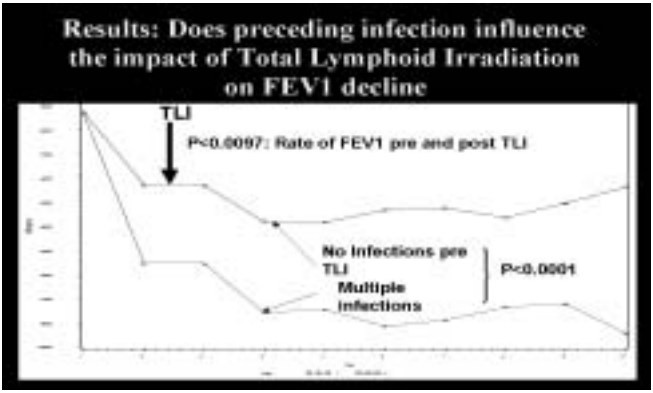
Figure 1. FEV1 decay curves for infection vs. no infection prior to TLI. Graph shows adjusted Mean FEV1's against time.



Conclusions: TLI is an effective treatment at halting the decline in FEV1 in lung transplant patients with CR. This benefit is experienced by patients irrespective of their age group, original indication or BOS stage. TLI is also effective for patients with multiple infections prior to TLI but the FEV1 decay curves display a significantly steeper rate of decline for the infection group. Mortality following TLI appears comparable to other case series.

Reduction of chronic vascular rejection by mycophenolate mofetil (MMF) after late treatment of acute pulmonary rejection in an allogenic rat lung transplant model

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Background: Chronic rejection (CR) represents the main long term limitation after solid organ transplantation and accounts for one third of late deaths after lung transplantation (LTX). In a low allogenic model of orthotopic left LTX in the rat (F344 > WKY) it could be shown that without immunosuppression (IS) acute pulmonary rejection (AR) with its maximum on postoperative day (pod) 14 is followed by severe CR, while using triple drug IS no AR and no CR results. In this experimental setting the influence of early and late treatment of AR by methylprednisolon boli (MP) and MMF was investigated.
Method: In group I (n = 20) 10 mg / kg MP was applied intraperitoneally (i.p.) on pod 9, 10 and 11, while in group II (n = 20) 10 mg / kg MP was given i.p. on pod 14, 15 and 16. In group III (n=20) the rats received in addition to the treatment of group II 30 mg / kg MMF i.p. daily beginning with pod 14. Cohorts of 5 animals each were sacrified on pod 20, 30, 60, and 100. In each group 5 syngneic transplants (WKY > WKY) were performed and these rats were sacrified on pod 100. The extend of AR and CR was graded according to the ISHLT working formulation using hematoxylin-eosin staining.
Results: In the allogenic lungs of group I AR was resolved after MP and no CR developed in the later course (ISHLT : pod 20: A 2,4 / B 0,8 / C 0 / D 0, pod 30: A 2,5 / B 1,0 / C 0 / D 0, pod 60: A 1,3 / B 0,9 / C 0,3 / D 1,0, pod 100: A 0 / B 0 / C 0,8 / D 0,4). In group II, application of MP resulted in a partial reversal of AR, however, followed by severe CR of the allografts (ISHLT : pod 20: A 2,5 / B 0,4 / C 0 / D 0, pod 30: A 2,6 / B 1,4 / C 0 / D 0, pod 60: A 0 / B 0 / C 3,2 / D 3,3, pod 100: A 0 / B 0 / C 3,6 / D 3,6). In group III, AR of the allograft was attenuated after application of MP and CR followed in the later course despite treatment with MMF, however, the extend of chronic vascular sclerosis was less than in group II (ISHLT : pod 20: A 2,6 / B 1,6 / C 0 / D 0, pod 30: A 1,2 / B 1,2 / C 0 / D 0, pod 60: A 0,8 / B 0,5 / C 3,3 / D 2,5, pod 100: A 0 / B 0 / C 3,6 / D 2,6). The syngrafts as well the native right lungs showed no histological evidence of AR or CR.
Conclusion: Preventive treatment with MP before the zenith of AR clearly diminishs the degree of AR after allogeneic rat LTX in the F344>WKY model and the graft recovers completely without any evidence of CR (group I), whereas the same treatment at the maximum of AR (group II) fails to control AR and severe CR develops. Additional application of MMF (group III) seems to be able to reduce the severity of acute vascular and bronchial rejection as well the extend of chronic vascular rejection, while no beneficial effects on the chronic bronchial rejection were seen.

Ex-vivo evaluation of non-acceptable donor lungs

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Despite all the improvements regarding donor management and organ preservation, still only about 20% of the potential candidates for lung donation are considered suitable donors. The number of lung transplantations performed worldwide is by far exceeded by the growing number of potential recipients on the waiting list. We have developed a method for ex-vivo evaluation with the potential for reconditioning of marginal and non-acceptable donor lungs. This is the result from evaluation of six lung donors who were deemed non-acceptable throughout the Scandiatransplant and Eurotransplant. The lungs are perfused ex-vivo with the lung evaluation-preservation solution, Steen Solution® (Vitrolife), mixed with red cells to a hematocrit of 15%. This extracellular solution is composed to have an optimal colloid osmotic pressure so that physiological pressure and flow can be maintained without development of pulmonary edema. The high colloid osmotic pressure has the potential of "drying up" wet lungs. Antibiotic is added to the perfusate to treat any infection without the risk of secondary organ dysfunction. An oxygenator connected to the extra-corporal circuit maintains a normal mixed venous blood gas of the perfusate. The lungs are ventilated and evaluated through analyses of pulmonary vascular resistance (PVR), oxygenation capacity and PaCO2 - end-tidal CO2 difference. The PaO2/FIO2 increased from 27 (17-34) kPa at the donor hospital to 57 (39-66) kPa during the ex-vivo evaluation. The PVR varied from 3,2 to 5,7 Wood units and the PaCO2 – ETCO2 difference was in the range of 1 to 2,5 kPa. The PaO2 improves significantly in this model. The importance of PVR and PaCO2-ETCO2 difference needs to be further evaluated.

High prevalence of pulmonary arterial thrombi in donor lungs rejected for transplantation: implications for lung dysfunction in donor lungs and lung recipients

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Background: The use of marginal donors has the potential to greatly increase the pool of organs available for lung transplantation. We previously reported that many donor lungs that were rejected for transplantation using standard criteria might actually have been suitable for transplantation (Lancet 2002;360:619). In order to develop better criteria for identifying potential lung donors, it is important to have a better understanding of the pathophysiologic mechanisms that contribute to donor lung dysfunction. Since organ donors are at high risk for venous thromboembolism, we hypothesized that pulmonary arterial thrombosis may impair the function of potential donor lungs. The primary objective was to prospectively quantify the incidence of pulmonary arterial thrombosis in donor lungs that were rejected for transplantation. The secondary objective was to better define the spectrum of histological abnormalities in the same lungs.

Methods: Lungs were procured from organ donors whose organs were used for transplantation, but whose lungs were deemed not suitable for transplantation by the California Transplant Donor Network. Lungs were resected at the time of organ procurement and transported to our facility at 4C. Lungs had not been flushed with a pulmonary preservation solution. A complete gross pathologic and histologic analysis of whole lung specimens was done prospectively on lungs from 17 donors.

Results: Overall, 35% of the donors had gross or microscopic evidence of pulmonary arterial thrombosis, pulmonary infarction or both. Clinical characteristics including oxygenation were not significantly different between donors who had thrombi or infarction and donors who did not. There was a trend toward more smokers in the group with thrombus or infarction (83%) compared to the group without thrombus or infarction (36%, $p = 0.13$). Other pathological findings included bronchopneumonia (focal/early in 4/17, moderate/severe in 8/17), respiratory bronchiolitis (7/17) and centriacinar emphysema (7/17). Pathological findings for each set of donor lungs were rated as normal or mild, moderately or severely abnormal. Overall, 47% were normal or had only mild abnormalities, 41% moderate abnormalities and 12% severe abnormalities.

Conclusions: Pulmonary arterial thrombosis and pulmonary infarction are very common in organ donors whose lungs are rejected for transplantation. The magnitude of this problem has not been previously appreciated. Pulmonary artery thrombosis in the organ donor could contribute to lung dysfunction both in (1) lung donors and (2) lung recipients. Further studies are needed to define the incidence of pulmonary arterial thrombosis in organ donors whose lungs are evaluated for potential transplantation and to better assess the potential adverse clinical consequences of donor pulmonary arterial thrombosis in lung transplant recipients. Therapies aimed at prevention of pulmonary arterial thrombosis in organ donors might lead to improved donor utilization rates and perhaps better function of transplanted lungs.

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Clinical applications of ET-Kyoto solution for lung transplantation in Kyoto University hospital

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Although Euro-Collins solution and University of Wisconsin solution have been frequently used in the clinical lung transplantation, the preservation limit is reported to be 10 hours. We have developed a new preservation solution ET-Kyoto solution, containing non-reducing disaccharide of trehalose, extracellular ion composition, to acquire effective use of the marginal donor organs and better management of organ function after transplantation. Since 2001 we have applied the solution to the clinical lung transplantation.

Material and methods: ET-Kyoto solution consists of Na+ 100 mmol/L, K+ 44 mmol/L, gluconate 100 mmol/L, phosphate 25 mmol/L, trehalose 41 g/L, and hydroxyethyl starch 30 g/L. In clinical practice, ET-Kyoto solution is used with dibutyryl cAMP (2 mmol/L) and nitroglycerin (0.1 g/L) as endothelial protective agents. Donor lungs were flushed with 2 liters of cooled ET-Kyoto solution antegradely and retrogradely. During flushing, the lungs were ventilated. Harve sted donor lungs were soaked in ice-cooled ET-Kyoto solution until transplants.

Results: We have applied ET-Kyoto solution to three clinical transplants. The first case (a 48 year-old woman with diffuse panbronchiolitis) underwent living-related donor lobar lung transplant in April 2002. The donors were her husband and son. Post operative PaO2 (FiO2=1.0) was maintained higher than 450 Torr, and there was no apparent reperfusion-injury. The second case was a 24 year-old woman with pulmonary and pelvic lymphangiomyomatosis. She developed spontaneous pneumothorax resulting in sudden respiratory arrest, and was resuscitated in June 2003. Due to severe respiratory failure from uncontrollable air leakage, and consequent septic shock, she underwent an emergent living-related donor lobar lung transplant. The donors were her sister and mother. The volume of the donor lungs was 55% of her predicted total lung volume. Although the preoperative condition was poor, reperfusion-injury was so mild that the post operative PaO2 (FiO2=1.0) was kept more than 380 Torr. Lung edema appeared at 12 hours after reperfusion, but disappeared within 24 hours without deterioration. The third case was a 38 year-old man with juvenile emphysema, who received bilateral lung transplant from a brain-death donor in February 2004. The donor was a 57 year-old man who was a heavy smoker and died of subarachnoidal hemorrhage. PaO2 (FiO2=1.0) after transplantation was kept over 400 Torr postoperatively, with maximum of 526 Torr. The Ischemic time was respectively 242min and 117min in the first case, 253min and 92min in the second case, and 544min and 613min in the third case. Histological examination of partially resected lung tissues of the case 3 revealed no apparent reperfusion injury after 10 hour-ischemia and 6-hour reperfusion.

Conclusion: We applied the ET-Kyoto solution for three clinical lung transplants including marginal cases with favorable results. ET-Kyoto solution can be a new option of reliable organ preservation.

Presensitization accelerates chronic allograft rejection in heterotopic rat tracheal allograft model

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Aims: In the field of transplantation, recipient sensitization to MHC antigens is among the most critical problems, and it has been known that sensitized recipient $B#s (B experience an increased rate of graft rejection, compared to unsensitized individuals, which is often irreversible and difficult to control by current used immunosuppressive agents. For better understanding of this problem, it is crucial to clarify the role of presensitization in the chronic graft rejection after transplantation. The purpose of this study is to determine the significant correlation between chronic allograft rejection and the humoral alloreactivity in sensitized recipients.
Methods: MHC fully incompatible combination was used in this study. Lewis (LEW) rats sensitized by transplantation with Brown Norway (BN) skin grafts twice per week received tracheal segments from Brown Norway rats heterotopically into the pouch in the back 7 days after the second skin transplant. Recipients were administered with the subcutaneous injection of CsA (25 mg.kg-1.day-1) for 3 days from the day of operation. Four allogenic groups were investigated $B!J (Bn=5 $B!K (B. Group1: nonsensitized recipients without CsA administration, Group 2: sensitized recipients without CsA administration, Group 3: nonsensitized recipients with CsA administration, Group 4: sensitized recipients with CsA administration. All recipients were sacrificed 21 days after implantation, and tracheal segments were extracted and histologically evaluated as follows: (1)Airway lining epithelial loss, (2)lymphocyte/plasma cell infiltration, and (3)luminal obliteration due to granulation tissue formation and/or fibrosis. $B!! (BIn order to analyze alloantibody responses, sera samples were tested with a flow cytometric cross-match (FCXM) technique.
Results: Histological findings revealed that the chronic rejection score in the sensitized recipients was significantly higher than that in nonsensitized recipients, especially when comparison between the recipients with CsA treatment was made (9.0+-1.2 vs. 3.0+-0.54, P<0.05). In other words, CsA therapy reduced rejection score in the nonsensitized recipients. In contrast, CsA did not work enough for sensitized recipients. Anti-donor IgG Abs were induced after presensitization by donor skin grafting. Heterotopic tracheal implantation also induced the IgG Abs production. This antibody elevation was significantly inhibited by CsA therapy in the nonsensitized recipient. Conversely, Ab levels were significantly higher in the sensitized recipient than in nonsensitized recipient, irregardless of CsA administration.
Conclusions: Our data showed that presensitization accelerates chronic allograft rejection with the marked elevation of donor specific IgG antibody. These results suggest that presensitization may be significant risk for the recipient and that IgG alloantibody might be correlated with chronic allograft rejection after lung transplantation.

Modifications of mitochondrial respiration from lung recipients' skeletal muscle: effects of rehabilitation

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Cellular and biochemical mechanisms responsible for limitation in VO2max in lung recipients (LR) remain obscure as well as the benefits gained from rehabilitation. The aim of this study is to evaluate the effects of rehabilitation by using a novel method of studies of mitochondrial respiration in small biopsies samples of skeletal muscle. Mitochondrial respiration is evaluated from Vastus lateralis permeabilized fibers after forceps biopsies from controls (n=17, 33±3 years old) and LR (n=14, 44±4 years old) before (D_0) and after (D_{90}) home rehabilitation. In parallel, immunohistochemistry is performed and morphometric data are collected. All results are given in means ± SEM. In LR, $VO2_{max}$ is 58±4 % of predicted (at Do) compared to the control group where $VO2_{max}$ is 104±4% of predicted. A different regulation of mitochondrial function in LR is shown by: 1. a significant decrease in the apparent Km for ADP: 91±9 µM vs 133±7 µM (in controls) ; 2. a weaker coupling of the mitochondrial creatine kinase (miCK) with the adenine nucleotide translocase (ANT) responsible for the stimulating effect of creatine (Cr) on respiration; 3. a non significant decrease of the mitochondrial maximal rate of respiration, Vmax. These results can be explained by a decrease in the number of type I fibers (type I: 17±12 % in LR vs 43±19 % in controls). After rehabilitation of the control group, bioenergetics parameters modified are an increase in the apparent Km for ADP (273±26 µM (D_{90}) vs 133±7 µM (D_0)) and a better control of mitochondrial respiration by Cr with no change of the fiber-type (type I: 36±13 % (D_{90}) vs 43±19 % (D_0)). The results obtained from LR (n=3) are similar to the control group ones after rehabilitation. Indeed, a striking 2–fold increase of the apparent Km for ADP and a stronger miCK/ANT coupling are observed. This demonstrates a higher degree of organization within intracellular energetic units (ICEUs) leading to better efficient energy transfers after rehabilitation and shows the diagnostic efficiency of the method used.

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Single lung transplantation in end-stage lung disease (ESLD) with secondary pulmonary hypertension (SPH): a survival assessment

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Introduction: Single lung transplantation (SLT) has been successfully performed in primary pulmonary hypertension with benefits on long-term survival. It has been proposed that the hemodynamic unloading of the native lung favors regression of the pathologic lesions resuming some its original function and then improving the outcome. The influence of previous SPH on the outcome of pts. with ESLD due to parenchymal lung disease receiving a SLT has not yet been established.
Objectives: to evaluate the influence of pre-SLT SPH on SLT recipients late survival
Methods: We analyze all SLT performed at a single center (Favaloro Foundation) during a ten years_period. Recipients diagnosis were COPD (n=24, 51 %), alfa-1 antitrypsin deficiency (n=5, 10.6%) and pulmonary fibrosis(n=18, 38.4 %). Patients (n=47) were divided into two groups depending on the presence (Group 1) or abscense (Group 2) of SPH (defined as a mean pulmonary artery pressure or mPAP ≥25 mmHg) at the moment of listing as LTx. Qualitative and quantitative variables were compared with the chi-square test or the Wilcoxon-Mann Whitney test, as appropriate. Survival was estimated by the Kaplan-Meier method, comparing the differences by the log-rank test.
Results: Group 1 (G1) included 12 patients (25.5%) , with G2 accounting for 35 pts. (74.5%). There were no significant diagnostics´, demographic or anthropometrical differences between the groups. Systolic and mean pulmonary artery pressure [PAPs, PAPm], and pulmonary vascular resistances [PVR] in G1 vs. G2 were respectively: 45±8 mmHg vs. 30±7 mmHg, 30±4 mmHg vs. 17±4 mmHg and 4.7±1.6 Wu vs. 2.2±1.1 Wu. Differences in functional assessment parameters were not significant between the groups (53±17% vs. 47±16%, 34±21% vs. 28±16%, 29±20% vs. 38±28% and 145±87 m vs 212±110 m for FVC, VEF1, DLCO and 6 minutes walk test respectively), but pts. in G1 had a lower PaO2 (58±16 mmHg vs. 70±17 mmHg, p= .05). Group 1 vs Group 2 in-hospital mortality rates were 2/12 (16%) vs. 6/33 (18.2%) p=0.6.
Late survival at 1, 3 and 5 years were respectively: 55.5%, 27.7% and 27.7% vs. 66.2%, 56% and 22.4% (p= 0.6).
Conclusions: There is a trend for patients with end-stage lung disease associated to SPH, to have a worse late survival after SLT than patients without SPH.

Pulmonary artery hypertension as a prognostic factor in patients with advanced lung disease on the lung transplant waiting list

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Objectives: To evaluate the incidence of pulmonary artery hypertension (PAH) in a population of patients with advanced lung disease (ALD) and its impact on the mortality of patients on waiting list for lung transplant (LTx).
Methods: A retrospective analysis of 243 patients diagnosed with ALD and referred to the Favaloro Foundation for their evaluation as lung transplant candidates, was performed. Patients with diagnosis of pulmonary vascular disease were excluded from the study. A hundred and sixty-four patients (67.2%) were accepted for LTx and placed on the waiting list. In twenty-five patients (15.2%) (most of them with a diagnosis of cystic fibrosis) right heart catheterization to monitor pulmonary pressures was not performed. The remaining population was divided into two groups depending on the presence of PAH (defined as a mean pulmonary artery pressure or mPAP ≥25 mmHg). Qualitative and quantitative variables were compared with the chi-square test or the Wilcoxon-Mann Whitney test, as appropriate. Survival was estimated by the Kaplan-Meier method, comparing the differences by the log-rank test. Death was predicted by the Cox regression model.
Results: PAH group (G1) included 54 patients (38.8%), and no-PAH group (G2) included 85 patients (61.2%). There were no significant demographic nor antropometric differences between the groups.Group 1 showed higher hematocrit levels (46±6% vs 41±4%; P<.001), a lower PaO2 (57.2±15 mmHg vs. 66.4±17 mmHg; P=.002); a lower SaO2 (87.4±8% vs. 91.8±4; P<.001) and a lower right ventricular ejection fraction (34.1±11% vs. 40.1±8 %; P=.002). Mortality on the waiting list at two years was 51.6% for G1 and 37.8% for G2 (P=.01). In these study population, the presence of PAH at the initial assessment predicted mortality on the waiting list (OR: 1.9; 95% CI: 1.1-3.3; P=.01).
Conclusions: Patients with PAH when placed on the waiting list for LTx showed a greater mortality compared to those without pulmonary arterial hypertension. Pulmonary arterial pressures monitoring might contribute to estimate the prognosis for p. with ALD placed in the LTx. waiting list

Lung mechanical changes in a lung transplant patient with impulse oscillometry system (IOS)

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Introduction: Pulmonary function of postoperative early day in a lung transplant patient is commonly evaluated by arterial blood gas analysis and forced expiratory volume in 1 second (FEV1). However, especially in the postoperative stage, pulmonary function is hard to be precisely evaluated, because a breathing effort is not sufficient by both the operation-related severe pain and the disease related muscle weakness. To overcome above-mentioned disadvantage, the MasterScreen IOS (Erich JAEGER GmbH) is used to measure respiratory resistance (R) relating to FEV1 in resting condition (i.e. normal tidal breathing situation). IOS outputs impulse-shaped sound signals, including a lot of frequency components (> 0 to 100 Hz), which are produced by an external generator. Time course of pressure and flow by Fast Fourier Transformation and quotient calculation transferred to the spectral course of R and reactance (X) related with pulmonary elasticity. IOS has an advantage in the point that respiratory resistance is divided into central and peripheral components by frequency analysis.

Methods: A 38 year-old man was diagnosed with juvenile pulmonary emphysema. He had a history of improvement of FEV1 after pulmonary aspergillus infection. Bilateral lung transplantation was performed in 2004.2.5. The increase of a feeling of dyspnea and CRP level and the decrease of PaO2, regarded as acute rejection, were recognized on the 15th postoperative day. Methylprednisolone 1g/day was administered via intravenous for three consecutive days. The respiratory impedance was measured with IOS several times every day after operation. The change of lung mechanics was evaluated by analyzing R5 (R at 5Hz), R20 (R at 20 Hz), X5 (X at 5Hz), Fres (Resonant frequency) and AX (low frequency reactance area, 5Hz to Fres).

Results: We can detect the dramatic decreasing changes in the lung impedance data including R and X, before and after the steroid administration.

Discussion: The increase of R5 was reported to be in proportional to decrease of FEV1. And X5 is related with pulmonary elasticity. We can detect the change in R5 and X5 by the portable IOS under the early post operative days and that the change regarded as acute rejection. Thus IOS may become a useful tool to detect the airway obstruction and the early stage of acute rejection.

Cytomegalovirus(CMV) Retinitis and Gastric ulcer perforation after Heart-lung Transplantation: a case report

Paik Hyo Chae

Introduction: Infection caused by cytomegalovirus (CMV) is a major cause of morbidity and mortality in recipients of organ allograft transplantation. Many forms of complications occur after the lung transplantation especially within six months after the operation. The incidence of CMV infection is quite high although near blindness by CMV retinitis is seldom seen. We have experienced a patient diagnosed as Eisenmenger's syndrome whom underwent heart-lung transplantations and succumbed to death due to a variety of complications such as CMV retinitis, post transplantation lymphoproliferative disease, and gastric ulcer perforation.

Case: A 41 year-old male was diagnosed as Eisenmenger's syndrome. Cardiac catheterization revealed pressures as follows; main pulmonary artery 130/80 mmHg, right ventricle 130/20 mmHg, right atrium mean 20 mmHg, and aorta 130/80 mmHg. Cardiac angiography showed huge right pulmonary artery with its diameter greater than 7 cm. The patient underwent heart-lung transplantation. The donor was a 24 year old male with intracranial hemorrhage and had negative viral markers except CMV immunoglobulin G (IgG). The recipient had negative viral markers except CMV IgG and Epstein-Barr Virus Early Antigen (EBEA) IgG. Under the cardiopulmonary bypass, heart-lung transplantation was done uneventfully. Patient's condition was stable with good oral feeding until the morning of planned discharge date (postoperative 20 days) when the patient complained of severe epigastric pain and abdominal wall guarding. An abdominal x-ray showed free air which necessitated an emergency laparotomy and primary repair of perforated stomach. The pathology specimen showed inclusion bodies near the gastric ulcer suggesting CMV enteritis. He was discharged on postoperative day 10 after the abdominal operation. A routine cardiac and lung biopsy showed grade 3 cardiac rejection. Steroid pulse therapy was given and cyclosporine was changed to tacrolimus (FK506) to maintain its level within the therapeutic range. Five months after the transplantation, he was admitted due to dyspnea on exertion and poor general condition. He also complained of blurred vision which rapidly deteriorated to near total blindness on both eyes. The chest x-ray showed multiple mass lesion in bilateral lung which was diagnosed as post-transplantation lymphoproliferative disease (PTLD) by needle aspiration biopsy. Ophthalmic examination revealed CMV retinitis. Foscarnet and gancyclovir was given intravenously and by intravitreus injection on both eye. PTLD was treated by decreasing the dosage of tacrolimus. Vision improved quite significantly three days after intravitreous injection of foscarnet although general condition and chest x-ray aggravated rapidly thereafter. On the thirteenth day following foscarnet therapy and on postoperative eight months, the patient expired due to multi-organ failure.

Conclusion: We have experienced a patient who succumbed to death by combination of PTLD, CMV retinitis, and gastric ulcer perforation. CMV infection was probably the initiating complication which ended in mortality and we strongly suggest long term prophylatic use of gancyclovir in order to prevent this disease.

Donor pretreatment using the aerosolized prostacyclin analogue iloprost optimizes postischemic function of non heart beating donor lungs

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Ischemia-reperfusion-injury accounts for one third of early deaths after lung transplantation. To expand the limited donor pool, lung retrieval from non-heart-beating donors (NHBD) has been introduced recently. However, due to potentially deleterious effects of warm ischemia on microvascular integrity, use of NHBD lungs is limited by short tolerable time periods prior to preservation. After intravenous prostanoids are routinely used to ameliorate reperfusion injury, latest evidence suggests similar efficacy of inhaled prostacyclin. Therefore, the impact of donor pretreatment using the prostacyclin-analogue Iloprost on postischemic NHBD lung function and preservation quality was evaluated.

Asystolic pigs (n=5/group) were ventilated for 180 minutes of warm ischemia (group 1). In group 2, 100 μg Iloprost were aerosolized during the final 30 minutes of ventilation using a novel mobile ultrasonic nebulizer (Optineb®). Lungs were then retrogradely preserved with Perfadex and stored for 3 hours. Following left lung transplantation and contralateral lung exclusion, hemodynamics, pO2/FiO2 and dynamic compliance were monitored for 6 hours and compared to sham-operated controls. Pulmonary edema was determined by wet-to-dry weight ratio (W/D), and extravascular-lung-water-index (EVLWI) was measured. Statistics comprised ANOVA analysis with repeated measurements.

Flush preservation pressures, dynamic compliance, inspiratory pressures and W/D were significantly lower in Ilomedin-treated lungs, while oxygenation and pulmonary hemodynamics were comparable between groups. EVLWI was within normal ranges in Iloprost-grafts.

Alveolar deposition of Iloprost in NHBD lungs prior to preservation ameliorates postischemic edema and significantly improves lung compliance. This easily applicable innovative approach using a mobile ultrasonic nebulizer offers an important strategy for improvement of preservation quality.

Effective application of ET-Kyoto Solution for Clinical Lung Transplantation

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The shortage of lung donors and ischemia-reperfusion injury following transplantation have been grave problems in lung transplantation (LTx). One of the most important strategies to solve these problems is the development of effective and highly reliable methods for lung preservation. Therefore, we have developed a new organ preservation solution, namely, the extracellular-type trehalose containing Kyoto (ET-Kyoto) solution. Trehalose is a cytoprotective non-reducing disaccharide. We have accumulated good results of ET-Kyoto solution in the experimental LTx, but its clinical application had to be suspended until the enforcement of the organ transplantation law in 1997 and the prevalence of LTx in Japan. We herein report the first experience of clinical application of ET-Kyoto solution for cadaveric LTx.

The recipient was a 38-year-old male diagnosed as pulmonary emphysema at 23 years of age. The donor, a 51-year-old male current smoker with smoking history of 62 pack-years, was dead of intracranial bleeding and had been mechanically ventilated for two and a half days. The ventilated donor's PaO_2 was 340 Torr (FiO_2 =1.0). The donor lungs were considered to be marginal to the currently accepted donor criteria. After diagnosis of brain death, the donor lungs were harvested. Heparin was administered intravenously and 1mg of prostaglandin E_1 was injected through the pulmonary artery. The pulmonary vasculature was flushed with 3L of ET-Kyoto solution supplemented with nitroglycerin and dibutyryl cAMP. The recipient underwent bilateral sequential LTx on cardiopulmonary bypass. Before transplantation, each lung was flushed with 2L of ET-Kyoto solution retrogradely. The ischemic time was 544/613 minutes for the left/right lung, respectively. PaO_2 (FiO_2 =1.0) was 385 Torr immediately after reperfusion. The donor lung was so large that bilateral partial resections were performed at 413 minutes (right) and 348 minutes (left) after reperfusion, respectively. Due to severe right pleural adhesion, it took long to control the blood oozing from the right chest wall. Postoperatively, PaO_2 (FiO_2=1.0) was 425, 456, 438, 433, 526, and 497 Torr at 12, 24, 36, 48, 60 and 72 hours after reperfusion, respectively. The arterial/alveolar oxygen tension ratio was also maintained so high as the mean value of 0.67 ± 0.07 during the first three days after reperfusion.

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Except for acute rejection on the 14th postoperative day, clinical course was almost uneventful. The histopathologic examination on the resected transplanted lungs showed almost normal lung structure. That is, neither alveolar thickening nor edema was seen in both transplanted lungs resected at six hours after reperfusion.

In conclusion, ET-Kyoto solution could be safely applied in clinical cadaveric LTx with marginal donor lungs and relatively long ischemic time. Functional and histopathological efficiency of ET-Kyoto solution was confirmed. Longer preservation with preserved quality using ET-Kyoto solution would increase the donor pool and enable semielective LTx.

Impact of an innovative preservation strategy on the use of non-heart-beating donors in experimental pig lung transplantation

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Lung transplantation is limited by severe scarcity of suitable donor organs. Currently, aside from living-related lobar donors, grafts are retrieved from brain-dead heart beating donors. To potentially expand the donor pool, lung retrieval from non-heart-beating donors (NHBD) using antegrade preservation has been reported recently. However, no NHBD studies exist using the novel approach of retrograde preservation with Perfadex solution through the left atrium.

Asystolic heparinized pigs (n=5/group) were continuously ventilated for 90, 180 or 300 minutes of warm ischemia. Lungs were then retrogradely preserved with Perfadex and stored at 4°C in inflation. After 3 hours of cold ischemia, left lung transplantation was performed. Hemodynamics, pO2/FiO2 and dynamic compliance were monitored for 5 hours. Intrapulmonary lung water was determined by wet-to-dry lung weight ratio (W/D ratio). All results were compared to sham-operated controls and to lungs obtained from standard heart-beating donors after retrograde preservation with Perfadex and 27 hours of cold ischemia. Statistics comprised ANOVA analysis with repeated measurements.

No mortality was observed. During flush preservation of NHBD lungs, continous elimination of blood clots via the pulmonary artery was observed. Oxygenation, hemodynamics, compliance and W/D ratio were comparable between groups.

Use of NHBD lungs is feasible and results in similar postischemic outcome when compared to sham controls and standard preservation procedures even after 5 hours of warm ischemia. Especially the NHBD with high risk constellations for intravascular coagulation might benefit from retrograde preservation by elimination of thrombi from the pulmonary circulation. This innovative technique might also be considered in situations where brain-dead organ donors become hemodynamically unstable prior to onset of organ harvest. Further trials with longer warm and cold ischemic periods are initiated to further elucidate this promising approach of donor pool expansion.

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Notes

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