7th International Congress on LUNG TRANSPLANTATION

Paris, september 14-15, 2006

Union Internationale des Chemins de Fer

16, rue Jean Rey, Paris XV

PROGRAM & ABSTRACTS

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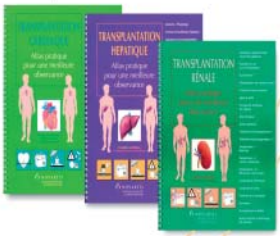

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dont l'objectif est l'échange entre transplanteurs et médecins spécialisés sur des thèmes d'actualités avec présentation de cas cliniques (donneur vivant, diabète, partage d'expériences avec des transplanteurs grecs).

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LUNG TRANSPLANTATION
Paris, september 14-15, 2006

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WELCOME ADDRESS

Dear Colleagues,

For the seventh time, the International Congress on Lung Transplantation is being held in Paris.

Besides plenary sessions and oral communications, we have two new presentations with controversies and basic science. The other topics : post-operative complications, aspergillosis and fungal infections, selection of candidate in difficult cases, molecular biology in lung transplantation, rejection and immunosuppression, unusual etiologies in transplantation 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.

Our Social Program is equally inviting, filled with Parisian treasures.

On behalf of the Organizing Committee, I am honoured to welcome you to Paris.

A. BISSON

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

If you are a speaker

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

GENERAL INFORMATION

Administrative Secretariat

Office hours :

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

After the Congress :

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

Badges

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

Certificate of attendance

A certificate of attendance for 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 14

DINNER AT "À LA MÈRE CATHERINE"
6, Rue Norvins (Place du Tertre)
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8:00 p.m

Price per person : 110 €
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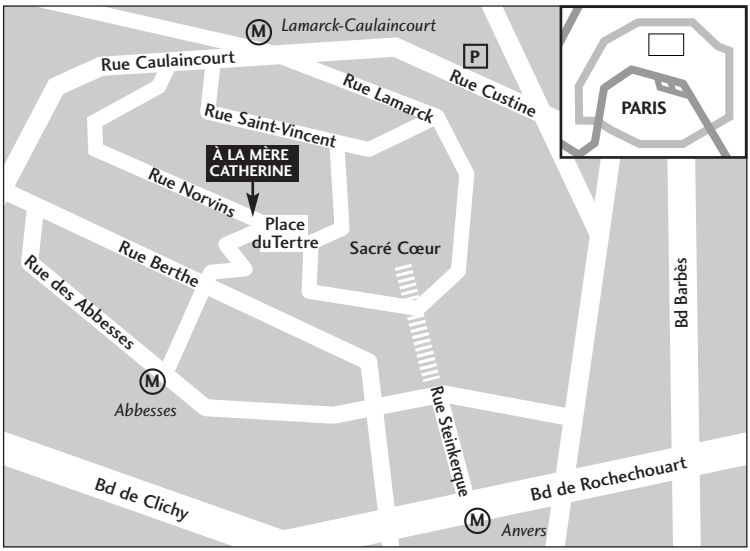

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SCIENTIFIC PROGRAM

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Thursday 14 September

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14:00 – 16:00	Rejection and Immunosuppression p 15	
16:00 – 18:00		Aspergillosis and other Fungal Infections p 17

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8:45 → 9:00 **Room Louis Armand**

Opening

A. BISSON (France)
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P. CORRIS (UK) **& R.D. DAVIS** (USA)
Presidents of the Congress

9:00 → 12:30 **Room Louis Armand**

Controversies in Lung Transplantation

Chairpersons: **P. CORRIS** (UK), **R.D. DAVIS** (USA)

9:00	**Emphysema : Unilateral versus Bilateral Lung Transplantation** H. Mal (France) – J. Dark (UK)	**L1**
10:00	Break	
10:30	**Systematic transbronchial biopsies: Pro /Cons** R.R. Hachem (USA) – A. Glanville (Australia)	**L2**
11:30	**Induction therapy in Lung Transplantation : Pro /Cons** R.D. Davis (USA) – B. Meiser (Germany)	**L3**

10:30 → 12:30 Room List & Stephenson

Communications

Chairpersons: **C. KNOOP (Belgium), M. REYNAUD-GAUBERT (France)**

10:30 **Evolution of pulmonary donor criteria between 2000 and 2005 and 1 year survival for transplanted patients in france** O1
C Cantrelle, D Tixier, B Loty, P Tuppin (France)

10:45 **Survival of lung transplant recipients in the modern era** O2
Mullen JC, Oreopoulos A, Modry DL, Weinkauff J, Stewart K, Winton T, Lien DC (Canada)

11:00 **Improved performance in lung transplantation: different patients or learning curve?** O3
Loirat P, Vinatier I, Thaler F, Hurel D, Djibre M, Fischler M, Chapelier A, Stern M (France)

11:15 **First romanian experimental lung transplantation experience** O4
Grigoroiu M, Scarlat C, Stanescu C, Apriotesei R, Merlusca G , Popescu A, Tulbure D, Popescu I (Romania)

11:30 **Intensive care unit (ICU) readmissions after lung transplantation. epidemiology and outcome** O5
Klin P., Klein F., Díaz J., Osses J., Bertolotti A., Favaloro R.R. (Argentina)

11:45 **Lung transplantation at ismett: results of a novel immunosuppression regimen** O6
F. Caronia, P. Vitulo, A. Bertani, R. Marchese, B. Gridelli (Italy)

12:00 **Peripheral consolidation and pleural thickening in chronic lung allograft rejection** O7
Corcoran D, Mittal T, Bell A, Carby M (USA)

12:15 **Graft versus host disease after heart-lung transplantation: an uncommon complication revealed by pancytopenia** O8
Ruppert A, Kessler R, Kraemer Jp, Massard G, Lioure B, Epailly E, On Behalf Of The Lung Transplant Group of Strasbourg (France)

14:00 → 18:00 **Room Louis Armand**

Rejection and Immunosuppression

With the support of Roche Pharma

Chairpersons: **A. GLANVILLE (Australia), M. ESTENNE (Belgium)**

14:00 **Calcineurin Inhibitor-free Immunosuppressive protocols** **L4**
H. Reichenspurner (Germany)

14:20 **m-TOR inhibitors** **L5**
A. Glanville (Australia)

14:40 **Inhaled Immunosuppression** **L6**
A. Iacono (USA)

15:00 **New approach of immunosuppressive drug's dose adjustment** **L7**
P. Marquet (France)

15:20 **Humoral rejection: lessons from the renal experience** **L8**
D. Glotz (France)

15:40 **Acute antibody-mediated rejection after lung transpantation: a clinical pathological entity** **L9**
C. Knoop (Belgium)

16:00 BREAK

16:30 **A randomized control trial of daclizumab versus anti-thymocyte globulin induction for lung transplantation** **O9**
Mullen JC, Oreopoulos A, Bentley MJ, Modry DL, Stewart K, Winton T, Jackson K, Halloran P, Lien D (Australia)

16:45 **Basiliximab as induction therapy of lung transplantation: a retrospective preliminary study of 21 following patients** **O10**
Clinckart F, Bulpa P, Delaunois L, Eucher P, Jamart J, Installé E, Evrard P (Belgium)

>>>>

17:00 **Monitoring of immunosuppression on circulating dendritic cells and t cells: an adjunct to therapeutic drug monitoring Humoral rejection: lessons from the renal experience** **O11**
Barten MJ, Bossert T, Bittner HB, Mohr FW, Gummert JF (Germany)

17:20 **Innate immunity in lung transplantation: antimicrobial peptides** **L10**
P. Corris (UK)

17:40 **Bronchiolitis obliterans syndrome: early surrogate markers, the real life** **L11**
M. Estenne (Belgium)

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

Aspergillosis and other Fungal Infections

Chairpersons: **B. PHILIPPE** (France), **S. HUSAIN** (USA)

14:00	**Aspergillus fumigatus : A review** J.P. Bouchara (France)	**L12**
14:30	**Pulmonary aspergillosis in lung transplant recipients: Foch experience** B. Philippe (France)	**L13**
15:00	**Pulmonary aspergillosis: basis for immunotherapy and vaccination** L. Romani (Italy)	**L14**
15:30	**Treatment of invasive aspergillosis: criteria of beginning and is there a place for prophylaxis** S. Husain (USA)	**L15**

8:00 → 12:30 **Room Louis Armand**

Postoperative Complications

Chairpersons: **D. VAN RAEMDONCK** (Belgium), **W. WISSER** (Austria)

8:00	**Primary Graft Failure: a new classification and now….** D. Van Raemdonck (Belgium)	**L16**
8:20	**Avoidance of reperfusion injury** F. Wagner (Germany)	**L17**
8:40	**Aprotinin attenuates ischemia-reperfusion injury in clinical lung transplantation** Bittner HB, Binner C, Kuntze T, Dahlberg P, Hertz M, Mohr FW (Germany)	**O12**
8:55	**Gelatinases and lung ischemia-reperfusion injury** P. Soccal (Switzerland)	**L18**
9:15	**ECMO and primary graft failure** W. Wisser (Austria)	**L19**
9:35	**Replacing cardiopulmonary bypass with extracorporeal membrane oxygenation in lung transplantation operations leads to significant differences in blood product management** Bittner HB, Kuntze T, Binner C, Richter M, Lehmann S, Mohr FW (Germany)	**O13**
10:00	BREAK	
10:30	**Postoperative bronchial complications** S. Schueler (UK)	**L20**
11:50	**Interventional bronchoscopy for the treatment of lung transplant bronchial complications** P. Vitulo, A. Bertani, F. Caronia, R. Marchese, B. Gridelli (Italy)	**O14**

>>>>

11:05 **Acute renal failure: Consequences** **L21**
R.D. Davis (USA)

11:25 **Postoperative renal dysfunction after lung transplantation: incidence and prognosis** **O15**
I. Vinatier, H. Salman, F. Thaler, D. Hurel, M. Djibre, D. da Silva, J.P. Grivois, P. Loirat (France)

8:00 → 10:10 **Room List & Stephenson**

Candidate Selection : Difficult Cases

Chairpersons: **P. CORRIS (UK), O. JEGADEN (France)**

8:00	**B. cepacia, Fungi and non tuberculous mycobacteria in Cystic Fibrosis patients** P.A. Corris (UK)	**L22**
8:20	**Lung or liver and lung transplantation in CF candidates** O. Soubrane (France)	**L23**
8:40	**Ischemic heart disease** R.R. Hachem (USA)	**L24**
9:00	**The effect of body mass index on postoperative outcomes and survival in lung transplant recipients** Mullen JC, Oreopoulos A, Tam-chung T, Bentley MJ, Lien DC, Weinkauf J, Jackson KB, Stewart K, Brown P, Taskinen A, Modry DL (Canada)	**O16**
9:15	**Lobar lung transplantation** P. Puyo (France)	**L25**
9:35	**Situs inversus** O. Jegaden (France)	**L26**
9:55	**Lung retransplantation for patients with bronchiolitis obliterans : single center experience** P. Jaksch, G. Lang, B. Zweytick, T. Fleck, W. Wisser, S. Taghavi, W. Klepetko **(Austria)**	**O17**

10:30 → 12:35 Room List & Stephenson

Basic science in Lung Transplantation

Chairpersons: **S. KESHAVJEE (Canada), D. ISRAËL-BIET (France)**

10:30	**Pharmacogenomics of immunosuppressive agents** D. Anglicheau (France)	**L27**
10:55	**The Lung Allograft Rejection Gene expression Observational (LARGO) study** S. Keshavjee (Canada)	**L28**
11:20	**Immune cell function Monitoring** N. Reinsmoen (USA)	**L29**
11:45	**Stem cell factor expression in the airways of lung transplant recipients** D. Israël-Biet (France)	**L30**
12:05	**NF-kB expression in human lung transplantation** A Roux, M. Stern, D. Grenet, F. Gonin, D. Israël-Biet (France)	**O18**
12:20	**A simple test early after lung transplantation predicts bronchiolitis obliterans syndrome** Van Besouw Nm, Van Hal Pthw, Quist L, Grijm K, Zuijderwijk Jm, Bekkers Ja, Weimar W (The Netherlands)	**O19**

14:00 → 16:00 **Room Louis Armand**

Lung Transplantation : Unusual Etiologies

Chairpersons: **J.F. MORNEX** (France), **S. SCHUELER** (UK)

14:00	**Langerhans' cell histiocytosis** G. Dauriat (France)	**L31**
14:25	**Lung transplantation in a 3 year old patient with langerhans cell histiocytosis** A. Bertani, P. Vitulo, F. Caronia, R. Marchese, A. Arcadipane, G. Burgio, B. Gridelli (Italy)	**O20**
14:40	**Lymphangioleiomyomatosis** M. Reynaud-Gaubert (France)	**L32**
15:05	**Non CF bronchiectasies** J.A. Nathan (UK)	**L33**
15:30	**Bronchoalveolar carcinoma** J.F. Mornex (France)	**L34**

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

Communications

Chairpersons: **R. HACHEM (USA), P. BONNETTE (France)**

14:00 **Automatic control of anesthesia for lung transplantation** **O21**
Michel-Cherqui M., Liu N., Puyo P., Bonnette P., Stern M., Chapelier A., Loirat P., Fischler M. (France)

14:15 **Postmortem heparinization followed by preharvest retrograde pulmonary flush improves pulmonary graft performance in the non-heart-beating-donor** **O22**
Van De Wauwer C, Neyrinck A, Geudens N, Rega F, Verleden Gm, Lerut T, Van Raemdonck D (Belgium)

14:30 **The lectin-like domain of thrombomodulin suppresses leukocyte infiltration in a murine lung ischemia-reperfusion injury model** **O23**
Geudens N, Van De Wouwer M, Vanaudenaerde B, Neyrinck A, Rega F, Van De Wauwer C1, Lerut T, Verbeken E, Verleden G, Conway E And Van Raemdonck D (Belgium)

14:45 **The impact on outcome of very long ischemic times in a new lung transplantation program** **O24**
Bittner HB, Kuntze T, Binner C, Wirtz H, Mohr FW (Germany)

15:00 **Il-8 is an unreliable marker of single lung transplantation viability from non-heart beating donor in pigs** **O25**
Bertolotti A, Gomez C, Lascano E, Negroni J, Cuniberti L, Yannarelli G, Laguens R, Favaloro R (Argentina)

15:15 **Unilateral radiographic abnormalities following bilateral lung transplantation: exclusion from the definition of primary graft dysfunction?** **O26**
Oto T, Levvey B, Williams T, Snell G (Australia)

EXHIBITORS LIST

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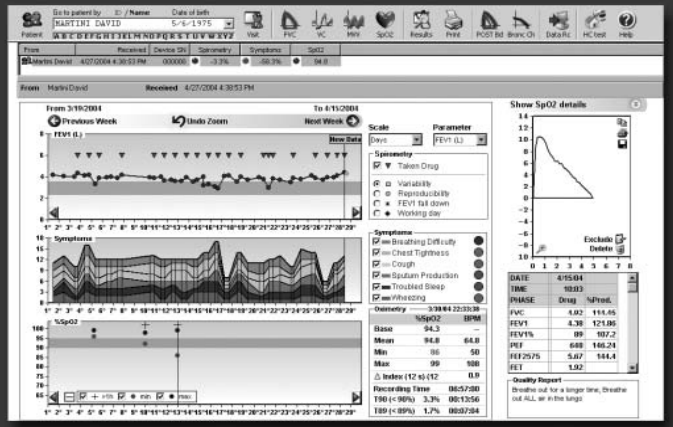

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ABSTRACTS

Evolution of pulmonary donor criteria between 2000 and 2005 and 1 year survival for transplan-ted patients in france

C Cantrelle ; D Tixier ; B Loty ; P Tuppin

Background: In the overall shortage context of organs, the release of organs donor criteria will be a solution to decrease the waiting time of the patients and increase the chances of graft survival. Despite the great need for suitable lung donors, only a minority of potential multi organ donors are used for lung donation in France (14%). A precedent study has shown a high national graft refusal level (66%) in French lung teams between 1996 and 2001. The level of lung graft has been increased since 2003 (+142%) and we wanted to see if it represented a modification of donor acceptability criteria and to assess the 1 year outcome.

Methods: This study of evolution of donor criteria in lung transplantation included all the 655 national lung grafts between 2000 and 2005.

Kaplan Meier curves were used to observe the influence of evolution of donor characteristics on 1 year outcome after lung transplantation by period (1987-2000 ; 2000-2002 ; 2003-2004) (n=1253).

Results: The causes of donor death have changed. Since 2 years, the number of traumatic in traffic accident has decreased in France (22.4% in 2003 and 16.8% in 2005). An increase in anoxia (6.6% in 2003 versus 12.5% in 2005) and in traumatic non traffic accident (13.2% in 2003 versus 19% in 2005) was observed.

The rate of donor aged more than 55 years has risen 13.2% to 15.2% between 2003 and 2005. We noted the apparition of donors aged more than 65 years since 2004.

In 2005, the donors were more likely than in 2003 to be female. (45.7% versus 35.5%) with a number of arterial hyper tension more important since 2001 (5.6% versus 13.6% in 2005) and the used of lungs from donor with smoking history is increased (17.1% in 2003 versus 33.7% in 2005).

The rate of donor cardiac arrest stable until 2003 (15.8%) increased in 2005 (24.5%).

The rate of unclear chest radiograph had still around 10%.

The proportion which had PaO2 < 300mm hg decreased since 2000 (10% versus 5.7% in 2005).

One year survival was 70% ,for the more recent cohort (2003-2004) and respectively 65% et 56% for 2000-2002 and <2000.

Conclusion: The French teams of lung transplantation released their criteria excepted those very associated with a reduced chance for successful lung procurement (arterial blood gases PaO2, unclear chest radiograph..).

The liberalization of donor criteria permitted to extend lung transplantation in France. The first results don't show a degradation on outcome after 1 year lung transplantation by period.

Survival of lung transplant reci-pients in the modern era

Mullen JC, Oreopoulos A, Modry DL, Wein-kauff J, Stewart K, Winton T, Lien DC

Background: Lung transplantation is the therapeutic option of choice for patients suffering from end-stage pulmonary disease. Over the past decade, there have been numerous advances made in the surgical techniques and postoperative management of lung transplantation. The purpose of this study was to examine survival outcomes of both single and double lung transplant recipients over time at our centre.

Methods: Retrospective analysis of 270 consecutive single and double lung transplant recipients at the University of Alberta Hospital from Dec 1989 to March 2006. Patients were divided into groups according to date of surgery: 1989-2000 and 2001-2006, separated by transplant type: single or double lung.

Results: There were 52 single and 48 double lung transplants performed between 1989 and 2000, and 30 single and 142 double lung transplants performed between 2001 and March 2006. One year survival for single lung transplants prior to 2001 was 71% compared to 79% after 2001 (p=0.6). One year survival for double lung transplants prior to 2001 was 71% compared to 88% after 2001 (p=0.02).

Conclusion: Survival in both single and double lung transplants has continued to increase over time, however survival post double lung transplant has had a significantly greater improvement. Advances in methods of organ preservation and postoperative management have substantially improved the outcome of lung transplantation. Progress in the fields of immunosuppression, combined with a better understanding of rejection, has also contributed to the success of lung transplantation.

Improved performance in lung transplantation: different patients or learning curve?

Loirat P, Vinatier I, Thaler F, Hurel D, Djibre M, Fis-chler M, Chapelier A, Stern M

International and national registries have documented improvements in survival after lung transplantation (LT) in recent years. This may be due to better selection or management of patients. A volume effect could also participate to learning curve.

Methods: A retrospective study of these variables was undertaken in the 250 LTs performed in our institution from 1988 to june. 2006 in 247 patients. 132 patients were transplanted from 1988 to 1999 (group 1), 115 from 2000 to 2006 (group 2). Immunosuppressive treatment (ALG induction, ciclosporin, steroids, azathioprin) did not differ between the 2 groups.

Results: The 2 groups differed in primary disease (emphysema 37.1 and 18.6%, cystic fibrosis 20.5 and 70.0%, fibrosis 19.7 and 10.1%, other 22.7 and 17.8%, $p < 0.0001$). Accordingly, significant differences were observed between the 2 groups concerning type of procedure (single 50.7 and 23.7%, double 48.4 and 75.4%, $p<0.0001$), sex ratio (M/W 2.1 and 1.2, $p=0.0258$), age (41.8 and 37.2y, $p<0.0001$). Death rate at 1 month was respectively 18.2 and 6.9% ($p=0.009$). Length of stay in the ICU or in hospital did not differ significantly. Survival at 5 years was 33.8 and 67.1% ($p<0.0001$). Patients' heath related quality of life, measured by the Nottingham Health Profile, patients' satisfaction, measured by the Perceived Quality of Life Scale, and risk factors for early death, (recipient age, sex mismatch, number of red pack cells received during the first 24 h following transplantation, ischemic time and PO2/FiO2 ratio in the 6 hours following LT), derived from a predictive model validated in a series of 683 patients, did not differ between the two periods when adjusted for disease. The number of LTs performed per year was similar between the 2 groups for emphysema (2.4 and 2.2), fibrosis (2.7 and 3.8) and other diagnosis (2.7 and 3.8) whereas it increased significantly (2.5 and 9.7, $p <0.01$) in cystic fibrosis patient. Whereas early death rate decreased in each diagnostic category, this was significant only in cystic fibrosis patients (18.5 and 3.2%, $p=0.0137$).

Conclusion: Apart from the increase in volume of procedure, no factor was recognized as relevant in order to explain improvement in survival.

First romanian experimental lung transplantation experience

Grigoroiu M, Scarlat C, Stanescu C, Apriotesei R, Merlusca G,
Popescu A, Tulbure D, Popescu I

Pulmonary transplantation is recommended for the patients within end stage, presenting progressive and irreversible respiratory failure, for whom other treatments became inefficient or do not exist. Romania remains one of the few European countries that has no practice related to this treatment procedure.

We are presenting the results of the porcine model experimental mono-pulmonary lung transplantation program, developed by the Surgical Experimental Centre, at Fundeni Clinical Institute from Bucharest. Between November 2005 – April 2006, 20 mono-pulmonary lung transplantation procedures where performed, on 40 domestic female swine, weighting 25-30 Kg. Five deaths were recorded: 2 donor difficult intubations, one donor death before heparin administration, caused by inadvertent cardiac manipulation and 2 receivers death, caused by the excessive right atria clamping. Three major complications were noted: two cardiac arrests, one resuscitated to a receiver caused by excessive right atria clamping and one to a donor after the heparin administration and the harvesting procedure were achieved on internal cardiac massage; one case of pulmonary graft parenchyma iatrogenic lesion, with secondary atelectasy. The only one minor complication was an allergic reaction at anaesthesia induction.

A total of 15 successful left orthotopic mono-pulmonary lung transplantation procedures were performed. The receivers were extubated at the end of the procedure and euthanatized 1-2 hours after.

The recorded parameters were: the learning curve, warm ischemic time, the bronchial anastomosis time and the vascular anastomosis times. The animal model experimental stage is the first compulsory step to be taken in any transplantation program implementation.

Intensive care unit (ICU) readmis-sions after lung transplantation. Epidemiology and outcome

Klin P., Klein F., Díaz J., Osses J., Bertolotti A., Favaloro R.R.

Introduction: Lung Transplantation (LT) evolved into an accepted therapeutic option for end stage respiratory failure patients (p). Short-term survival has improved dramatically over the last years, with most of the p. being discharged postoperatively. Nevertheless, a significant number of p. require to be readmitted to the ICU because of different complications.
The aim of our study was to analyse the epidemiology, outcome and risk factors for LT p. readmitted to the ICU after their initial discharge.
Methods: All LT p. from a single centre (Favaloro Foundation) who were initially discharged from ICU and who needed to be readmitted were studied from 02/20/1996 until 05/29/06. Collected demographic data included type and date of LT, best post-LT FEV1 , last pre-ICU readmission FEV1, admission diagnosis, mechanical ventilation (MV) use, rejection episodes and opportunistic infections. For statistical analysis, Fisher and X2 tests were used. Actuarial survival rates were calculated with Kaplan Meier curves.
Results: Since 1996 and until 05/29/06, from a total of 103 LT p. discharged from the ICU, 41 p.(39.8%) were readmitted. Males represented 53.6% (22 p.) with a mean age of 42 years (15-66). In these population, indications for LT were Emphysema (E) in 13 p. (31.7%), Idiopathic Pulmonary Fibrosis (IPF) in 8 p.(19.5%), bronchiectasis in 5p. (12.2%),Cystic Fibrosis (CF) in 5 p. and others in 7 (17%). Seventeen p. were bilateral LT, right LT in 11 (26.8%) and left LT in 8 p (19.5%) while 5 p. Heart-Lung Transplantations (HLT). Respiratory failure (RF) was the most frequent admission diagnosis (28 p. (68.3%)), followed by seizures (3 p. (7%) and septic shock (2 p.)(4.8%)). The rest of the causes included acute abdominal emergencies, atrial fibrillation, high-risk bronchoscopy , neumothorax, syncope and acute cellular rejection therapy. Mechanical ventilation was required in 35 p. (85.3% during their ICU admission. Overall ICU mortality for readmitted p. was 68.3% (28 p.) with a one, three and five years actuarial survival rate of 67.3%, 62.9% and 47.4%. The survival median was 1761 days (1134-2388). In the mechanically ventilated p., a 1, 3 and 5 years actuarial survival rate of 63.1%, 58.9 and 44.2% was found with a median survival of 1618 days (132-3104). When compared with the survivors subpopulation, the de-ceased p. required significantly more MV (71.4% vs 38.5%; p: 0.044(X2); OR: 4; CI: 95%; 1-15.99). Emphysema was not more prevalent in the deceased group (32.1% vs. 30.8%; p: 1 by Fisher Test), neither a less than 2000 ml pre-ICU readmission FEV1 (54.2% vs. 33.3%; p: 0.238 X2) nor the occurrence of opportunistic infections (39.3% vs. 38.5 %; p: 0.96). A statistically significant correlation was found between steroid resistant acute cellular rejection (SRACR) and mortality. No SRACR was reported among survivors.
Conclusions: ICU readmission is frequent among LT p. In our study group, RF was the more prevalent admission diagnosis. The need of MV was associated with a worse prognosis as well as a history of SRACR episodes.

Lung transplantation at Ismett: results of a novel immunosuppression regimen

F. Caronia, P. Vitulo, A. Bertani, R. Marchese, B. Gridelli

We present the preliminary results of the lung transplant program at Ismett-UPMC Italy (Mediterranean Institute for Transplantation and Highly Specialized Therapies) after the first year of activity. The Ismett program opened in June 2005 with the aim to cover for the needs of patients requiring a lung transplant (LTX) in the south of Italy and in the countries of the Mediterranean basin. In this abstract special attention is given to the description of the immunosuppression protocols used on transplanted patients.

Patients were put on the list according to standard international guidelines for LTX.

Between June 2005 and June 2006 17 lung transplants were performed, 16 double lungs and one single lung. The indications were cystic fibrosis (N=6), idiopathic pulmonary fibrosis (N=5), Emphysema (N=2), Bronchiectasis (N=2), Langerhans cell Hystiocytosis (N=1), and retransplantation for OB (N=1). The median age was 39 yrs (range = 3-63); patients had a median weight of 52.5 kg (range 11-96) and height of 1.65 m (range 0.94-1.85). the median time spent on the waiting list was 86 days (range 2-445) The antibiotic prophylaxis regimen was based on double antibiotic coverage possibly according to preoperative sputum coltures. All patients received anti-fungal prophylaxis with Fluconazole. Both antibacterial and antifungal regimens were given until the donor coltures became available and confirmed absence of microorganism growth. Viral prophylaxis was undergone using a strict pre-emptive protocol with weekly CMV antigenemia and DNA-emia determination. The immunosuppression regimen was based on Basiliximab induction (2 doses of 20 mg each), and maintenance with Tacrolimus (0.08 mg /kg then adjusting for blood levels of 12-15), steroids (20 mg for the first 3 weeks and MMF

At a mean follow-up time of 146.5 days (range 0-366) 14/17 patients are alive and doing well (gross overall survival of 82%). Acute cellular rejection occurred in 5 patients out of 17 (29%) at a median timing of 60 days post transplantation (range 25- 96). The grade of these rejection episodes was higher than ISHLT 2 in 1 case. All rejection episodes were diagnosed via transbronchial biopsy except in 1 case, were clinical diagnosis was performed. All the episodes of ACR were successfully treated with steroid pulses (10 mg /kg for 3 days). We observed three episodes (17%) of CMV diseases that were successfully treated by iv DHPG therapy. We tailored the immunosuppression protocol according to primary disease and infectious disease pattern, i.e. avoiding MMF in cystic fibrosis patients with multi resistant microorganisms.

We conclude that the initial experience with lung transplantation has been satisfactory. The immunosuppression protocol that we are currently adopting seems to well balance the need of adequate immunologic protection and protection from infection. ACR episodes seem to be low grade rather than high grade rejections. Viral and bacterial infections seem to be well controlled and managed using this immunosuppressive approach.

Peripheral consolidation and pleural thickening in chronic lung allograft rejection

Corcoran D, Mittal T, Bell A, Carby M.

The radiological features of chronic lung allograft rejection are widely described.
We report on 3 patients followed up over a 6 year period at this transplant centre. All cases had bronchiolitis obliterans syndrome and had expiratory air trapping on high-resolution computed tomography (HRCT). Unusually peripheral consolidation with associated pleural thickening was present.

Case 1. 46 year old man had heart/lung transplantation for Eisenmengers in 1998. Lung function deteriorated in 2004. HRCT showed areas of peripheral consolidation merging with the thickened pleura. Thickening of the interlobular septa with traction bronchiectasis was also present. Transbronchial biopsy (TBB) revealed clumps of dense fibrin with alveolar cell hyperplasia. Thoracoscopic biopsy showed pleural fibrosis, patchy old parenchymal scarring, focal organising pneumonia and patchy chronic inflammation. The patient died from a respiratory tract infection 7 months later.
Case 2. 44 year old diabetic man had bilateral sequential single lung transplantation for cystic fibrosis in 2000. Right main bronchial stenosis developed post transplant and was treated with cryotherapy. In 2006, HRCT showed peripheral consolidation predominantly in the right upper lobe (RUL). TBB of the RUL showed many alveoli filled with fibrin and patchy interstitial infiltrates of lymphocytes, plasma cells and eosinophils. Pseudomonas aeruginosa infection was isolated but HRCT changes persisted despite treatment. The patient died from a respiratory tract infection 2 months later.
Case 3. 53 year old diabetic lady had bilateral sequential single lung transplantation for alpha-1 antitrypsin deficiency emphysema in 2001. Mycobacterium Gordonii was isolated in 2002 and 2003 but was not clinically significant. TBB showed organising pneumonitis but no granulomas were detected. HRCT in 2004 showed RUL pleural thickening and consolidation. No infections were identified on sputum cultures. The patient is still alive.

All these cases showed decline in their lung function with pleural thickening and associated peripheral consolidation on HRCT. In 2 cases histology revealed parenchymal fibrinous and inflammatory changes, death followed only months after the peripheral consolidation was detected. In 2 cases no obvious infective cause was identified These HRCT features may be part of a spectrum of lung damage caused by chronic allograft rejection and may be a future marker of poor outcome.
Keywords: Lung transplant rejection, peripheral consolidation

(HRCT images will be present on poster)

Graft versus host disease after heart-lung transplantation: an uncommon complication revealed by pancytopenia

Ruppert A, Kessler R, Kraemer JP, Massard G, Lioure B, Epailly E, On Behalf Of The Lung Transplant Group Of Strasbourg

Introduction: Graft versus host disease (GVHD) is caused by allogenic immunocompetent T cells introduced during transplantation in an immunocompromised host. It mainly occurs after bone marrow transplantation (BMT). Solid organ transplantations are rarely concerned due to the small amount of lymphoid tissue. To our knowledge, only 5 cases have been reported after lung transplantation. In GVHD, activated donor T cells recognize the host antigen presentation cells and differentiate into T-helper 1 and cytotoxic T cell lymphocytes. We report a case of GVHD after lung transplantation revealed by a severe pancytopenia.

Case report: A forty year old woman presenting a localized left atrial rhabdomyosarcoma was treated by surgical resection and adjuvant chemotherapy (EPIRUBICIN – IFOSFAMIDE). She underwent 6 months later a heart-lung transplantation for residual tumour in the left pulmonary vena. Induction immunosuppression included anti-thymocyte globulin (ATG), methylprednisolone (MP), cyclosporine (CsA) and mycofenolate mofetil (MMF). On day 14 post-transplant a severe bicytopenia occurred (withe blood cell count WBC 0, 23 x 109/liter; platelet 35 x 109/ liter). Improvement was noted after treatment by G-CSF and temporary stop of MMF and cotrimoxazole. On day 30 she presented fever (39°C), nausea and diarrhoea. Blood analysis showed a relapse of grade 4 neutropenia and thrombopenia (WBC 0, 3 x 109/l, platelet 18 x 109/l) and grade 2 anemia. A moderate cholestatic hepatitis was noted. The next days a maculopapular rash spread out. Implication of the bone marrow, the skin, the gastro-intestinal tract and the liver alluded to GVHD. Skin biopsy and chimerism studies confirmed the diagnosis of GVHD (donor lymphocytes 90%, host lymphocytes 10%). Treatment with high dose pulse MP therapy associated to G-CSF was started and maintenance immunotherapy by CsA and MMF was continued. She however remained pancytopenic and died at day 109 post-transplantation of a systemic cytomegalovirus infection.

Discussion: GVHD should be considered in case of pancytopenia associated with fever, gastro-enteritis, dermatitis or hepatitis. Differential diagnoses include infectious diseases (especially CMV infection), drug related reactions, post transplant lymphoproliferative diseases, transfusion associated GVHD and graft rejection. An early differential diagnosis between GVHD and drug related pancytopenia is crucial, since immunosuppression should be intensified in the case of GVHD but reduced

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in the case of leucopoenia. Pulse MP, ATG, methotrexate, increased doses of CsA or tacrolimus or a combination of these are typically used. Depletion of donor T cells from the graft or therapies focusing on activated T cells like anti-CD25 monoclonal antibodies could also be an option. In our case, as in the prior reports, prognosis was poor mainly resulting of bone marrow dysfunction and its life threatening infectious complications.

Conclusion: GVHD is an uncommon complication after heart-lung transplantation. It should be considered in case of any pancytopenia particularly if associated with fever, gastro-enteritis, dermatitis or hepatitis. Early diagnosis is warranted since immunosuppression should be increased in GVHD. Prophylaxis is not recommended due to the low prevalence of GVHD in solid organ transplantation. GVHD is still associated with a high mortality but therapy based on monoclonal antibodies directed against T cells seems a promising approach.

A randomized control trial of daclizumab versus anti-thymocyte globulin induction for lung transplantation

Mullen JC, Oreopoulos A, Bentley MJ, Modry DL, Stewart K, Winton T, Jackson K, Halloran P, Lien DC

Purpose: To test the efficacy and safety of Daclizumab (DZM) versus Anti-thymocyte Globulin (ATG) as a component of induction therapy.

Methods: Fifty adults undergoing single or double lung transplantation were randomized to receive either ATG or DZM during induction therapy. Patients in the DZM group received an initial dose of 2mg/kg i.v. at the time of transplant and 1mg/kg i.v. on post-op day 4. Patients were followed for 1 year after transplant.

Results: Average absolute lymphocyte and platelet counts were significantly higher in the DZM group (lymphocyte count ATG: 0.6 ± 0.3 x 109/L vs. DZM: 0.9 ± 0.5 x 109/L, p=0.05; platelet count ATG: 151 ± 10 per mm3, DZM: 212 ± 19 per mm3, p=0.006). CMV mismatch was significantly higher in the DZM group (7 vs. 1, p=0.05). Other donor characteristics and intra-operative variables did not differ significantly between groups. Total drug, ICU and hospital costs did not differ. One patient in the ATG group developed thrombocytopenia and lymphopenia as an adverse reaction. There was no significant difference in number of rejections, malignancy or steroid-induced diabetes. The DZM group did have a higher number of infections (82 vs. 49 in the ATG group, p=0.02), however the number of CMV infections was also significantly higher (18 vs. 6 in the ATG group, p=0.03), corresponding to greater CMV mismatch. There was one incidence of malignancy in each group; both were post-transplant lymphoproliferative disease. Two patients in the ATG group were re-transplanted, one 6 days post op due to graft failure and the other after 2 months due to anastomosis dehiscence. One year survival was excellent in both groups: 96% in the DZM group and 92% in the ATG group.

Conclusion: Daclizumab is a safe component of induction therapy in lung transplantation. Significant infections were more frequent in the DZM group however this was likely due to a higher incidence of CMV mismatch. Both methods of induction therapy worked well with excellent one-year survival.

Basiliximab as induction therapy of lung transplantation: a retrospective preliminary study of 21 following patients

Clinckart F, Bulpa P, Delaunois L, Eucher P, Jamart J, Installé E, Evrard P

Background: Basiliximab is a chimeric anti-interleukin II monoclonal antibody. It has shown safety profile and efficacy to prevent acute rejection in liver, renal and heart transplantation. The aim of the study was to present our results of its utilisation in lung transplantation (LT).

Methods: Between March 2003 and July 2005, 21 patients (pts) were treated with Basiliximab 20mg on day 0 and 4 for induction immunosuppression after LT. The immunosuppression was completed with Cyclosporine, Azathioprine and corticosteroids. We reviewed retrospectively the safety of basiliximab, the occurrence of acute rejection, bacterial and CMV infections, and the outcome of pts.

Results: The safety profile of Basiliximab was excellent with no cytokine-mediated reaction, no hematological toxic effect. The survival rate was 65% at one year. The incidence of acute rejection during the first week was 47% (10/21) treated with a pulse steroids therapy. We had a peak of incidence on days 2 and 3 after LT. After the first week, 6 other acute rejections appeared during the first year (6/21). There was one bronchiolitis obliterans syndrome (BOS). Forty-three infections were noted (2.01/patients) : 7 septicemia in 6 pts, 17 pneumonia in 14 pts, 11 bronchitis in 9 pts, 4 invasive aspergillosis in 4 pts, and 4 other infections in 4 pts (1 pericarditis, 2 peritonitis, 1 Herpes pneumonia). The survival curve without septicemia was similar to one representing all the groups. The incidence of CMV infections was 0% when donor and recipient were negative (D-/R-), 100% when D+/R-, 88.8% when D+/R+, and finally 66.6 % when D-/R+.

Conclusions: This retrospective study showed a good safety profile of Basiliximab in LT. There was a large incidence of CMV infections during the first year post-transplantation and an important number of bacterial infections. Before concluding that was an effect of Basilixmab, a control group with another drug for the induction of immunosuppression (such as Anti-thymocyte Globulin) is necessary to evaluate the incidence of infections.

Monitoring of immunosuppression on circulating dendritic cells and T cells: an adjunct to therapeutic drug monitoring

Barten MJ, Bossert T, Bittner HB, Mohr FW, Gummert JF

Aims: Since its introduction into the clinic 25 years ago, cyclosporine (CsA) is still the most used basis-immunosuppressive drug after heart transplantation (HTx). Newer potent agents like tacrolimus (TRL) or everolimus (ERL) offer e.g. the opportunity to treat recipients which suffer from CsA side effects. However, due to their small therapeutic window measuring blood drug concentrations is mandatory. Recently, it has been shown that monitoring immune functions could enhance such a therapeutic drug monitoring (TDM). Therefore, in this study we assessed the effects of different immunosuppressive drugs on dendritic cells (DCs) and T cells (TCs) in chronically treated HTx recipients.

Methods: Blood of HTx recipients receiving either a basis-immunosuppression of CsA (n=30), of TRL (n=17) or of ERL (n=10) was obtained before morning drug intake (trough-values). Blood drug concentrations were measured with LC-MS and flow cytometry analysis was used to assess cytokine production of DCs (IL-1ß, TNF-?__; IL-8, IL-12) and TCs (IFN-g, TNF-a, IL-2, IL-4) in peripheral blood.

Results: For all recipients blood drug concentrations were in the respective target ranges (±SEM): CsA:115.7±4.7ng/ml; TRL:8.8±1.1ng/mL and ERL:4.1±0.6µg/L.
Effects of ERL were significant lower on cytokine production of TCs (%expression±SEM) compared to effects of both CsA and TRL ($p<0.05$):
TNF-a: ERL:26.3±4.2; CsA:16.5±2.3; TRL:17.8±3.6;
IL-2: ERL:25.3±3.8; CsA:18.7±2.2; TRL:15.5±1.8.
However, effects of ERL on cytokine production of DCs were significant different compared to the effects of CsA or TRL ($p<0.05$):
IL-1ß: ERL:24.9±3.1; CsA:18.9±2.2; TRL:16.0±1.4;
IL-8: ERL:45.5±2.3; CsA:36.7±2.8; TRL:34.8±2.9;
IL-12: ERL:5.6±0.4; CsA:10.8±1.5; TRL:10.0±1.6.

Conclusion: For the first time, we found different effects on circulating DCs and TCs of a basis-immunosuppression with ERL compared to a basis-immunosuppression of either CsA or TRL in chronically treated HTx recipients. Moreover, the results show that monitoring of circulating DCs and TCs could be an adjunct to TDM based on measuring blood concentrations to enhance drug efficacy and safety after HTx.

Aprotinin attenuates ischemia-reperfusion injury in clinical lung transplantation

Bittner HB, Binner C, Kuntze T, Dahlberg P, Hertz M, Mohr FW

Objectives: Severe reperfusion injury and acute graft failure following lung transplantation (LTX) is one of the major causes for the markedly high early morbidity/mortality rate. Use of Aprotinin (Apt) in experimental LTX models suggest attenuation of the specific transplant ischemia-reperfusion injury (TRI) cascade and improved gas exchange, however, its efficacy in clinical LTX is not well established.

Methods: We used the lung transplant database of two LTX centers in order to investigate the incidence of severe TRI of 152 lung-grafts (controls, 112 patients, single LTX 64%, 54 ±8 years, ischemic time 231 ±14 min) who underwent LTX for emphysema/COPD, IPF, and miscellaneous lung diseases. These LTX were compared to 97 lung-grafts of 68 patients (single LTX 58%, 55 ±9 years, ischemic time 290* ±46 min) who recently underwent LTX for the same diagnosis and who were managed perioperatively with high-dose Aprotinin (Hammersmith protocol) as routinely used in cardiac surgery (the Apt-group). Pulmonary infiltrates and the PaO2/FIO2 ratio of less than 200 mm Hg in the absence of infection or rejection was used for the diagnosis of TRI . (ANOVA, t-tests, *=p<0.05=significant).

Results: The incidence of severe TRI in the control group was 18% vs. 8%* in the Apt-group associated with a significantly higher rate of graft dysfunction, ECMO support (12% vs. 4.5 %*), and 90-day mortality in the controls (38% vs. 9%*).

Conclusions: These data document a clear advantage of using Aprotinin for the perioperative lung transplant patient management leading to a significant decrease in TRI and 90 day mortality without adverse effects. The significantly extended ischemic times in the Aprotinin group did not affect outcome adversely. Aprotinin might therefore be of great benefit in lung transplantation, where TRI continues to be a challenging problem.

Replacing cardiopulmonary bypass with extracorporeal membrane oxygenation in lung transplantation operations leads to significant differences in blood product management

Bittner HB, Kuntze T, Binner C, Richter M, Lehmann S, Mohr FW

Objective: Cardiopulmonary bypass (CPB) support is required in some lung transplantation (LTx) operations. CPB support and full dose heparin increases the risks of bleeding and early graft dysfunction. We report our experiences of replacing CPB with heparin-bound low dose heparin extracorporeal membrane oxygenation (ECMO) support in LTx procedures.

Methods: From 2003 until the end of 2005 47 lungs (56% single) were transplanted and extracorporeal circulation support was necessary in 40% secondary to severe primary or secondary pulmonary hypertension (P or SPHTN) and right heart dysfunction or hemodynamic instability. There were 7 LTX procedures with CPB and 8 implantations with ECMO support. CPB (high dose heparin) and ECMO support (ACT 160-220 sec) was always set up through the left femoral venoarterial canulation. All LTX patients were managed with same aprotinin, immunosuppression, and medical protocol. All patients had limited access thoracotomies without transsection of the sternum. Normothermia was maintained in all patients. CPB patients: PPH 15%, COPD 15%, IPF with mean PAP > 40 mm Hg 70%. ECMO patients: PPH 13%, COPD 13%, IPF with severe PAP pressure elevation 74%.

Results: Five thousand units of heparin was injected intravenously during the femoral vessels cannulation, but no more was used during the first 24 h of ECMO support. If necessary, as in patients undergoing single LTx for end-stage pulmonary hypertension, the ECMO support was directly extended into the postoperative period until reperfusion edema of the graft lung subsided. Red blood cell transfusion requirements during the operation and the first 24 hours were 13.25 +/- 4.4 vs. 3.1 +/- 2.2 U on CBP (p=0.001). Operative time was longer (p=0.11) in the ECMO LTX (451 min +/- 76 vs. 346 +/- 140). The increased 90-day mortality rate of the ECMO patients showed a trend toward significance (p=0.056), which was related to infectious complications (3 vs. 1 patient). Severe ischemia/reperfusion injury occurred in 95 in the CPB vs. 13% ion the ECMO group.One year survival was significantly reducedcin ECMO patients (p=0.004, log-rank test).

Conclusions: The advantages of femoral canulation rather than conventional central connections in lung transplantation procedures led to an undisturbed operative field. A significantly higher blood product amount was required in ECMO patients, which might lead to increased infection and mortality rates. CPB obviously appears to remain the standard of support technique if extracorporeal circulation is required for lung transplantation surgery.

Interventional bronchoscopy for the treatment of lung transplant bronchial complications

P. Vitulo, A. Bertani, F. Caronia, R. Marchese, B. Gridelli

Bronchial stenoses and leaks are among the most frequent complications of lung transplantation. The incidence rate of these complications is attested approximately at 15% in most of the largest world series. Being the surgical technique standardized in the last 10 years, the pathophisiology of these events is probably related to the ischemic damage at the site of the anastomosis between the donor and recipient bronchus.

With the beginning of the lung transplant program at Ismett-UPMC Italy, we have implemented a diagnostic and interventional bronchoscopy service for the management of bronchial complications in our lung transplant recipients cohort. Between June 2005 and June 2006 17 lung transplants were performed, 16 double lungs and one single lung.

Bronchial complications occurred in 4/17 patients. One was a R very small (1-2 mm) anastomotic fistula. Two stenoses of the bronchus intermedius and a complex case of diffuse obstruction of both bronchial trees were also diagnosed. They occurred at a mean timing of 95 days after the transplant (range 35- 193). The diagnosis was suspected on the base of worsened PFTs (decreased FEV1) in 3/3 cases and based on the appearance of clinical symptoms of obstruction (wheezes, cough) in 2/3. The diagnosis was established via fiberoptic bronchoscopy and CT scan with tridimensional reconstruction of the bronchial tree. The fistula was an occasional finding observed after a CT scan in the complete absence of clinical symptoms. The treatment of the two BI stenoses was performed with the temporary placement of a Silastic Dumont stent under rigid bronchoscopy. Usually a balloon dilatation is performed first, and then an appropriate size stent is placed taking care to preserve the right upper lobe uptake and the origin of the right middle lobe and superior segment. A meticulous preoperative planning of the procedure is mandatory in order to choose the best site for the stent placement and the correct size of the prosthesis. In both cases the stents were removed after 41 and 55 days, respectively. By using this strategy, both complications healed very well with excellent anatomic and functional results.

The patient with bilateral diffuse stenosis required a more complicated and prolonged treatment. Dumon and metal stents were repeatedly placed Unfortunately, the patient developed subsequent bilateral upper lobe stenoses which at the moment are still determining a functional impairment of the respiratory function.

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The patient with the small right anastomotic fistula did not require any treatment and at a follow up CT scan performed two months after the diagnosis revealed a complete healing of the fistula.

Also, cases from other transplant center were referred to our unit for the treatment of post lung transplant bronchial complications. 2 anastomotic stenosis were successfully treated using Dumont stents.

We conclude that the preliminary experience with lung transplantation at Ismett showed a rate of bronchial complications which is comparable to international benchmarks. The treatment of these complications is a complex multidisciplinary task involving the surgeon and the pulmonologist. We were able to resolve most of the bronchial complications with interventional bronchoscopy. The treatment of complex and diffuse bronchial stenoses remains a challenging task even in the most experienced hands.

Postoperative renal dysfunction after lung transplantation: incidence and prognosis

I Vinatier, H Salman, F Thaler, D Hurel, M Djibre, D Da Silva, JP Grivois, P Loirat

Renal function has rarely been assessed in the early post-transplantation period. The aim of this study was to assess the incidence and prognosis of early renal dysfunction following lung transplantation.

Methods

The charts of the 105 patients who received a LT between 2000 and 2005 were reviewed. Following data were recorded : creatinine levels (before LT, worst value in the first month following LT and one year level), factors susceptible to influence renal function (operative procedures, hemodynamics, drugs) and renal function at one year. Initial renal dysfunction was defined by a doubling of pre LT creatinine level. Late renal function was assessed by Cockroft formula.

Results

Pre LT renal function was normal in all patients. A doubling of creatinine level was observed in 31.4%. Maximum post LT values exceeded 200 mmol/L in 21.9% and 300 mmol/L in 8.6%. 7 patients required dialysis. In monovariate analysis, occurrence of renal dysfunction was linked ($p<0.05$) to preexisting diabetes, existence of perioperative hemodynamic problems, use of catecholamines, number of red cell packs received during the first 24h, length of mechanical ventilation, ischemic time, pO2/FiO2 ratio in the 6 first hours and maximum trough levels of CsA. Age, preexisting hypertension, type of surgical procedure and pulmonary disease were not linked to the occurrence of renal dysfunction.

In multivariate analysis, occurrence of renal dysfunction was linked to total ischemic time ($p=0.0348$), post-operative hemodynamic problems ($p=0.0343$), use of aminosides ($p=0.0042$) and trough levels of CsA greater than 300 mg/L ($p=0.0059$).

Patients with renal dysfunction had higher ICU ($p=0.0002$) and initial hospital ($p=0.0041$)) lengths of stay.

Renal dysfunction was linked to early survival: survival at 1 month was 98.6% with normal renal function, 91.7% when maximum S creatinine was lower than 300 mmol/L and 55.6% when S creatinine exceeded 300 mmol/L. In multivariate analysis, early death was associated with ischemic time, number of red cell packs received during the first 24 hours following LT, duration of mechanical ventilation and only severe renal dysfunction (S creatinine >300 mmol/L $p=0.039$).

Actuarial survival showed significant differences according to maximum initial creatinine levels ($p<0.0001$), and survival at one year was respectively 92.9%, 74.2%, and 33.3%.

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At one year, among the 85 survivors, renal function was normal in 61.2%, moderately impaired (Cockroft clearance 30-60 ml/min/1.73m2) in 37.6% and severely impaired (30.0 ml/min/1.73m2) in one patient. There was no end stage renal failure. There was no link between initial renal function and renal function at one year.

Conclusion

Renal dysfunction is frequent during the first month following lung transplantation. Its occurrence depends on hemodynamic and toxic factors. Patients with renal dysfunction consume more resources and have higher mortality rates.

The effect of body mass index on postoperative outcomes and survival in lung transplant recipients

Mullen JC, Oreopoulos A, Tamchung T, Bentley MJ, Lien DC, Weinkauf J, Jackson KB, Stewart K, Brown P, Taskinen A, Modry DL

Background: Obesity is commonly cited as a significant comorbidity in lung transplantation. In some programs a body mass index (BMI) >30 and <18.5 kg/m2 are absolute contraindications while in others they are listed as relative. A statement from the International Society for Heart and Lung Transplantation recommends patients with body weight <70% and >130% should strive to either gain or lose weight to be eligible for transplantation. The purpose of this study was to examine the effect of BMI on postoperative outcomes and survival following lung trasplantation.

Methods: We retrospectively reviewed 276 consecutive single, double, and living donor double lung transplants performed at the University of Alberta between December 1989 and March 2006. Patients were grouped according to the World Health Organization BMI categories: underweight <18.5 kg/m2, normal BMI 18.5-24.9 kg/m2, overweight 25.0-29.9 kg/m2, and obese ≥30 kg/m2.

Results: One hundred and ninety transplants were double lungs, 82 were single lungs, and 4 were living donor double lungs. There were 41 underweight, 126 normal, 78 overweight, and 31 obese patients. Only 4 of the obese patients had BMI>35 kg/m2. Overweight and obese patients were older than the normal BMI and underweight patients: underweight: 48 ± 3 years, normal 52 ± 2 years, overweight 60 ± 1 years, and obese 58 ± 2 years ($p<0.0001$). The ratio of males to females was not significantly different between groups. Intensive care unit length of stay was highest in the overweight group (15 ± 2 days, $p=0.06$), however total postoperative length of stay was not significantly different between groups ($p=0.3$). Intubation time was significantly higher in the obese group (234 ± 63 hours, $p=0.02$). Most recent 6-minute walk test (mean 1.7 years post transplant) was also significantly lower in the overweight and obese groups: underweight 576 ± 22m, normal 612 ± 25m, overweight 497 ± 26m, and obese 458 ± 39m ($p=0.002$). One-month survival was 93%, 95%, 91%, 87% ($p=0.4$), and one year survival was 81%, 77%, 78% and 89% in the underweight, normal, overweight and obese categories respectively ($p=0.6$). In the 4 patients who had BMI≥35 kg/m2, survival at one year was 75%. Actuarial survival with Kaplan Meier analysis revealed no significant differences in 5-year survival between BMI categories (log rank comparison $p=0.5$).

Conclusions: Contrary to previous reports that state BMI>30 and <18.5 are predictors for decreased survival following lung transplantation, one-year survival was not significantly different between underweight, normal BMI, overweight and obese patients (81%, 77%, 78% and 89% respectively). Obese patients had significantly higher intubation times. Patients with high BMI also had lower 6-minute walk distances, which may have been a result of older age and/or reduced function in the overweight and obese groups.

Lung retransplantation for patients with bronchiolitis obliterans: single center experience

P. Jaksch, G. Lang, B. Zweytick, T. Fleck, W. Wisser, S. Taghavi, W. Klepetko

Introduction and methods: Despite significant increase of short and longterm survival after lung transplantation more than 50% of patients develop BO(S) 5 years postoperativly. Lung retransplantation is the only therapeutic option for endstage bronchiolitis obliterans but its value remains still discussed controversly. Between 1989 and 2005 a total of 600 lung transplantations were performed at the Vienna transplant centre, 28 of these procedures were retransplantations because of BO(S).
The files of all patients who received a retranplantation for chronic allograft dysfunction were analysed retrospectivly. Demographics: m/f = 11/17., age 35,6 ±15,2 years. Primary indications for LuTX were COPD (n=4), IPF (n=8), PPH (n=5) , CF (n=7) and others (n=9). All ReTX candidates were ambulatory and non-ventilated at the time of reoperation. The mean time to retransplantation were 36,2±24,5 months. Patients survival and recurrence of BO(S) were calculated using Kaplan Meyer survival analysis.

Results: The retransplantation procedure was SLuTX in 17 patients and DLuTX in 11 cases. Five patients received a contralateral and 2 ispilateral ReTX after primary SLuTX and 10 patients had a single lung transplantation after primary bilateral LuTX . The medium follow up were 1830±1242 days after retransplantation. The overall survival was 70% , 65% and 65% after 1, 3 and 5 years, respectively.. Causes of death were bacterial infections in 6 cases (55%), primary organ failure, intracerebral bleeding , BO, cardiac arrest and intraoperative in the other patients. 17 patients after ReTX are still alive and have a good functional status. There was no higher incidence of BO(S) after ReTX and the actual freedom from BOS (grade 1, 2 or 3) was 94%, 83 % and 75% after 1, 3 and 5 years, respectivley. Three patients are actualy in BOS stage 1 and just one in BOS stage 3.

Discussion: Lung retransplantation offers a viable therapeutic option for selected patients with BOS. Survival rates and incidence of BOS were comparable to patients after primary lung transplantation.

NF-KB expression in human lung transplantation

A. Roux, M. Stern, D. Grenet, F. Gonin, D. Israël-Biet

Rationale: Bronchiolitis obliterans syndrome (BOS) remains the major obstacle to long term survival of lung transplants (LTx). Its pathogenesis is not elucidated but clearly involves sustained inflammatory and fibrogenic responses through mediators partly regulated by NF-kB. Specific inhibition of the latter largely attenuates the development of BOS in animal models. The aim of this study was to evaluate the expression of NF-kB in relation with the evolution of human lung transplantation.

Methods: Two LTx populations were studied. One retrospective (R), including 11 subjects with BOS and 13 without, and one (P) in which 11 subjects have been prospectively included (median follow-up : 12 mo; no BOS at the present time). NF-kB was quantified in peripheral blood mononuclear cells (PBMC) of all subjects at 2 time points (before (T1) and after (T2) BOS in group R, and at similar time points in P) using Nuclear Factor kit assay. In addition, the IL-8 and MCP-1 content of PBMC culture supernatants was determined in group P by ELISA. All data were analyzed in relation with clinical events (acute complications and BOS).

Results: In group R, NF-kB was markedly lower in BOS+ than in BOS- subjects at T1 ($p<0,005$). While it remained stable in the latter, it reached a 10-fold increase at T2 in BOS+ pts, indicating an escape from the strong immunodepression of these pts. In group P, NF-kB remained undetected in most samples except in 9, while IL-8 and MCP-1 were highly released at both time points, suggesting a role for other regulators in their production.

Conclusion: NF-kB overexpression might play a role, although not exclusive, in the development of BOS. Other transcription factors (AP-1, MAPK for instance), potential therapeutic targets, also warrant investigation. The ongoing follow-up of the P cohort will help to evaluate relationships between continuous inflammatory activation, NF-kB expression and the outcome of the graft.

A simple test early after lung transplantation predicts bronchiolitis obliterans syndrome

Van Besouw NM, Van Hal P, Quist L, Grijm K, Zuijderwijk JM, Bekkers JA, Weimar W

Despite the advances in surgical techniques and immunosuppressive medication, long term survival after lung transplantation is limited by the occurrence of bronchiolitis obliterans syndrome (BOS). Early identification of patients at risk for BOS may enable preemptive intervention, e.g. changing immunosuppressive or antibiotic therapy. Peripheral blood monitoring after lung transplantation may support to identify patients at risk for BOS. We investigated whether donor-specific reactivity would be an useful marker to identify lung transplant recipients at risk for developing BOS. The T-cell reactivity of peripheral blood mononuclear cells (PBMC) to donor and third-party cells was tested in 8 lung transplant recipients 1.5 months (range: 1-2 months) and 12 months (range: 12-19 months) after transplantation. We performed mixed lymphocyte cultures (MLC) and IFN-_ and IL-10 Elispot assays. BOS gradation was determined according to the decline in forced expiratory volume in 1 second (FEV1). Six patients had stable post-transplant FEV1 (BOS grade 0), and 2 patients developed BOS (grade 1: FEV1 66% and 70%, respectively) approximately 1 year post-transplant. Shortly (1.5 months) after transplantation, patients with BOS grade 1 had higher donor-specific reactivity in MLC (stimulation index (SI) 287 and 211) compared to patients with BOS grade 0 (median SI 5.6 (range 0.6-18.7)). One year after transplantation, the donor-specific reactivity decreased in patients with BOS grade 1 (SI 78 and 114, respectively), but remained higher than in patients with BOS grade 0 (SI 0.5 (range: 0.2-25.0)). Third-party specific MLC, and number of IFN-γ or IL-10 producing cells reactive to donor or third-party cells did not discriminate between patients with and without BOS.

In conclusion, our data suggest that BOS can be predicted with a rather simple test, the donor-specific MLC, performed one month after transplantation.

Lung transplantation in a 3 year old patient with langerhans cell histiocytosis

A. Bertani, P. Vitulo, F. Caronia, R. Marchese, A. Arcadipane, G. Burgio, B. Gridelli

Lung transplantation is an established option for the treatment of end stage respiratory failure deriving from a number of primitive diseases such as cystic fibrosis, COPD and pulmonary fibrosis. Among the other indications to lung transplantation there are a number of rare isolated disorders such as Langerhans cell Histiocytosis. Langerhans cell histiocytosis (LCH) is a rare proliferative disorder of pathological Langerhans cells, whose aetiology and pathogenesis remain largely unknown. It can affect single organs such as the lung or the liver, or show a more disseminated pattern involving the lymphatic system. We describe here the case report of a patient who underwent lung transplantation at out institution for Langerhans cell histiocytosis.

A three year old boy was referred to our institution with LCH with lung involvement. He had received several courses of chemotherapy but showed recurrent relapse of the disease. He had also recurrent pnuemothoraces and had progressed to end stage respiratory failure. He underwent a complete preoperatory workup to rule out possible contraindications to a LTX and was completely restaged to exclude involvement of the disease to other organ sites. He was finally put on the waiting list and received a double lung transplant from a 2 year old donor of correct size and blood type match. His postoperative course was uneventful and he was extubated early on POD #4. He was treated for an episode of ACR on POD 15, and he responded very well to a steroid pulse x 3 . On POD 18, he started complaining of persisting vague abdominal pain and received the standard workup and treatment for viral enteritis. No microorganism or virus was ever isolated from the stools. On POD 22, he suddenly developed acute respiratory failure requiring mechanical ventilation. We were able to perform a BAL that showed no bacterial or fungal growth but a strongly positive immunofluorescence stain for Adenovirus. H was started on an aggressive regime of Cidofovir and Ribaviri. The following day he required VV Ecmo support for the worsening of respiratory function despite maximal ventilatory support. His clinical status slowly worsened and he was never able to recover a satisfactory respiratory function. He was kept on full support for 19 days, and eventually expired from what was interpreted as a primary cardiac event. An autopsy was performed that revealed no other macroscopic organ damage than a complete destruction and consolidation of lung parenchyma. Pathological review is still pending.

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We conclude from this case that 1) lung transplantation in infants is a technically feasible operation with acceptable mortality rates. 2) young children undergoing lung transplantation can have an excellent functional recover from the operation. 3) it is still unclear whether a pure viral disease or other issues determined the final exitus. It must not be completely excluded that recurrence of primary disease might have influenced the final outcome.

Automatic control of anesthesia for lung transplantation
Michel-Cherqui M., Liu N., Puyo P., Bonnette P., Stern M., Chapelier A., Loirat P., Fischler M.

Introduction: Use of closed-loop titration of a hypnotic agent (propofol) guided by an EEG monitor the Bispectral Index (BIS) has recently been reported during various types of surgical procedures (Anesthesiology 104:686-95, 2006). We describe our experience of this technique of anesthesia during lung transplantation (LT).

Method: After IRB approval, informed and written consent, 20 patients, America Society of Anesthesiologists risk IV, who were scheduled for lung transplantation were included in this study. The goal was to reach a BIS target at 50 during the induction and to maintain it between 40 and 60 during the maintenance using a closed-loop titration of propofol. Other anesthetic agents were administered by the anesthesiologist in charge of the patient (remifentanil, atracurium). A thoracic epidural catheter was inserted if no contra-indication was present. All patients were ventilated without nitrous oxide. Performance of the controller was assessed by the Global Score (Anesthesiology 104:686-95, 2006). Data were presented as mean ± SD.

Results: Eleven unilateral LT, 6 bilateral LT and 3 bilobar LT were performed. Patients were suffering from cystic fibrosis (9 cases), emphysema (8 cases) and fibrosis (3 cases). Fourteen patients had an intraoperative epidural analgesia. Mean duration of anesthesia was 346 ± 121 minutes. The closed-loop controller maintained anesthesia during a total of 114 hours during which 2687 propofol concentrations were made automatically. Eleven patients were extubated in the operating room; one was reintubated during the first 48 postoperative hours. Closed-loop controller avoids overdosing of the hypnotic agent, the performance of the closed-loop system is summarized in the Table:
BIS < 40 (%) 13 ± 16
BIS > 60 (%) 2 ± 1 40 <
BIS < 60 (%) 85 ± 17
Global Score 27 ± 18
%: % of maintenance time

Conclusion: Automatic control of consciousness using the BIS is clinically feasible and reliable throughout anesthesia during LT and facilitates extubation in the operating room. This new technology appears to be an attractive way to improve the patient care during LT.

Postmortem heparinization followed by preharvest retrograde pulmonary flush improves pulmonary graft performance in the non-heart-beating-donor

Van De Wauwer C, Neyrinck A, Geudens N, Rega F, Verleden GM, Lerut T, Van Raemdonck D

Objective: The use of non-heart-beating donors (NHBD) has been propagated as an alternative to overcome the scarcity of pulmonary grafts. Formation of microthrombi after circulatory arrest, however, is still a concern for the development of reperfusion injury. In this isolated lung reperfusion study we evaluated the effect of postmortem heparinization and preharvest pulmonary flush on graft performance.
Methods: Domestic pigs (n=6/group) were sacrificed by ventricular fibrillation and left untouched for 1 hour followed by lung retrieval. In the control group no heparin and no pulmonary flush were administered [C]. In group II lungs were flushed with Perfadex® in a retrograde way [R] via the left atrium prior to explantation. In group III heparin [H] (300IU/kg) was administered via the central venous line 10 minutes after cardiac arrest, then closed chest massage was performed during 2 minutes. In group IV animals were heparinized in an identical manner and the lungs were explanted after a retrograde flush [H-R]. After 3 hours of cold storage, the left lung was assessed during 60 minutes in our ex-vivo reperfusion model.
Results: Pulmonary vascular resistance (PVR) was significantly lower and flow was significantly higher in [R], [H] and [H-R] compared to [C]. Graft haemodynamics were superior in [H-R] versus [H] at 40 and 45 minutes of reperfusion. No significant differences were observed for the other parameters [Table]. No differences in Wet-to-dry weight ratio at the end of reperfusion were observed between groups.

Reperfusion Time: 40’ 45’ 50’ 55’ 60’

Pulmonary vascular resistance (dynes*sec*cm-5)

C	1482?61	1418?76	1351?87	1448?82	1435?95
R	1387?85	1225?54	1249?57	1186?69†	1145?56†
H	1614?166	1325?104	1159?53	1076?34#	1103?43#
H-R	1118?98‡	1038?76?‡	1054?95	1036?85?	1007?65?

Flow (L/min)

C	0.74?0.05	0.80?0.05	0.83?0.04	0.84?0.04	0.85?0.04
R	0.85?0.06	0.96?0.05	1.01?0.04†	1.04?0.04†	1.06?0.04†
H	0.69?0.09	0.82?0.07	0.94?0.04	0.98?0.03#	0.99?0.03#
H-R	0.99?0.06?‡	1.03?0.05?‡	1.04?0.04?	1.05?0.04?	1.04?0.04?

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Plateau airway pressure (cmH2O)					
C	14?1	14?1	13?1	14?1	14?1
R	13?1	13?1	13?1	13?1	13?1
H	13?1	13?1	13?1	13?1	12?1
H-R	12?1	12?1	12?1	12?0	12?0

Compliance (ml/cmH2O)					
C	17?1	18?2	18?1	18?1	17?2
R	20?2	21?3	22?3	20?3	24?3
H	18?3	18?3	18?2	18?1	21?3
H-R	21?2	21?1	20?1	21?1	20?2 ?:

p<0.05 H-R vs C, #:
p<0.05 H vs C , †:
p<0.05 R vs C and ‡:p<0.05 H-R vs H

Conclusion: Postmortem heparinization followed by preharvest retrograde flush improves pulmonary graft performance in lungs from the non-heart-beating donor. We speculate that the lowered PVR upon reperfusion results from less thrombi formation in the pulmonary microvasculature during warm ischemia and a better wash-out during flush.

The lectin-like domain of thrombomodulin suppresses leukocyte infiltration in a murine lung ischemia-reperfusion injury model

Geudens N , Van De Wouwer M, Vanau-denaerde B, Neyrinck A, Rega F, Van De Wauwer C, Lerut T, Verbeken E, Verle-den G, Conway E, Van Raemdonck D

Background: The warm ischemic period preceeding cold preservation of lungs from a non-heart-beating donor (NHBD) may increase the risk of ischemia-reperfusion injury compromising the outcome after lung transplantation. During this ischemic period, inflammatory cells become an important trigger of the pro-inflammatory processes occurring after reperfusion. Thrombomodulin (TM) is a vascular endothelial cell receptor that is a cofactor for thrombin-mediated activation of the anti-coagulant and anti-inflammatory protein C. The N-terminal lectin-like domain of TM has distinct anti-inflammatory properties and is important in leukocyte infiltration in different organs. AIM: We investigated the importance and specificity of the N-terminal lectin-like domain of TM towards leukocyte infiltration in the murine lung after ischemia and reperfusion.

Methods: In all study groups, animals underwent the same ischemia reperfusion protocol. After left thoracotomy, the hilum of the left lung was clamped to induce warm in situ ischemia for 90 minutes, followed by 4 hours of reperfusion. After sacrifice, saline was instilled in the left lung and BAL was obtained for leukocyte cell count. Part 1: Wild-type [TMwt/wt] mice were compared with transgenic [TMLeD/LeD] mice, lacking the N-terminal lectin-like domain of TM (n=6/group). Part 2: A vector containing the DNA sequence for the lectin-like domain of TM was administered to SWISS outbred mice by hydrodynamic gene delivery via the tail vein (n=6) [LeD vector]. In the control group [Empty vector], 6 animals received the same vector, but without the DNA sequence for the lectin-like domain of TM. The ischemia-reperfusion protocol was executed 24 hours after gene delivery, when the expression of the protein was at the highest level.

Results:

Part 1: BAL (mean±SD) Cells (x103/ml) Macrophages (x103/ml) Lymphocytes (x103/ml) Neutrophils (x103/ml)

TMwt/wt	60.0±13.8	45.5±11.0	10.6±3.8	3.9±2.1
TMLeD/LeD	87.1±10.3**	63.6±12.4*	9.3±4.3	12.7±3.1***

*: $p<0.05$, **: $p<0.01$ and ***: $p<0.001$ versus [TMwt/wt]

The number of cells, macrophages and neutrophils was significantly higher in transgenic mice, lacking the lectin-like domain of TM, compared to wild-type mice.

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Part 2: BAL (mean±SD) Cells (x103/ml) Macrophages (x103/ml) Lymphocytes (x103/ml) Neutrophils (x103/ml)

Empty vector	121.7±38.4	88.3±25.2	18.3±11.7	15.3±4.8
LeD vector	48.3±8.2**	39.6±6.5**	7.2±2.4*	1.6±0.9***

*: $p<0.05$, **: $p<0.01$ and ***: $p<0.001$ versus [Empty vector]

The number of inflammatory cells was significantly lower in animals, receiving the vector with the DNA sequence for the lectin-like domain of TM, compared to control animals.

Conclusion: The N-terminal lectin-like domain of TM dampens the inflammatory cellular respons after ischemia and reperfusion in the mouse lung. This domain could be an interesting therapeutic target to modulate the inflammatory status following lung transplantation.

The impact on outcome of very long ischemic times in a new lung transplantation program

Bittner HB, Kuntze T, Binner C, Wirtz H, Mohr FW

Objectives: Establishing a lung transplantation program is challenged by lack of team experience and organizational structure limitations, which can lead to extended ischemic times affecting clinical outcome adversely.

Methods: We used the prospectively collected data of 2.5 years of a new lung transplant (LTX) unit in order to investigate the incidence of severe post-transplant reperfusion injury, early mortality rate, and outcome of 39 lung transplant patients. The data were compared to the ISHLT data bank. The lung procurement and transplantation was performed by the same surgeon.

Results: Donor age (15-64, mean 39 ±14 years)/recipient age (22-68, mean 53 ±11 years) was relatively high. High-risk patients with end-stage lung disease due to IPF with high secondary PAP prevailed predominantly (50%), COPD (39%), CF (8%), PPH (3%). Cold ischemic time for single lung (320 ±45min), sequential bilat. (591 ±70 min) was significantly longer compared to ISHLT-reporting. CPB/intra-op ECMO was used in 40%, allowing controlled reperfusion. Sternum sparing bilat. antero-lat. incisions were performed in sequential bilateral LTX (42%) requiring repositioning and turning/re-draping in 20%.
Severe ischemia-reperfusion injury assessed by ISHLT-working group criteria (P/F ratio < 200) was seen in 13% of patients. Graft failure requiring delayed ECMO occurred in 10%. Overall, the 90-day and 1 year mortality rate was 18 % and 29% (vs. ISHLT 14% and 24%) and unrelated to long ischemic times and caused predominantly by infectious complications in 45% (viral sepsis: CMV, varicella, herpes> 50%). One rejection was seen within 252 cummulative patient months.

Conclusion: These data document clearly that very long ischemic times do not affect lung transplant outcomes adversely. The use of Aprotinin in the perioperative management shows beneficial effects attenuating lung graft reperfusion injury. The high viral infection rate requires a change in the anti-viral therapy and prophylaxis.

Il-8 is an unreliable marker of single lung transplantation viability from non-heart beating donor in pigs

Bertolotti A, Gomez C, Lascano E, Negroni J, Cuniberti L, Yannarelli G, Laguens R, Favaloro R

Background: Lung transplantation is limited by organ shortage. An alternative to expand the pool of potential donors is to use grafts from non-heart beating donors. Recently, it has been shown that interleukins 8 and 10 have been proposed as predictors lung viability in lung transplantation (Rao JN et al, Eur J Cardiothor Surg 2003, Gómez CB et al, J Heart Lung Transplant 2005). Likewise, Il-1 has been used for ex vivo assessment of viability in non-heart beating donors (NHBD) in pigs (Rega FR et al, J Heart Lung Transplant 2005). However, the viability in the recipient is unknown.

Objective: The purpose of this study was to assess IL-8 as an indicator of functional performance in left single-lung transplantation from NHBD in pigs. Methods: Young adult pigs were divided in two groups: a) HBD (N=7): the heart-lung block was excised immediately after thoracotomy; b) NHBD (N=10): death was induced by fibrillation, and after 30 min warm ischemia the lungs were topically cooled through thoracic drains during 3 h before harvesting. Thereafter, the same procedure was followed in both groups. Left lungs were flushed with Perfadex and stored at 3-4º C up to a total 3 h ischemic period. The inflammatory markers, IL-8 and IL-10 were measured in basal bronchoalveolar lavage (BAL) in the donor and at 30 and 120 min in the recipient. Hemodynamic and graft functional measurements were performed in the recipient at 0, 10, 30, 60, 90 and 120 min reperfusion. Variables were calculated as percent of basal donor values and expressed as mean of the reperfusion period. Biopsies from the donor right lung and the transplanted left lung were taken to measure myeloperoxidase (MPO) as injury marker and the wet/dry weight ratio (W/D) to estimate edema. Presence of intraalveolar edema, polymorphonuclear nuclei, atelectasis and increase in alveolar wall thickness were scored from 0-4 according to the degree of severity, and the histologic score was obtained adding the points corresponding to each feature of injury.

Results:

Pulmonary function	% Pa/Fi	% PAPm	% PVR	% Cst	% Cdy
HBD	100.2±22.2	104.4±17.9	138.9±80.1	81.7±9.4	88.4±7.4
NHBD	86.8±23.3	115.1±36.7	197.0±128.5	88.9±20.8	89.7±16.4

Pa/Fi: Blood O2 partial pressure/fraction of inspired O2.

PAPm: mean arterial pulmonary pressure.

PVR: pulmonary vascular resistance.

Cst: static lung compliance.

Cdy: dynamic lung compliance.

Mean±SD.

Viability	% IL-8	% IL-10	% MPO	% W/D	Histologic score
HBD	306.2±238.0*	208.5±93.8#	145.9±22.7	133.4±23.6	3.25±1.03
NHBD	119.3±32.8	88.9±35.4	168.3±58.2	172.6±69.9	3.9±2.47

Mean±SD, *P<0.05; #P<0.01 (HBD vs. NHBD, t test).

Conclusions: Similar pulmonary function and histologic score in both groups indicate that 3 h topical cooling following 30 min warm ischemia preserves the graft efficiently and confirms that NHBD and HBD lungs can be employed with a comparable degree of safety. However, IL-8 evidenced a paradoxical result indicating that it does not reliably assess transplantation outcome in these experimental conditions.

Unilateral radiographic abnormalities following bilateral lung transplantation: exclusion from the definition of primary graft dysfunction?

Oto T, Levvey B, Williams T, Snell G

Introduction: Unilateral infiltrates on chest X-ray are occasionally seen after bilateral lung transplantation (BLT). In the Primary-Graft-Dysfunction (PGD) grading system, the presence or absence of a radiographic abnormality is crucial in determining the incidence and severity of PGD. However, no consideration is given as to whether unilateral infiltrates have the same impact and relevance as bilateral infiltrates. This study aims to describe the incidence, features, and outcomes of post-transplant unilateral infiltrates and their effect on the novel PGD grading system.

Method: Depending on post-transplant radiographic appearance, 144 BLTs were divided into 3 groups: no infiltrates (Clear), unilateral infiltrates (Unilateral) or bilateral infiltrates (Bilateral).

Result: Radiographic abnormalities were seen in 43 % of donors and 61 % of post-transplant recipients (sensitivity = 76 %, specificity = 50 %). The percentage of recipients in the Unilateral, Clear, and Bilateral groups was 26 %, 39 % and 35 %, respectively. Lower post-transplant oxygenation ($p< 0.05$), longer intubation hours and ICU days ($p<0.0001$) were seen in the Bilateral compared to that in the Unilateral and the Clear groups. A significant difference in the prevalence of PGD ($p<0.0001$) was seen, depending on whether unilateral infiltrates were included or excluded from the PGD grading.

Conclusion: The incidence of unilateral infiltrates is relatively high after BLT. The early post-transplant outcomes of the unilateral infiltrates are similar to that in the clear chest X-ray group and significantly better than that in those with bilateral infiltrates. In BLT, only bilateral infiltrates should be used as part of the PGD Definition.

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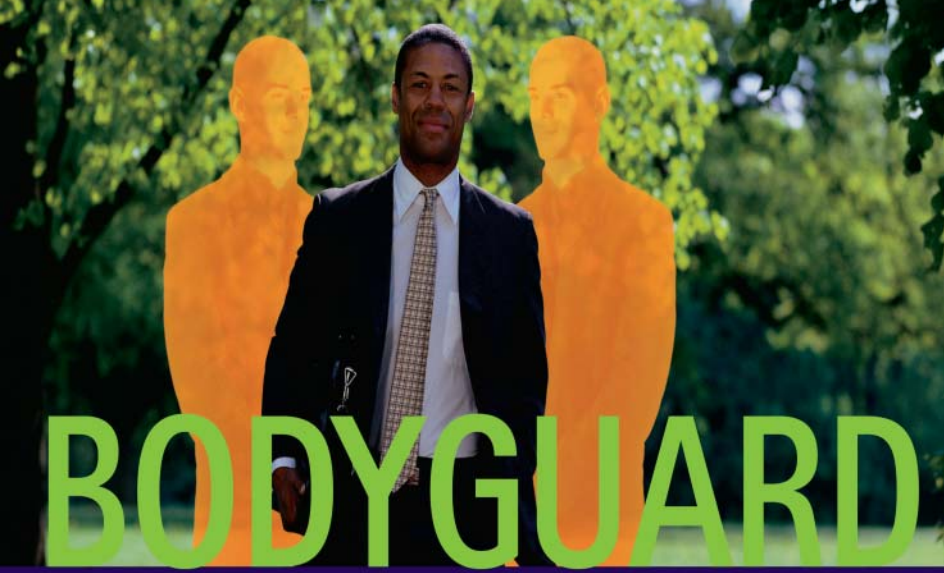

Valcyte effectively protects transplantation patients from the danger of CMV infection and disease in a convenient once-daily oral dose

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Not recommended in patients on haemodialysis (see SmPC). Safety and efficacy have not been established in paediatrics, the elderly or patients with hepatic impairment. **Contraindications:** Hypersensitivity to valganciclovir or excipients, ganciclovir, aciclovir or valaciclovir. Lactation. **Use in Pregnancy and Lactation:** Safety in pregnancy not established. Ganciclovir is a potential teratogen. Use only if benefit to patient outweighs potential risk to the foetus. In women effective contraception should be used during treatment and in men barrier contraception should be used during and for at least 90 days following treatment. Breast-feeding must be discontinued. **Special warnings and precautions:** Potential teratogen, mutagen and carcinogen. May cause suppression of female fertility and temporary or permanent inhibition of spermatogenesis. Severe leucopenia, neutropenia, anaemia, thrombocytopenia, pancytopenia, bone marrow depression and aplastic anaemia may occur. Complete blood and platelet counts should be monitored during therapy especially in patients with renal impairment. Therapy should not be initiated if absolute neutrophil count is less than 500 cells/mL, platelet count less than 25000/mL or haemoglobin level less than 8 g/dL. Dose interruption should be considered if severe bone marrow suppression occurs. The bioavailability of ganciclovir from 900 mg valganciclovir is approximately 60% compared with approximately 6% from 1000 mg oral ganciclovir (as capsules). Valcyte tablets cannot be substituted for ganciclovir capsules on a one-to-one basis. Dose modification required for renal impairment (see SmPC). Convulsions have been reported in patients taking imipenem-cilastatin and ganciclovir. Valcyte should not be used concomitantly with imipenem-cilastatin unless potential benefit outweighs potential risk. Limited experience in lung and intestinal transplant patients. **Undesirable effects:** Effects associated with ganciclovir can be expected with Valcyte. Greater risk of neutropenia and leucopenia with Valcyte compared with oral ganciclovir. Severe neutropenia occurs more frequently in CMV retinitis patients than in solid organ transplant patients during treatment with Valcyte. Diarrhoea occurs more frequently with Valcyte and oral ganciclovir than with IV ganciclovir. Adverse reactions: Very common (>10%); severe neutropenia, anaemia, dyspnoea, diarrhoea. Common (1-10%); oral candidiasis, sepsis, cellulitis, urinary tract infection, severe anaemia, severe thrombocytopenia, severe leucopenia, severe pancytopenia, appetite decreased, anorexia, depression, anxiety, confusion, abnormal thinking, headache, insomnia, dysgeusia, hypoaesthesia, paraesthesia, peripheral neuropathy, dizziness, convulsions, macular oedema, retinal detachment, vitreous floaters, eye pain, ear pain, cough, nausea, vomiting, abdominal pain, dyspepsia, constipation, flatulence, dysphagia, severe hepatic dysfunction, raised alkaline phosphatase, raised AST, dermatitis, night sweats, pruritis, back pain, myalgia, arthralgia, muscle cramps, decreased creatinine clearance, renal impairment, fatigue, pyrexia, rigors, pain, chest pain, malaise, asthenia, weight decreased, raised blood creatinine. See SmPC for uncommon (0.1-1%) adverse reactions. The following adverse reactions have been reported in clinical trials with a frequency ≥5% include; neutropenia, diarrhoea, anaemia, detatitisand nausea. Other adverse reactions with an incidence ≥2% reported during valganciclovir Valcyte clinical trials include; thrombocytopenia, leucopenia, pancytopenia, decreased appetite, weight decrease, depression, anxiety, headache, insomnia, taste disturbance, hypoaesthesis, paraesthesia, peripheral neuropathy, macular oedema, retinal detachment, vitreous floaters, cough, vomiting, oral candidiasis, abdominal pain, abnormal hepatic function, night sweats, pruritus, back pain, fatigue, pyrexia and dizziness (See SmPC for ganciclovir adverse events). **Drug Interactions:** As Valcyte is converted to ganciclovir, interactions associated with ganciclovir will be expected with Valcyte. Probenecid - decrease in renal clearance of ganciclovir, monitor for ganciclovir toxicity. Zidovudine - increase in zidovudine AUC increasing the risk of neutropenia and anaemia. Didanosine - increase in didanosine plasma concentrations, monitor for didanosine toxicity. Mycophenolate Mofetil - potential for increase in MPAG and ganciclovir plasma levels, MPA levels were unaffected, increased risk of neutropenia and leucopenia, monitor FBCs and patients with renal impairment for possible additive toxicity. Zalcitabine – has the potential to cause peripheral neuropathy with ganciclovir. Toxicity of Valcyte may be enhanced when co-administered with drugs that inhibit replication of rapidly dividing cells, e.g. trimethoprim which has myelosuppressive potential, or drugs that might reduce renal clearance of ganciclovir, and concomitant use should only be considered if the potential benefits outweigh the risks. **Overdose:** In the event of overdose, haemodialysis and hydration may be of benefit in reducing blood plasma levels. **Legal Category:** Local information. **Presentation and cost:** Pink, film-coated, convex oval tablets, embossed with VGC and 450. Bottle of 60 tablets local information. **Marketing Authorisation Number:** Local information. **Marketing Authorisation Holder:** Local information. Full prescribing information is available on request. **Date of Preparation:** May 2003.

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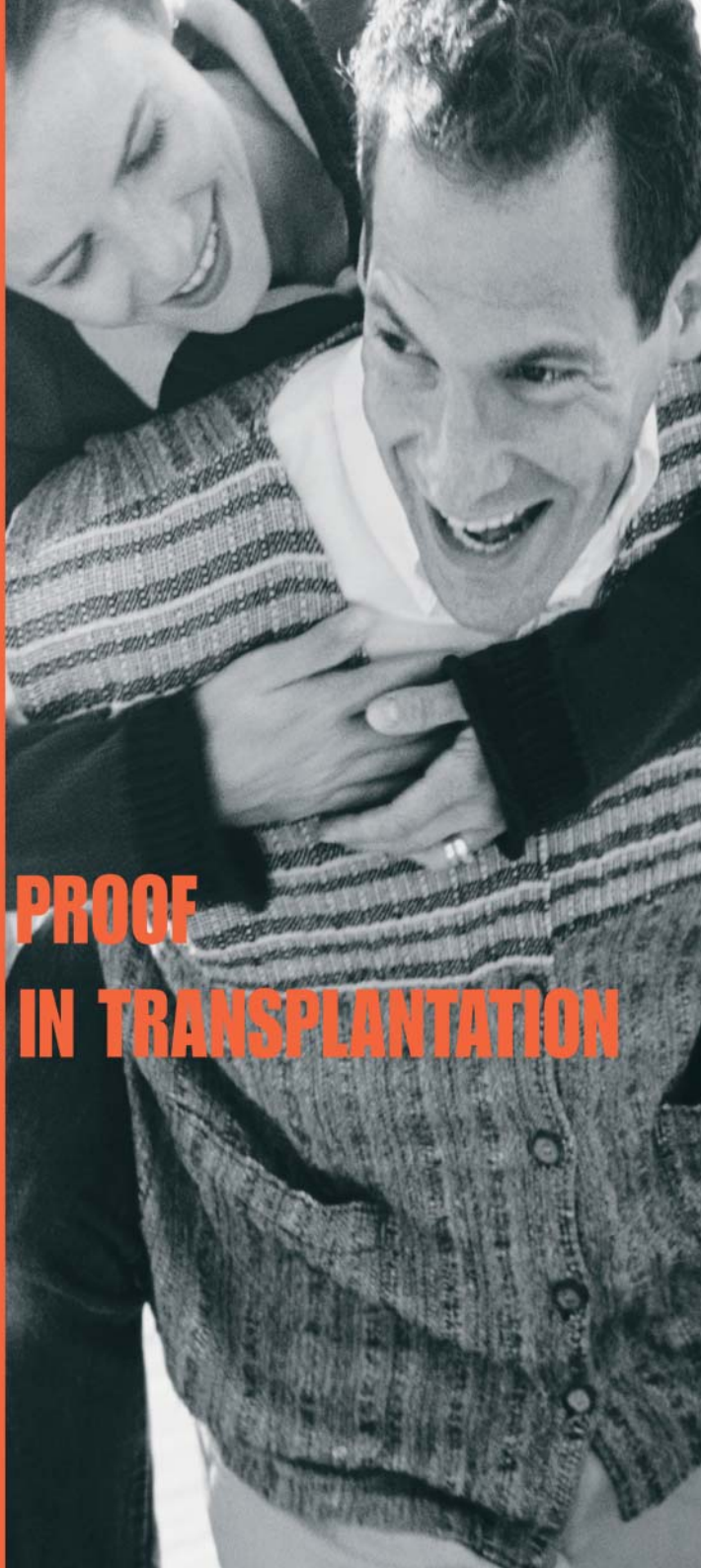

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