269. Lung transplantation

P2437
LSC 2011 Abstract: T helper 17 cell involvement in COPD and lung transplantation patients
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Background: COPD is associated with airway and systemic inflammation and end stage disease is a major indication for lung transplantation (LTx). The novel T helper 17 (Th17) subset was recently implicated in the pathogenesis of COPD and is also associated with allograft rejection. To date, little is known about the cytokine profile of circulating T cells in COPD and LTx patients.

Aim: To determine the cytokine profile of circulating T cells in patients with COPD and in stable LTx patients.

Methods: Peripheral blood mononuclear cells of COPD patients, before and 1 year after LTx and of healthy controls were shortly stimulated in vitro and T cells were analysed by flow cytometry for intracellular cytokine production.

Results: We found no differences in proportions of Th17 cytokines (IL17A, IL22, IL17F) in stable COPD patients when compared to healthy controls. In the LTx patients, proportions of IFNγ and TNFα producing T cells did not differ from those in healthy controls. However, IL22 production by CD4+ and CD8+ T cells was increased in LTx patients. Also, an increase in the proportions of IL17+IL22+ and IL17+IFNγ+ double positive T cells was found in stable LTx patients when compared with healthy controls.

Conclusions: Remarkably, T cells of LTx patients have the capacity to produce high levels of proinflammatory cytokines despite immunosuppressive drug treatment. In particular, IL22+ T cells and specific populations of IL17+ cells co-expressing IL22 or IFNγ are high in LTx patients, while IFNγ and TNFα single positive T helper cells are not increased. These findings indicate that there is no general systemic inflammatory state but that specific Th17-linked subpopulations may play a role in stable LTx patients.

P2438
Comparison between referral and explant diagnoses in lung transplant recipients: Discrepancies and additional findings
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Background: LungTX is an accepted therapeutic option for a range of pulmonary infections, carcinomas (n=10), cystic adenomatoid dysplasia (n=1) and carcinoid (n=1). However, short- and long-term survival was not different in patients with different diagnoses, malignancies or implanted infections. Interestingly all mycobacterial infections and all malignancies occurred in patients with COPD.

Conclusions: On account of this high rate of discrepancies and its possible influence on survival, frequently repeated clinicopathologic investigations should be performed during the waiting list period.

P2439
Mortality in idiopathic pulmonary fibrosis (IPF) on the waiting list for lung transplantation in the Netherlands
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Background: Idiopathic Pulmonary Fibrosis (IPF) is a progressive disease with a poor prognosis of 2.5 to 5 years. IPF is not responsive to medical treatment and lung transplantation is the only therapeutic option to prolong life.

Objective: The aim of this study was to examine waiting list mortality of IPF in the Netherlands.

Methods: Data were retrospectively collected from September 1989 till June 2010 of all IPF patients registered for lung transplantation in the Netherlands. Patients were included after revision of the diagnosis based on the IPF criteria set by the ATS/ERS. Clinical data and lung function measurements were collected at the time of screening.

Results: 167 IPF patients were referred for lung transplantation. After evaluation for contraindications and screening, 90 patients were listed for lung transplantation. During the waiting list period 33.3% of IPF patients (n=30) died compared to 13.8% in Cystic Fibrosis (CF) (p = 0.0018) and 16.3% in Chronic Obstructive Pulmonary Disease (COPD) (p = 0.003). Analysis of lung function showed a mean FVC%-predicted of 51.1% (SD 19.0) and mean DLCO%-predicted of 27.1% (SD 9.4) at time of screening. Five patients were taken off the list due to new comorbidities and deterioration of physical condition, 51 were transplanted and 4 IPF patients were still on the waiting list.

Conclusions: This study revealed a significantly higher waiting list mortality for IPF compared to COPD and CF. DLCO%-predicted at time of screening was considerably lower than international guidelines for lung transplantation. This indicates that timing of referral of IPF for lung transplantation can be improved.

P2440
The impact of resistant bacteria in respiratory secretions on the outcome of lung transplantation
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Introduction: Antibiotic treatment may cause growth of resistant bacteria in respiratory secretions. We assessed the association between antibiotic treatment of lung transplant recipients and acquisition of quinolone resistant gram negative bacteria (QR-GNB), and the impact of such colonization on mortality and lung rejection (BOS).

Methods: We examined data from lung transplant recipients for antibiotic treatment, GNB in respiratory secretions, BOS, and mortality.

Results: 126 patients were included. Median percentage of days with antibiotics was 2.8% in patients with no growth, 11.1% in patients with quinolone sensitive GNB (QS-GNB), and 26% in patients with QR-GNB. Age adjusted mortality hazard ratio was 9.2 (95% CI: 1.27-78.9) for patients with QR-GNB compared with QS-GNB. Age adjusted hazard ratios for BOS were: 3.6 (1.1-11.6) for QR-GNB compared with no growth, and 3.7 (1.33-10.3) for QR-GNB compared with QS-GNB.
P2441 Anxiety, depression and coping in patients awaiting lung transplantation
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Results:
Knowledge is scarce about the mental aspects of living with terminal lung disease. We aimed to assess anxiety, depression and coping in patients waiting for lung transplantation.

Material and methods: A national cohort of 121 consecutive patients were evaluated by psychometric instruments, Hospital Anxiety and Depression Scale (HADS) and General Health Questionnaire (GHQ). 89 (45 females) had COPD, 18 (9 females) fibrosis, and 14 (8 females) various other lung diseases. Mean (SD) age was respectively 56 (5), 52 (6) and 46 (8) years. Patients with cystic fibrosis were excluded.

Results: See table.

For all groups, mean values were within the normal range. However, the ranges were wide. Males tended to be more depressive than females (mean (SD) HAD score 4.1 (3.0) vs 3.1 (2.5), p=0.07), and have higher restrained coping scores than females (mean (SD) GHQ score 1.05 (0.05) vs 0.93 (0.05), p=0.038). The association between anxiety and restrained coping was highly significant, p<0.0001 as well as the association between depression and restrained coping.

Conclusions: Antibiotic treatment was associated with QR-GNB. Airway colonization with QR-GNB was associated with mortality and with BOS. We suggest that narrow spectrum antibiotics should be preferred in lung transplant recipients.

P2442 Significance of a spirometric obstructive pattern immediately after lung transplantation
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Obstructive pattern is associated with earlier development of BOS and might worsen the outcome after double lung transplantation. The OP in association with increase TLC and donor history suggests that the obstruction was of donor origin. Factors like smoking status, age of the donor lung and P/F02 were indicators of a later obstructive pattern in recipients.

P2443 Probe-based confocal laser endomicroscopy in acute lung allograft rejection
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Several aspects of normal alveolar tissue in probe-based confocal laser endomicroscopy (pCLE) have been elucidated: a description of the alveolaroscopic findings in different pulmonary disorders is still largely lacking. In a prospective study, we evaluated 40 lung transplant recipients using probe-based confocal laser endomicroscopy (pCLE) preceding BAL and bronchoscopic biopsy (TBLB). In 6 patients (15%) acute rejection (AR) was diagnosed using TBLB. The recordings of the pCLE images were digitally processed and analyzed for the following parameters: alveolar duct diameter, alveolar elas tine thickness, macrophage diameter, number of macrophages per microscopic field and quantification of the autofluorescence signal of macrophages.

In 5 out of 6 AR cases, a diffuse infiltration of autofluorescent cells with a mean diameter of 26.2±13.3 μm, was recognized in all examined segments. The number of macrophages per microscopic field and their autofluorescence intensity were significantly higher in the AR group than in the non-AR group (p<0.001 and p = 0.03 respectively). In all affected segments there appeared to be more than 100 cells per microscopic field, frequently presenting as clustering cells. The elastin network in the alveolar ducts of AR appeared to be of a normal architecture (alveolar elas tine thickness mean 8.3±4.9 μm, alveolar mouth diameter mean 371±131 μm), and did not differ from the patient group without AR (7.8±3.7 μm and 323±69 μm, respectively).

In the lung transplant recipient group studied, our preliminary findings suggest that pCLE is able to detect an alveolaroscopic pattern that might correlate with AR.

P2444 Frequency and characteristics of prolonged viral shedding of influenza A/H1N1 virus in lung transplant recipients
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Influenza infection may harm lung transplant recipients (LTR) because it potentially triggers allograft rejection. Prolonged viral shedding (PVS) is defined as positive detection of influenza A/H1N1 virus (H1N1) by real-time reverse-transcriptase polymerase chain reaction (RT-PCR) at least 7 days after diagnosis. The aim was to quantify and characterize PVS of H1N1 infections among LTR in consecutive influenza seasons.

Methods: Influenza vaccination is routinely offered at follow-up visits in our outpatient clinic. LTR are also instructed to contact and visit our clinic when signs of infection occur or home lung function deteriorates 10% or more. We then frequently perform nasopharyngeal swabs (NPS) for viral and bacterial analysis. In
Lung transplantation for pulmonary silicosis: The Israeli scene

P2445

Opto-electronic plethysmographic study of the chest volume changes after lung transplantation

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Background: Lung transplantation is the established surgical therapy for pulmonary end-stage disease.

Aims: Even though the pulmonary function after lung transplantation is well studied, the chest volume changes remain uninvestigated. The aim of the present study was to examine such changes by the opto-electronic plethysmography (OEP), a non-invasive technology.

Methods: Seven patients with end-stage pulmonary disease were studied before and after lung transplantation by OEP during quiet and forced breathing. Standard pulmonary function tests were also obtained. Three patients with pulmonary fibrosis had single lung transplantation and four patients with cystic fibrosis had bilateral.

Result: The functional tests demonstrated increasing in pulmonary function (e.g. FEV1% from 44±15 to 83±6). After bilateral transplantation, the OEP revealed a volume rearrangement: a decrease was noted in functional residual capacity (FRC: -2.14±1.3L), in vital capacity (-1.1±1.1L), in total lung capacity (-2.59±1.6L). The chest wall volume reduction was different in the upper thorax, lower thorax and abdominal compartment (e.g. FRC: -0.68L, -0.13L, -1.59L respectively). After single lung transplantation the pattern was similar but less evident.

Conclusions: This first, preliminary, study of the chest wall volume changes reveals a rearrangement of such volumes after single or double lung transplantation. Facing the dramatic improvement in spirometric value, OEP recorded a decrease in volume parameters; such decreases were inhomogeneous through the different thoracic compartments.

P2446

Lung transplantation for pulmonary silicosis: The Israeli scene

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Background: Silicosis is a rare indication for lung transplantation (LT). The number of patients with silicosis in Israel is increasing due to improper processing of a new quartz stone Caesartone.

Methods and materials: We retrospectively reviewed the files of patients that were transplanted in Rabin Medical center (RMC) and compared the data to that of the ISHLT.

Results: According to the ISHLT registry out of 24,090 transplants 50 patients were transplanted for Silicosis between 1994-May 2009. Out of 336 lung transplantations in RMC between 1997- 2010 8 patients underwent LT for silicosis. There were more patients transplanted for silicosis in RMC compared to the ISHLT (p=0.01).

All of our patients were men, their average age being 50.5. Four underwent left LT and 1 bilateral sequential LT. Before transplantation their average FEV1 and DLCO were 298.9 and 28.58, one patient was treated with ECMO. In all the patients the native lung extraction was difficult because of severe pleural adhesions. Three patients died, due to technical failure, recurrent pneumothorax, and recurrent infections. Three patients had intra-operative bleeding, one of them needed a second operative procedure.

Post operative complications also included severe infections in 3 patients, severe primary graft dysfunction in 2 patients, injury to the phrenic nerve and diaphragm paralysis in 2 patients. According to the ISHLT 6 of 36 patients needed additional surgical procedure, and 20 out of 39 were treated for infection.

Conclusions: Compared to the ISHLT registry, in Israel there are more transplantations for silicosis. LT in patients with silicosis is technically difficult with higher morbidity and mortality.
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**P2450**

The use of extracorporeal membrane oxygenation (ECMO) in severe delayed graft dysfunction after lung transplant

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**Introduction:** Delayed graft dysfunction is an uncommon but serious complication in the first few days following successful lung transplantation and is associated with significant mortality. ECMO has been used in initial graft dysfunction with some success, but there have been few studies on its use in delayed graft failure.

**Objectives:** To review the experience of using veno-venous (V-V) ECMO in patients with delayed graft dysfunction at Harefield Hospital from January 2010 to January 2011.

**Methods:** A retrospective review of five cases of severe delayed graft failure requiring V-V ECMO was carried out.

**Results:** Five cases of lung transplant were COPD (2 patients), hypersensitivity pneumonitis (2 patients), pulmonary fibrosis and alpha-1 antitrypsin deficiency. Four patients (80%) were eventually discharged from hospital and are currently well with stable lung function and good functional status. One patient (20%) died 112 days after ECMO explantation. Mean transplant to implantation date was 11±9.1 days. Mean PatO2/FiO2 ratio was 9.9±3.8 kPa on mechanical ventilation. All patients had initial extensive bilateral pulmonary infiltrates on chest radiograph or HRCT scan. Three patients had abnormal radiological changes that persisted after discharge. Mean duration of ECMO support was 9.2±2.7 days. Only one patient had positive microbiology – rhinovirus on viral PCR. Mean length of stay in ITU was 56.2±30.0 days. Mean length of stay in hospital was 90.8±25.3 days.

**Conclusion:** In severe delayed graft dysfunction refractory to mechanical ventilation, a short period of V-V ECMO can be highly effective in supporting patients during recovery of acute lung injury.

**P2451**

Validation of a non-invasive CO measurement in an isolated lung model

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**Introduction:** Carbon Monoxide (CO) is a key mediator in ischemic - reperfusion injury. Its role as a potential diagnostic and therapeutic target in organ transplant is increasing. We tried to validate a new CO measurement on isolated perfused and ventilated lungs.

**Methods:** After euthanasia, swines lungs (n=2, 19.5±0.1 kg) were removed. Trachea was intubated and the pulmonary artery was linked to an extracorporeal membrane oxygenation. Lungs were then progressively ventilated and perfused to a steady state (tidal volume 8ml/kg, respiratory rate 15/min, PEEP 5mmHg and cardiac output 70ml/kg/min). CO measurements were made by Optical-Feedback Cavity-Enhanced Absorption Spectroscopy. This laser based technique allows non-invasive and real time measurements with high sensitivity (0.002ppm). We measured gas taken directly from the end of the trachea. To validate our model, we compare our CO cavity peak with the CO level in air and in ventilated lungs.

**Results:** CO peak was obtained during expiratory phase and initial average CO concentration thanks to mixed gas injection in the ambient air. A MRI was repeated two weeks later, documenting a significant improvement both of the cerebral and the occipital-parietal and frontal regions of the brain; a minor alteration was also present in the thalamus. ADC (i.e. Apparent Diffusion Coefficients) mapping showed wide areas of vasogenic and cytotoxic edema.

**Conclusion:** We here describe a case of PRES in a 26-year-old woman, 5 days after she received bilateral lung transplantation for cystic fibrosis. She had been administered tacrolimus since the transplantation was performed. While in ICU, she suddenly developed mental status alterations, acute pulmonary deterioration and hypercannia, with need of mechanical ventilation. A head CT scan and MR were performed, detecting subcortical white matter lesions and patchy, bilaterally symmetric areas of abnormally increased signal on the T1-weighted images within the cerebellum and the occipital-parietal and frontal regions of the brain; a minor alteration was also present in the thalamus. ADC (i.e. Apparent Diffusion Coefficients) mapping mapped wide areas of vasogenic and cytotoxic edema.

**P2452**

BODE index as a predictor of survival in lung transplantation

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**Introduction:** Chronic obstructive pulmonary disease (COPD) is one of the most frequent indications for lung transplantation (LTx), but survival benefit is still under debate. We analysed the survival impact of LTx in COPD using the BODE (body mass index, airway obstruction, dyspnea, exercise capacity) index.

**Aims:** The aim of our study was to analyse the survival impact of lung transplantation in COPD patients. We compared the post-transplant survival with the survival predicted by the BODE index as measured during pre-transplant clinical evaluation.

**Methods:** Retrospective review of 59 consecutive lung transplants performed for COPD in our centre between June 1st 1999 and December 30th 2010. The pre-transplant BODE score was calculated for each patient. Predicted and observed post-transplant survival was then compared.

**Results:** 59 COPD patients were analyzed. Mean age was 57±6 years, 51 (86%) men, 52 (88%) patients had a BODE ≥ 7 and 7 (11.9%) <7. The overall survival time was 70.82 months ±8.1. BODE <7 had a overall survival time of 19.5 and BODE ≥ 7 was 73±2.8±6. In the subgroups with a BODE score ≥7 and <7, the 4-year survival was 57±4.18 and 57±5.08 respectively.

**Conclusions:** The results of this study showed a significant survival benefit of LTx in our cohort of COPD patients. Patients with BODE ≥7 will be the ones who benefit the most from the procedure.

**P2453**

Early development of posterior reversible encephalopathy syndrome post lung transplantation

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**Introduction:** Tacrolimus is a calcineurin inhibitor and has been proven highly effective in preventing graft rejection after transplantation of solid organs. Its major adverse effects are nephrotoxicity and neurotoxicity: the most severe form of the latter is PRES (Posterior Reversible Encephalopathy Syndrome). We here describe a case of PRES in a 26-year-old woman, 5 days after she received bilateral lung transplantation for cystic fibrosis. She had been administered tacrolimus since the transplantation was performed. While in ICU, she suddenly developed mental status alterations, acute pulmonary deterioration and hypercannia, with need of mechanical ventilation. A head CT scan and MR were performed, detecting subcortical white matter lesions and patchy, bilaterally symmetric areas of abnormally increased signal on the T1-weighted images within the cerebellum and the occipital-parietal and frontal regions of the brain; a minor alteration was also present in the thalamus. ADC (i.e. Apparent Diffusion Coefficients) mapping mapped wide areas of vasogenic and cytotoxic edema.

**Conclusion:** In our model, CO arises during expiratory phase and its concentration is not changed by low or high CO level in ambient air. Thus, we are able to quantify CO produced by the lungs.

**P2454**

Lung transplantation in Portugal: 2008-2010 results

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**Introduction:** Lung transplant is the final therapeutic option for patients with end stage lung disease, to whom no other therapeutic is available.

**Purpose:** Evaluation of a lung transplant center results.

**Material and methods:** The authors reviewed the results of all patients to lung transplantation at the only center in Portugal, between 2008-2010 (after reorganization of the program). Demographic data, diagnosis at referral, time on waiting list and survival at first year were analyzed.

**Results:** Twenty five patients were submitted to a lung transplant (72% male), with a medium age of 43.3 years (range 17 to 63). Ten procedures were bilateral and 15 unilateral. Twelve patients had terminal lung fibrosis, five cystic fibrosis, three COPD, three bronchiectasis and two had silicosis. The average time on waiting list

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was 181 days and 20% of these patients were on mechanical ventilatory support (invasive or non-invasive) at the time of transplantation. Six patients died (5 in the first month after procedure). The 1 year survival rate was 78.4% (Kaplan-Meier curves).

Conclusion: After reorganization in 2008, the Portuguese Lung Transplantation program results are comparable to the results published by the International Society of Heart and Lung Transplantation.

P2455
Characterization of a population referred to a lung transplantation centre in Lisbon
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Introduction: Lung transplantation is the therapeutic option for patients with end stage lung disease. An appropriate referral contributes to a better post surgery survival.

Purpose: Characterization of the patients referred to the only lung transplantation centre in Portugal.

Material and method: The authors evaluated patients referred from January 2008 to December 2010. The following data was determined: demographics, lung disease and evaluation result. Reasons for refusal were also analyzed.

Results: A total of 199 patients were referred (61% male), with an average age of 45.5 years (range 11 to 69). Thirty per cent had the diagnosis of terminal lung fibrosis, 21% COPD, 13% cystic fibrosis, 12% bronchiectasis and the last 23% other diagnosis. After evaluation 24.6% of patients were accepted (49 patients, 25 of which already transplanted and 5 died on waiting list) and 45.3% were refused, mostly due to severe cardiac impairment or very poor general condition. Of the remaining patients, 9.5% are under current evaluation, 6.5% present a relative contraindication and 5% still don’t meet criteria for transplantation.

Conclusion: Despite the considerable number of patients referred, only 45.7% were eligible for lung transplant. The important number of patients refused due to medical contraindications should alert the attending physicians for an earlier referral.

P2456
Effect of BIPAP on diaphragm paralysis after single lung transplantation
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Diaphragm is a chief muscle of inspiration and its unilateral or bilateral paralysis can lead to dyspnea and affect ventilator function. Here, we are reporting management of an emphysematous patient who is undergone single lung transplant and was suffering from diaphragmatic paralysis.

A 53 year old male emphysematous patient was transplanted in 2009 and had no significant complication after transplantation. He was admitted 3 months and 9 months after transplantation due to acute rejection and received corticosteroid pulse therapy which the results were acceptable. 14 months after transplantation an elevated hemi diaphragm on chest x-ray was suggestive of diaphragmatic paralysis which was confirmed by paradoxical upward movement of right hemi diaphragm during fluoroscopic imaging. He had dyspnea with minimal exercise, reduced pulmonary function test (FVC from 63% to 38%) and oxygen saturation fall to 75% in rest without any oxygen supplement. Considering hypoxia and CO2 retention, polysomnography was performed to look for sleep apnea. Patient apnea hypopnea index (AHI) was 17 with 5 hypopnea, 5 central and 7 obstructive sleep events. After titration test, bi-level positive airway pressure apparatus (BIPAP) (PE=15, PEl=11, st back up=14) was administered by oronasal mask. Although the authors worried about over expansion of high compliance emphysematous native lung with using BIPAP, pulmonary function test result improved significantly (FVC from 38% to 58%) and oxygen saturation during exercise increased to greater than 88% dramatically without expanding the native lung. We claim that BIPAP could be recommended for management of these patients without any considerable side effects.

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