Lung Transplantion: Indications in 2016

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SSP/SSC Lausanne 2016
Adult Lung Transplants
Number of Transplants by Year and Procedure Type

- **Bilateral/Double Lung**
- **Single Lung**

Number of Transplants by Year:
- 1985: 0
- 1986: 0
- 1987: 0
- 1988: 0
- 1989: 0
- 1990: 0
- 1991: 0
- 1992: 0
- 1993: 0
- 1994: 0
- 1995: 0
- 1996: 0
- 1997: 0
- 1998: 0
- 1999: 0
- 2000: 0
- 2001: 0
- 2002: 0
- 2003: 0
- 2004: 0
- 2005: 0
- 2006: 0
- 2007: 0
- 2008: 0
- 2009: 0
- 2010: 0
- 2011: 0
- 2012: 0
- 2013: 0

The chart shows the number of adult lung transplants from 1985 to 2013, with a significant increase in the latter years.
CURT: 2004-2015 (n=200)

Zurich (USZ: 2004-2015, N=316)
Specific constraints for organ transplantation from a deceased donor

• Limited availability of the treatment
• Unknown time frame
• Non reversible therapy
• A disease is replaced by another one
• Quality control of the therapy = the organ?
Questions raised about a lung transplant candidate

- Life expectancy with standard of care?
- Life expectancy after transplantation?
- Expecting time on the waiting list?

- Complete work-up. Predictive equation of survival
- Comorbidities. Local results, international data
- Allocation system
- Height, blood group
Indications
General indications: consensus

• Chronic and progressive lung disorders
• Failure of established therapies (pharmacological, surgical and others)
• The main goal of lung tx is to give the patient a survival benefit

Practical case 1

- 63 yr-old woman
- COPD since 1998
- Presently GOLD IV, FEV1 23% pred.
- 2010: mechanical ventilation in the ICU for acute exacerbation
- 2-3 exacerbations/year
Case 1 (continued)

Actual treatment:
Acide folique 5mg 2X/semaine,
calcium Sandoz D3 1cpr 2Xj,
Neo-mercazole 5mg 1Xj,
Solmucol 600mg 1Xj,
Zithromax 250mg 3Xsemaine,
Seretide 1 dose 2Xj, Spiriva 0.018mg/j,
lisinopril 10 mg/j,
Nexium 20 1xj,
lexotanil 1,5 mg en R,
prednisone 10 mg 1x j à sevrer progressivement,
Ensure plus 2xj,
Would you refer this patient to a LuTx Centre?

1. Yes
2. No
3. I need further information
Would you refer this patient to a LuTx Centre?

1. Yes

2. No

3. I need further information
Check list before LuTx referral (COPD)

- BODE Index ?
- Smoking abstinence ?
- Rehabilitation attended ?
- Previous thoracic surgery ?
- Any obvious comorbidity/ risk factor ?
Check list before LuTx referral (COPD)

- BODE Index? 7/10
- Smoking abstinence? Yes, since 9 years, verified
- Rehab attended? Yes, in and outpatient
- Previous thoracic surgery? Yes, right thoracotomy for suspicion of cancer dg: COP
- Any obvious comorbidity/ risk factor? Hypertension, Hypothyroid, Osteoporosis
COPD

**TX referral**
- BODE > 5
- Worsening despite therapy
- PaCO₂ > 50 mmHg
- PaO₂ < 60 mmHg
- FEV1 < 25% of PV
- LVRS not feasible

**Listing**
- BODE ≥ 7
- FEV1 < 20% (DLCO < 20% or homogenous emphysema)
- > 3 hospitalisations/yr
- Severe Exacerbations with acute hypercapnic resp failure
- PH > 35 mmHg mPAP

Case 2

- 30 years old, female
- Cystic fibrosis (CF) (ΔF508/G542X)
- CF-associated chronic sinusitis
- CF-associated arthritis
- Exocrine pancreatic insufficiency
- FEV$_1$ before transplantation: 1.14L (34%)
- Respiratory failure 02. March. 2012
Transplantation Window of Opportunity:
ideal world and the reality

*Chest*. 1990. 

“Transplant window”

Too Soon

Too Late

Clinical course vs. Time
Cystic fibrosis

Referral

• FEV1 < 30% or fast ↓ c/o patient infected with par NTM, B Cepacia Complex and/or diabetes
• 6’mwt:<400m
• PH MPAP>35 mmHg
• Clinical deterioration with:
  - NIV
  - ↑ exacerbations: ATB+ R
  - pneumothorax
  - recurrent hemoptysis despite embolisation

Listing

• Respiratory failure:
  - PaO₂ < 60 mmHg
  - PaCO₂ > 50 mmHg
• NIV
• PH
• Frequent hospitalisations
• Fast ↓ PFT
• World Health Organisation Functional Class IV

Cystic Fibrosis

Impact of the new medications (Ivacaftor, lumacaftor) on listing?

No data so far
Case 3 Sarcoïdosis stage IV

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<tr>
<th></th>
<th>mesuré</th>
<th>predit</th>
<th>% predit</th>
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<tbody>
<tr>
<td>FEV1</td>
<td>1.54</td>
<td>3.35</td>
<td>46</td>
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<tr>
<td>FVC</td>
<td>2.15</td>
<td>4.19</td>
<td>51</td>
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<tr>
<td>TLC</td>
<td>3.77</td>
<td>6.74</td>
<td>56</td>
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<tr>
<td>DLCO</td>
<td>4.5</td>
<td>9.6</td>
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Weigth/Heigth: 96 kg 175 cm BMI: 31 kg/m2

**Lungs**

NYHA: III

PaO₂ 62 mmHg SaO₂ 88% PaCO₂ 24 mmHg

6 mwt: 270 mètres : SaO₂ : 90 ( 4lt d’O2) Borg : 5 (2)
Would you refer this patient for Lung Tx evaluation?

- No, sarcoïdosis has a slow mostly benign course
- No, I would first try anti-TNF and Cellcept
- I do not know
- Yes, this patient is at high risk
Would you refer this patient for Lung Tx evaluation?

- No, sarcoïdosis has a slow mostly benign course
- No, I would first try anti-TNF and Cellcept
- I do not know
- Yes, this patient is at high risk
Because sarcoidosis tends to have a chronic and variable natural course, the optimum timing to refer a patient for transplantation is difficult to define. Factors

RISK FACTORS
• African-American
• Hypoxemia
• Pulmonary hypertension with high RAP
Case 3 sarcoidosis

RISK FACTORS

• African-American
• Hypoxemia
• Pulmonary hypertension

• No
• Yes: SaO2 88%
• No: mPAP 17 mmHg
## Case 3 Sarcoïdosis stage IV

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- **poids/taille:** 96 kg 175 cm
- **BMI:** 31 kg/m²

**Lungs**
- **NYHA:** III
- **PaO₂:** 62 mmHg  **SaO₂:** 88%  **PaCO₂:** 24 mmHg

- **6 mwt:** 270 mètres : **SaO₂:** 90 (4lt d’O₂)  **Borg:** 5 (2)
Contra-indications
Contre-indications absolues (1)

• Cancer avec rémission < 2 ans
• Dysfonction grave d’un autre organe: cœur, rein, foie...
• Athérosclérose avancée
• Instabilité hémodynamique
• Troubles sévères de la coagulation
• Infection non contrôlée à germes résistants, tuberculose active
Contre-indications absolues (2)

• Déformation thoracique sévère
• Obésité avec BMI >35 kg/m²
• Non adhérence thérapeutique « réfractaire »
• Maladie psychiatrique invalidante
• Absence de tout soutien social
• Fragilité (frailty) rendant une récupération post greffe hypothétique
• Tabagisme dans les 6 derniers mois, toxicomanie
The impact of BMI

A

Adjusted risk of death at 1 year

Body mass index at transplantation, kg/m²

p = 0.02
nonlinear p = 0.02

B

Adjusted risk of death at 5 years conditional on 1 yr survival

Body mass index at transplantation, kg/m²

p = 0.35
nonlinear p = 0.04
How to deal with smokers?
Substance abuse or dependence (e.g., alcohol, tobacco, marijuana, or other illicit substances). In many cases, convincing evidence of risk reduction behaviors, such as meaningful and/or long-term participation in therapy for substance abuse and/or dependence, should be required before offering lung transplantation. Serial blood and urine testing can be used to verify abstinence from substances that are of concern.
Practical attitude (CURT)

- TX work-up only when $\geq 6$ months abstinence
- When abstinence is $< 2$ yrs, and in fragile patients, a specialized consultation is requested
- Ex-smokers are informed that unscheduled tests will be performed (cotinine, anabasine, CO ex)
Zurich Experience (Jan 2007 – Oct 2013, N=26)

Inci I et al. Transplantation, 2015
Extracorporeal Membrane Oxygenation in Awake Patients as Bridge to Lung Transplantation

Thomas Fuehner, Christian Kuehn, Johannes Hadem, Olaf Wiesner, Jens Gottlieb, Igor Tudorache, Karen M. Olsson, Mark Greer, Wiebke Sommer, Tobias Welte, Axel Haverich, Marius M. Hoepfer, and Gregor Warnecke

A

Secondary intubation (n=7)

Died on ECMO (n=6)

Successful bridging to LuTx (n=4)

Died after LuTx on ICU (n=3)

Discharged from hospital (n=3)

Awake ECMO to LuTx group (n=26)

Not intubated (n=19)

B

Intubation to LuTx group (n=34)

Died before LuTx (n=10)

Successful bridging to LuTx (n=24)

Died after LuTx on ICU (n=12)

Discharged from hospital (n=12)

Secondary ECMO (n=4), Secondary ECLA (n=14)

Survival

Time (days)

Am J Respir Crit Care Med  Vol 185, Iss. 7, pp 763–768, Apr 1, 2012
Copyright © 2012 by the American Thoracic Society
Case 4: COPD

• 63 year-old male
• 170 cm, 60 kg,
• BMI: 21 kg/m2
• 150 py (gave up 2001)
• CT Thorax: Diffuse emphysema

• September 2008:
  FEV1 0.78 L(26%),
  TLCO 21%
  PaO2 7.67 kPa
  PaCO2 4.61 kPa
  mPAP : 29 mmHg
  6MWT: 375 m
  Lung perfusion: r/l:34%/66%
Case: LVRS bridge to TPL

• 18.12.2008: LVRS rechts
• Listed for TPL: 08/2011
  (68kg, BMI:23.5 kg/m2)
    – FEV1:24%
    – TLCO: 15%
    – mPAP: 21 mmHg
Case: LVRS bridge to TPL

- 02/2012: bilateral lung transplantation
- 68 years old
- 38 months after LVRS
- Survived 3 years (37 months)
- Cause of death: CLAD
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</table>
| 5. Age | If the donor age is less than 40 years then recipients less than 40 years old are privileged.  
D.Age < 40 Years AND R.Age < 40 Years  
Otherwise (No age privilege). | EDI 8.1 c  
EDI 8.2 | 1 |
| 6. Pulmonary Fibrosis | Recipients with pulmonary fibrosis are privileged.  
R.HasPulmonaryFibrosis = Yes  
Otherwise (recipients without pulmonary fibrosis). | EDI 8.1 d | 1 |

Following priority levels must be applied for urgent and non-urgent recipients, but for urgent recipients these rules have to be applied as second priority if the most urgent recipient can’t be determined.

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<tbody>
<tr>
<td>7. Multi Transplant</td>
<td>Recipients who need the lung and at least one more other organ are privileged.</td>
<td>EDI 9.1.a</td>
</tr>
<tr>
<td></td>
<td>Otherwise (recipients who need only the lung).</td>
<td></td>
</tr>
</tbody>
</table>
| 8. ECMO | Recipient with an ECMO are privileged  
R.ECMO = Yes AND R.Urgent = Yes  
Otherwise (no ECMO) | EDI 9.1c | 1 |
| 9. O, B Blood group priority | Recipient of blood group O or B are privileged if the donor blood group is O.  
D.BloodGroup = 0 AND R.BloodGroup ∈ \{0,B\}  
Otherwise (No O, B blood group priority). | EDI 9.1.b | 1 |
| 10. Wait time | Recipients with the longest wait time are privileged.  
For urgent recipient the wait time is calculated from the date the recipient is urgent. For non-urgent recipient the waiting time is calculated from the date the recipient has been set on the waiting list.  
w.t = Wait time in days for the lung | EDI 9.1.c  
EDI 3 | 9999-wt |
Interstitial lung disease

Timing of referral:

- Histopathologic or radiographic evidence of usual interstitial pneumonitis (UIP) or fibrosing non-specific interstitial pneumonitis (NSIP), regardless of lung function.
- Abnormal lung function: forced vital capacity (FVC) <80% predicted or diffusion capacity of the lung for carbon monoxide (DLCO) <40% predicted.
- Any dyspnea or functional limitation attributable to lung disease.
- Any oxygen requirement, even if only during exertion.
- For inflammatory interstitial lung disease (ILD), failure to improve dyspnea, oxygen requirement, and/or lung function after a clinically indicated trial of medical therapy.
Timing of listing:

- Decline in FVC $\geq 10\%$ during 6 months of follow-up (note: a 5\% decline is associated with a poorer prognosis and may warrant listing).
- Decline in D\textsubscript{L}CO $\geq 15\%$ during 6 months of follow-up.
- Desaturation to < 88\% or distance < 250 m on 6-minute-walk test or $> 50$ m decline in 6-minute-walk distance over a 6-month period.
- Pulmonary hypertension on right heart catheterization or 2-dimensional echocardiography.
- Hospitalization because of respiratory decline, pneumothorax, or acute exacerbation.
Lung transplantation and disease recurrence

- CF: No
- COPD: No time enough!
- Sarcoidosis: Yes - benign
- IPF: Very rare
- LAM: Yes
- Histiocytosis X: Yes - severe
Spare case if time permit

- A1AT deficiency, born 1949
- Listed for double lung Tx in nov 2008
- Blood group 0. 186 cm 61 kg
- January 2012, still on the waiting list!
- Meanwhile: dyspnea III $\rightarrow$ IV
  New hypercapnia
  Increase in oxygen need
  But no admission in emergency
Case 5 continued

• The patient:
  « Doctor, am I still on the waiting list? Why so many patients listed after me have already been transplanted? »

• The referring pulmonologist:
  « John-David, I know you are a nice guy: can you please push up my patient on the list; he deserves it »
SOAS = Swiss Organ Allocation System

- when donor < 40 yrs: priority to recipient < 40 yrs

= invasive mechanical ventilation in the ICU
Benchmarking

- Wait time (weeks)
- Survival on wait list
- 1 year survival
- 3 year survival
- % lung used
- LTX/107

- ABM
- SwissTX
- UNOS
In conclusion

• BPCO, Mucoviscidose et Fibrose sont les principales indications à la TX pulmonaire
• Les critères pour adresser le patient à un centre de TX diffèrent selon les pathologies
• La TX pulmonaire est une forme de traitement avec un rationnement explicite
# Equations de prédiction de survie (préTX)

<table>
<thead>
<tr>
<th>Maladie</th>
<th>Nom/paramètre</th>
<th>Auteurs</th>
<th>Validation prospective</th>
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</thead>
<tbody>
<tr>
<td>COPD</td>
<td>BODE</td>
<td>Celli 2004</td>
<td>oui</td>
</tr>
<tr>
<td>Mucoviscidose</td>
<td>Âge, sexe, FEV1, pancréas, infections</td>
<td>Liou 2001</td>
<td>Oui (ped + adulte)</td>
</tr>
<tr>
<td>Hypert. Art. Pulm.</td>
<td>mPAP, OD, CI</td>
<td>Thenapan 2010</td>
<td>non</td>
</tr>
<tr>
<td>IPF</td>
<td>Composite physiological index Path, DLCO, FEV1,FVC</td>
<td>Wells 2003</td>
<td>non</td>
</tr>
</tbody>
</table>
**Mucoviscidose:**
VEMS < 30% ou ↘ rapide du VEMS
NTM, B Cepacia Complex et/ou avec diabète
Augmentation des exacerbations/hosp:AB +R
Pneumothorax/Hémoptysies
6':<400m

**BPCO:**
BODE > 5
Évolution progressive malgré ttt
PaCO₂ > 50 mmHg
PaO₂ < 60 mmHg
VEMS < 25% de la VP

**Pneumopathie interst.:**
Evidence Rx ou histol NSIP/UIP
CVF < 80% de la VP ou DLCO < 40% de la VP
Dyspnée ou limitation fct liée à la maladie interstitielle
O₂ pendant pas au ttt

**Référer à centre de Tx**

**Maladies vasc pulm:**
NYHA III-IV
Maladie progressant rapidement
Ttt iv
Susp- maladie veino occlusive
Susp- maladie veino capillaire