Lung Transplantation: Who to Refer? How to Refer?

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Success
Just Ahead
Who to Refer? How to Refer?

• Transplant activity

• Transplant indications and outcomes

• Guidance on selection of candidates

• The Assessment Process
Adult and Pediatric Lung Transplants
Number of Transplants by Year and Procedure Type
Adult Lung Transplants
Major Indications By Year (Total Number)
Adult Lung Transplants Kaplan-Meier Survival by Diagnosis (Jan 1990 – June 2011)
Optimal Use of a Scare Resource
Selection of Candidates
A Balance of Risks

Mortality Risk from Lung Disease
Impairment in Quality of Life

Operative Mortality Risk
Risk of post-operative morbidity
Chance of long term survival
The Transplant Window

- Functional Status / Disease Severity
- Time in years

Transplant Window

A

B

Death
Assessment Pathway

Evaluation of Referral by Consultant Lung Transplant Physician

Discussion at MDT

Out –patient Assessment

In-patient Assessment

Declined for Transplant
Transplant Assessment

1. Does the patient require a transplant?
2. Is the patient physiologically/physically strong enough to survive a transplant?
3. Which operation and when, what degree of risk?
4. Does the patient want a transplant?
International Guidelines

- General Guidance
- Disease-Specific Guidance
- Contraindications

A consensus document for the selection of lung transplant candidates: 2014—An update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation

J Heart Lung Transplant 2015;34:1–15
ISHLT General Guidance

- Advanced lung disease (WHO III/IV)
- Refractory to maximal medical therapy
- No other appropriate surgical option

- High (>50%) risk of death from lung disease within 2 years if lung transplantation is not performed.

- High (>80%) likelihood of surviving at least 90 days after lung transplantation.

- High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function.
Absolute Contraindications

• Current smoking (min 6 months abstinence)
• Serious dysfunction of kidney or liver
• Active extrapulmonary infection
• Uncontrolled systemic disease (physical or psychiatric)
• Substance Abuse including drugs and alcohol
• Active Malignancy (min 2-5 years disease free)
• Progressive neuromuscular disease
• Acute medical instability
• Poor rehabilitation potential
• Absence of adequate support social support network
• Current non-adherence to treatment
• BMI>35
Relative Contraindications

• Any other uncontrolled disease process
• Oral corticosteroids >20mg daily
• BMI <18 or >30
• Established osteoporosis
• Pan-resistant organisms or invasive fungal disease
• HIV / Hepatitis B or C infection
• Poor compliance or psychological adjustment
• Age >65
Possible outcomes of assessment

1. Currently above the threshold for consideration – to be followed up closely by local +/- transplant team
2. Suitable – onto active waiting list
3. Suitable but issues to resolve
4. Currently above the threshold for consideration – re-refer when indicated
5. Not suitable due to contraindications being identified
Recipient Age Distribution
Jan 1985 – June 2012
Recipient Age Distribution by Era

1985-1989 (N=327)
1990-1994 (N=4,413)
1995-1999 (N=6,971)
2000-2005 (N=11,782)
2006-6/2012 (N=19,930)

% of Transplants

Recipient Age

18-24 25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-65 >65

JHLT. 2013 Oct; 32(10): 965-978
Age as a Risk Factors For 1 Year Mortality
Hazard Ratio (95% Confidence Limits)

Recipient Age

Hazard Ratio of 1 Year Mortality

p < 0.0001

2013 Oct; 32(10): 965-978
Lung Transplant Survival Advantage for IPF

Thabut et al J Thor Cardio Vasc Surg 2003; 126(2):469
Pulmonary Fibrosis
Disease Specific Guidance

Referral Criteria:
• Fibrotic NSIP on biopsy or UIP on CT or biopsy
• FVC <80% predicted
• TLCO <40% predicted

Listing Criteria:
• Desaturation $\text{SpO}_2 < 88\%$ or <250m in 6 min walk test
• >15% fall in TLCO in 6 months
• >10% fall in FVC in 6 months
• Pulmonary Hypertension on RHC or Echo
• Hospitalisation due to lung disease
IPF Recipient Age Distribution

Number of >65:
2000-2005 = 138
2006-6/2012 = 1,061
Survival for IPF Lung Transplant Recipients by Age Group (Jan 1990 – June 2011)

Survival (%)

Years

0 1 2 3 4 5 6 7 8 9 10

Survival (%)

IPF 18-49 (N=1,936)
IPF 50-65 (N=5,582)
IPF >65 (N=1,010)
IPF Recipient Age
as a Risk Factors For 1 Year Mortality

Hazard Ratio of 1 Year Mortality vs. Recipient Age

$p < 0.0001$
Survival by Diagnosis and Age Group Conditional on Survival to 3 Months

Survival (%) vs Years

COPD 18-49 (N=1,750)
COPD 50-65 (N=8,985)
COPD >65 (N=666)
IPF 18-49 (N=1,563)
IPF 50-65 (N=4,630)
IPF >65 (N=906)
Single vs Bilateral

- 1339 patients with IPF
- 31.7% listed for bilateral only
- 41.0% listed for single only
- 27.3% listed for either

- Patients listed for bilateral has increased risk of death on the waiting list (p=0.003)

Nathan SD et al, JHLT 2010
Connective Tissue Disease ILD

• 284 patients with CTD associated ILD underwent lung transplant over 18 years
• Survival worse than for COPD
• Survival comparable to IPF
• No evidence of disease recurrence
• Extra-pulmonary flares of CTD rare

Takaqish T et al, J Clin Rheum 2012
Pathway for Patients with Pulmonary Fibrosis
Freeman Hospital 1987-2012

- 486 Referrals
- 480 Assessed
- 273 Waiting List
- 144 Transplanted (29% referrals)
- 207 Unsuitable
- 133 Died
144 Transplants for Pulmonary Fibrosis

- Mean age 52.8 years (range 17.8-65.6)
- 28% female
- 78% were on pre-op immunosuppressive therapy

<table>
<thead>
<tr>
<th>Test</th>
<th>Mean (SD)</th>
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<tbody>
<tr>
<td>6 min walk (m)</td>
<td>246 (135)</td>
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<tr>
<td>FEV1 % (L)</td>
<td>50.2 (16.6)</td>
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<tr>
<td>FVC % (L)</td>
<td>48.7 (18.8)</td>
</tr>
<tr>
<td>TLC %</td>
<td>50.2 (14.7)</td>
</tr>
<tr>
<td>DLCO %</td>
<td>30.1 (12.0)</td>
</tr>
<tr>
<td>PaO2 (kPa)</td>
<td>8.5 (2.7)</td>
</tr>
<tr>
<td>PaCO2 (kPa)</td>
<td>5.2 (0.8)</td>
</tr>
<tr>
<td>BMI</td>
<td>25.9 (5.6)</td>
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144 Transplants for Pulmonary Fibrosis
Freeman Hospital

- 36 bilateral, 106 single and 2 heart-lung transplants
- 5 year survival was 46.0%, compared to 57.1% for all other indications (p<0.0001).
- 5 year survival in bilateral recipients was higher than in singles (67.9% vs 42.0%, p=0.005).
Example Case - COPD

- 56 year old female with severe COPD
- Ex-smoker with 35 pack year history, stopped 2 years ago
- Very breathless on exertion
- Poor quality of life
- 2-3 exacerbations /year
- Anxiety symptoms
- Osteoporosis

- On inhaled therapy in line with NICE guidelines
- Oral therapy
- FEV1 29% predicted, FEV1/VC 58%, DLCO 36%
Does this patient need referral for lung transplant assessment?

1. No, it's too soon to refer this patient

2. No, there are numerous relative contraindications to transplant

3. Yes, she should be formally assessed

4. Yes, she is a good candidate and needs to move to waiting list as soon as possible
Assessment

• PaO$_2$ 8.4kPa on air, PaCO$_2$ 5.2kPa
• BMI 17.1
• 6 min walk = 110m desaturating to 92%
• BODE score =7
• Bone density T score -2.1 spine; -1.6 Hip
• Echo RV size and function normal
• No history of Type 2 respiratory failure or NIV
Outcome of assessment

Not for listing – re-refer if condition deteriorates

• Needs Pulmonary Rehabilitation
• Needs Ambulatory oxygen assessment
• Needs nutritional support
• Consider Azithromycsin therapy
• Social circumstances assessment
COPD – Disease Specific Guidance

- **Referral Criteria:**
  - Progression despite maximal medical therapy
  - Not suitable for LVR surgical or medical
  - Bode Score 5-6
  - PaO2 <8 kPa and/or PaCO2 >6.6kPa
  - FEV1<25%

- **Listing Criteria:**
  - Bode Score >7
  - 3 or more severe exacerbations within 12 months
  - Hospitalisation with hypercapnic respiratory failure
  - Moderate to Severe Secondary PH despite LTOT
  - FEV1 <15-20% predicted

*Journal of Heart and Lung Transplantation July 2014*
COPD Survival By Procedure Type (1990 – June 2011)

N at risk at 10 years = 628
N at risk at 10 years = 331

p < 0.0001
Conclusions

• Lung Transplant activity worldwide is increasing
• Age>60 is an independent risk factor but not an absolute contraindication
• ILD and COPD patients require careful assessment to determine suitability and timing of potential listing
• Consider the overall condition of the patient beyond the lung disease
Institute of Transplantation
http://transplant.tv
Patients < 60 years had equivalent survival to those > 60 years (p=0.44).

Survival in those with preoperative pulmonary hypertension (PH) was similar to those with no PH (p=0.69).

62.5% of patients with secondary PH had bilateral lungs compared to 20% in non-PH patients.