LUNG TRANSPLANT: UPDATE ON RECENT ADVANCES AND ETHICAL CONSIDERATIONS

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Dr. Gordon Yung is currently the Medical Director of Lung and Heart-Lung Transplant Program and Director of Advanced Lung Disease Program, at UCSD Medical Center. He joined the University of California, San Diego as a fellow in Pulmonary and Critical Care Medicine in 1995. After his fellowship, he stayed on for a one year fellowship in Pulmonary Vascular diseases. He is currently Clinical Professor of Medicine at the university and is actively involved in many areas of research and academic activities.

His clinical roles involve the evaluation and management of patients for lung transplantation, as well as other end stage lung diseases. He has a diverse interest in clinical and translational research in pulmonary hypertension, interstitial lung diseases, emphysema and lung transplantation. He is a member of the Medical Advisory Committee for the local organ procurement agency and Medi-Cal Advisory Committee on Anatomic Transplants (MACAT) on Cardiothoracic Transplantation. His clinical expertise was recognized by his peers and trainees, and has been given the Award of Clinical Excellence in 2004 for his work at UCSD, as well as 'Honorable Mentioned' in Graduating House Staff Teaching Award for Excellence in the education of medical residents in 2001 and 2002.

OBJECTIVES:

Participants should be better able to:

1. Understand the epidemiology and logistics of lung transplantation within the US and in other parts of the world.

2. Understand the four distinct stages of lung transplantation.

3. Consider different ways to increase the availability of donor lungs for transplantation.

4. Discuss the ethical considerations inherent to lung transplantation.

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Lung Transplantation: Recent Advances and Ethical Considerations

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Dr. Yung has received research grants from Gilead Science, Astra Zeneca, Roche, Bristol-Myers Squibb, and CMS, and is on the Speakers’ Bureau at Roche/Genentech but these do not create a conflict of interest related to the following presentation.
Disclosures

- No relevant financial conflicts of interests
- No treatments ever been approved by FDA: (almost) any discussion of treatment is non-FDA approved

Objectives

- Overview of lung transplants in US/World
- Understand the 4 stages of transplant
- Ways to increase organ availability
- Ethical considerations in lung transplant
Number of Transplants in US: 2011

- Kidney: 16,813
- Liver: 6,342
- Heart: 2,322
- Lung: 1,822
- Heart-Lung: 27

Adult and Pediatric Lung Transplants
Number of Transplants by Year and Procedure Type

NOTE: This figure includes only the lung transplants that are reported to the ISHLT Transplant Registry. As such, this should not be construed as representing changes in the number of lung transplants performed worldwide.
Adult Lung Transplants
Average Center Volume by Location
(Transplants: January 2000 – June 2013)


Indications for Single Lung Transplants
(Transplants: January 1995 – June 2013)

*Other includes:
- Pulmonary Fibrosis, Other: 4.4%
- Bronchiectasis: 0.4%
- Sarcoïdosis: 1.8%
- Connective Tissue Disease: 1.2%
- OB (non-Rtx): 0.7%
- LAM: 0.9%
- Congenital Heart Disease: 0.4%
- Miscellaneous: 1.7%

For some retransplants, diagnosis other than retransplant was reported, so the total percentage of retransplants may be greater.

Adult Lung Transplants
Indications for Bilateral/Double Lung Transplants
(Transplants: January 1995 – June 2013)

*Other includes:
Pulmonary Fibrosis, Other: 3.6%
Bronchiectasis: 4.0%
Sarcoidosis: 2.1%
Connective Tissue Disease: 1.5%
OB (non-Retx): 1.3%
LAM: 1.1%
Congenital Heart Disease: 1.1%
Miscellaneous: 2.0%

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Adult Lung Transplants
Kaplan-Meier Survival (Transplants: January 1990 – June 2012)

Median survival = 5.6 years

N = 43,501
Four Stages of Transplant

1. Transplant Referral & Evaluation
2. Waitlist
3. Transplant surgery
4. Post-Transplant Care

Stages of Transplant:
1. Referral and Evaluation
Ethical Dilemma: Who Should Receive Transplant?

- Sickest?
- Best survival?
- Age?
- Contribution to society?
  - Death row inmates?
- US citizens/residents vs foreign nationals?

Adult Lung Transplants
Kaplan-Meier Survival by Gender
(Transplants: January 1990 – June 2012)

- Male (N=23,855)
- Female (N=19,644)

\[ p < 0.0001 \]

Med. survival (years): Male = 5.4; Female = 5.8

N at risk: Male = 88, Female = 78
Ethical Dilemma: Who Makes the Decision?
Ethical Dilemma: Who Decides?

- **Patients**: “I have NOTHING to lose”
- **Doctors**: conflict of interests
- **Government**: judges?

Decision to Transplant (Risks and Benefits)

- **Without Transplant**
  - Patients know best!

- **With Transplant**
  - DM, infections, malignancies, renal failure/dialysis, rejection, GI, HTN Hospitalizations...
  - 80-85% with no limitations in daily activities

**Survival**

**Quality of Life**
Stage 2 of Transplant: WAITLIST

- LAS= Lung Allocation Score, range 0-100
- Risks of death without vs after transplant
- Age>12

*Other factors: ABO, size, PRA etc.

Serial Spirometries: Where and How Fast
Six Minute Walk Test

- With ‘normal’ oxygen
- ATS guidelines
- Oxygen requirement at rest and during ‘exertion/exercise’

Who Gets The Organ?

Local vs regional offer
Blood type
Lung Allocation Score
Lung size and type of transplant

Tentative Acceptance

Organ Visualization

Final Acceptance
How To Increase Transplant?

Ethics: Should we increase or even do transplant?

Donation After Cardiac Death

- ‘Near brain dead’ or severely brain injured donors
- Compassionate extubation
- Cardiac death = brain death
Increasing Organ Donation: Ex-Vivo Lung Perfusion
Cold Preservation vs. Warm Perfusion

- Cold static storage allows for injury due to cold and ischemia
- No capability for optimizing organ condition
- No means of assessing organ function
- Limits organ utilization
- Results in compromised clinical outcomes

- Warm, functioning/living preservation
- Organ condition can be optimized ex-vivo
- Online organ viability/function assessment
- No time limitation
- Expands organ utilization
- Improves clinical outcomes

Living Organ Transplant: Organ Cara System

OCS Device  Heart Perfusion Module  Maintenance Solution Set
Stages of Transplant:
3. Surgery- Making The Right Choice

- Single
- Double (bilateral sequential)
- Heart-lung
- Living (related) donor lobar

Stage 3: Transplant Surgery
Surgery

- Connect
  - Airway(s): trachea or bronchus
  - Pulmonary artery
  - Pulmonary vein
- Not connect
  - Bronchial artery/vein
  - Nerves
  - Lymphatics

Stage 3: Transplant Surgery
Advances in Peri-operative Management: Age Selection

- Older patients are being transplanted
- Replacing ‘chronologic’ with ‘physiologic’ age limits.
  - 2004: 6.9% (81/1172) ≥ 65 yo
  - 2010: 24.7% (399/1618) ≥ 65 yo
- Average survival for ≥ 70 yo ~ 3 years
Advances in Peri-operative Management

- Replace ‘clamshell’ approach with bilateral thoracotomies
- Less exposure but better patient recovery
- Less use of CP bypass → less bleeding and renal dysfunction

Implications To Management

- Anastomosis: ET tube and suctioning
- Bleeding: Bronchoscopy before extubation
- Tracheo-bronchial necrosis: Day 7-10 post-op
- Impaired/absent cough reflex: months to years ?permanent

Hyperinflation in COPD/Single Lung Transplant
Advances in Rejection Treatment:
Once upon a time, in ancient Egypt.....

Photopheresis

White blood cells are treated with methoxsalen and exposed to UVA light.

Blood is separated by centrifugation and red blood cells are returned.

The UVAR XTS instrument draws blood from the patient.

The photoactivated white blood cells are returned to the patient.
Q1: Which organ has the largest number of transplant in US?

a) Lung
b) Heart
c) Kidney
d) Liver
Q2. Approximately, what is the average survival after lung transplant?

a) 3 years  
b) 5 years  
c) 7 years  
d) 9 years
Q3. Which of the following is **NOT** a potential benefit of Ex-Vivo Lung Perfusion?

a) Increase number of donor lungs  
b) Increase marginal organ’s function  
c) Allows more time for arrangement of transplant surgery  
d) Save cost for transplant

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