

Lung Transplantation

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Disclosure

- I have financial relationships with Astellas (researcher) and Takeda (advisor).
- I will be discussing off-label medication uses.



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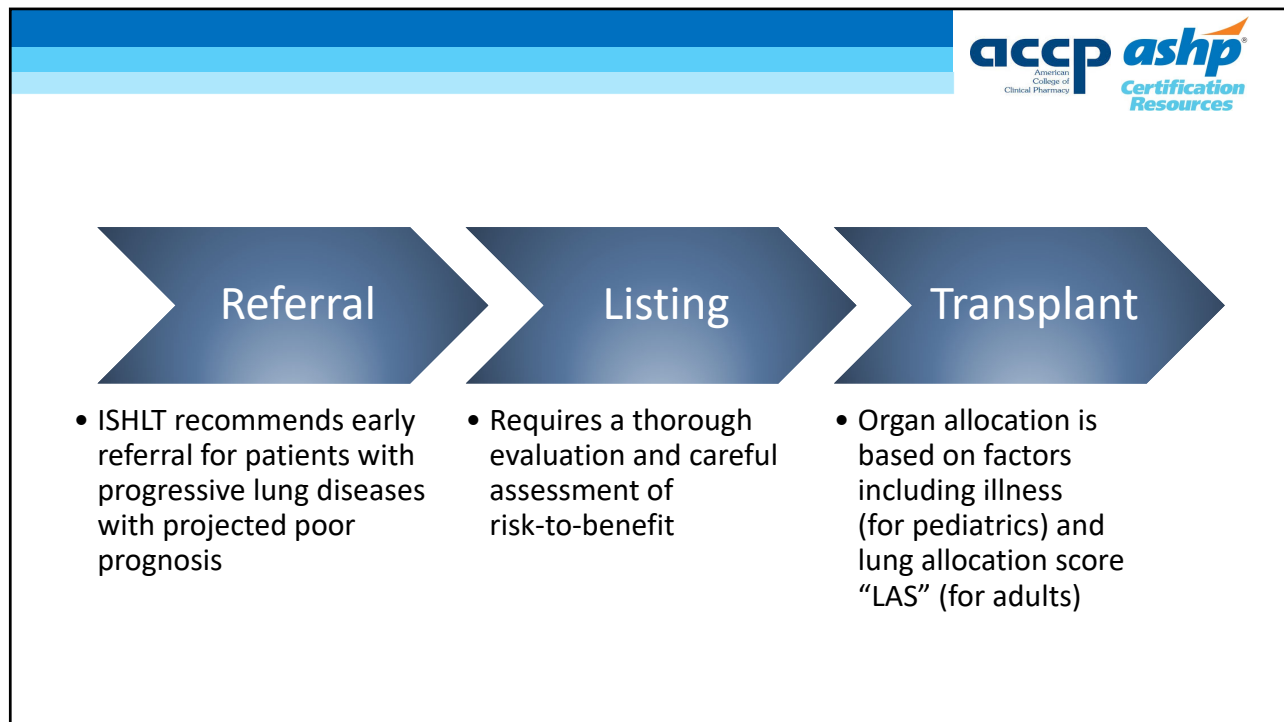
Learning Objectives

- Describe diagnoses that may lead to end-stage lung disease and referral for lung transplantation.
- Identify indications, absolute contraindications, and relative contraindications for lung transplantation.
- Formulate a medication regimen for a lung transplant recipient, taking into account immunologic risks and needs, preventative needs, and comorbid diseases.
- Explain the objective testing used to evaluate lung allograft function.
- Summarize the presentation and management of common immunologic complications after lung transplantation.
- Summarize the presentation and management of common non-immunologic complications after lung transplantation.

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Illnesses Leading to End-Stage Lung Disease

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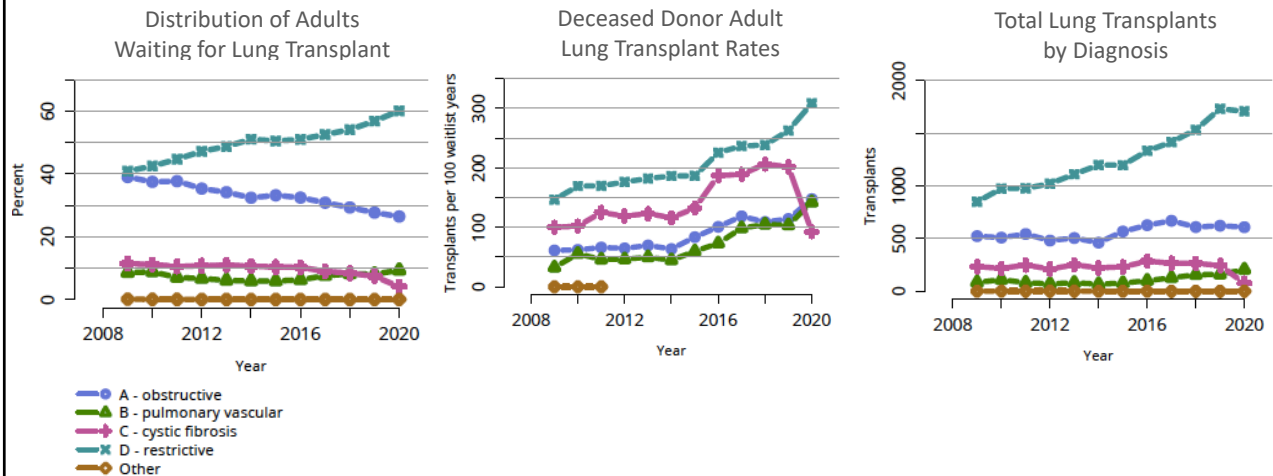
Who Needs a Transplant?

- Group A diagnoses: obstructive lung disease (e.g. COPD, emphysema, bronchiectasis)
- Group B diagnoses: pulmonary vascular disease (e.g. pulmonary hypertension)
- Group C diagnoses: cystic fibrosis or immunodeficiency disorders (e.g. CF, common variable immune deficiency)
- Group D diagnoses: restrictive lung disease (e.g. idiopathic pulmonary fibrosis, retransplant)

Valapour M, et al. OPTN/SRTR 2020 Annual Data Report: Lung. *Am J Transplant* 2022; 22(S2): 438-518.

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Who Needs a Lung Transplant?



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Question 1:

Which of the following is the leading indication for lung transplant in the United States?

- a) Chronic obstructive pulmonary disease
- b) Cystic fibrosis
- c) Pulmonary fibrosis
- d) Pulmonary arterial hypertension

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Lung Transplant Indications and Contraindications

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Lung Transplant Listing Criteria: Indications

Chronic, end stage lung disease (ESLD) with:

- >50% risk of death from lung disease within 2 years if lung transplant is not performed
- >80% likelihood of surviving 5 years post-transplant from a general medical perspective, provided there is adequate graft function

Leard LE, et al. *JHLT* 2021; 40(11): 1349-79.

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Lung Transplant Listing Criteria: Absolute Contraindications

- | | |
|---|---|
| <ul style="list-style-type: none"> • Lack of patient willingness or acceptance of transplant • Malignancy with high risk of recurrence or death related to cancer • GFR <40 unless being considered for multi-organ • ACS or MI within 30 days • Stroke within 30 days • Liver cirrhosis with portal HTN or synthetic dysfunction unless being considered for multi-organ • Acute liver failure • Acute renal failure with rising SCr or on dialysis and low likelihood of recovery • Septic shock • Active extrapulmonary or disseminated infection | <ul style="list-style-type: none"> • Active tuberculosis infection • HIV infection with detectable viral load • Limited functional status (e.g. non-ambulatory) with poor potential for post-transplant rehabilitation • Progressive cognitive impairment • Repeated episodes of non-adherence without evidence of improvement (note: not an absolute contraindication for pediatric candidates) • Active substance use or dependence including current tobacco use, vaping, marijuana smoking, or IV drug use • Other severe uncontrolled medical condition expected to limit survival after transplant |
|---|---|

Leard LE, et al. *JHLT* 2021; 40(11): 1349-79.

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Lung Transplant Listing Criteria: Factors with High or Substantially Increased Risk

- Age >70 years
- Severe CAD that requires CABG at transplant
- Reduced LVEF <40%
- Significant cerebrovascular disease
- Severe esophageal dysmotility
- Untreatable hematologic disorders including bleeding diathesis, thrombophilia, or severe bone marrow dysfunction
- BMI <16 or >35 kg/m²
- Limited functional status with potential for post-transplant rehabilitation
- Psychiatric, psychological, or cognitive conditions with potential to interfere with medical adherence without sufficient support systems
- Unreliable support system or caregiving plan
- Lack of understanding of disease and/or transplant despite teaching
- *Mycobacterium abscessus* infection
- *Lomentospora prolificans* infection
- *Burkholderia cenocepacia* or *gladioli* infection
- Hepatitis B or C infection with detectable viral load and liver fibrosis
- Chest wall or spinal deformity expected to cause restriction after transplant
- Extracorporeal life support
- Retransplant <1 year following initial lung transplant
- Retransplant for restrictive CLAD
- Retransplant for AMR as etiology for CLAD

Leard LE, et al. *JHLT* 2021; 40(11): 1349-79.

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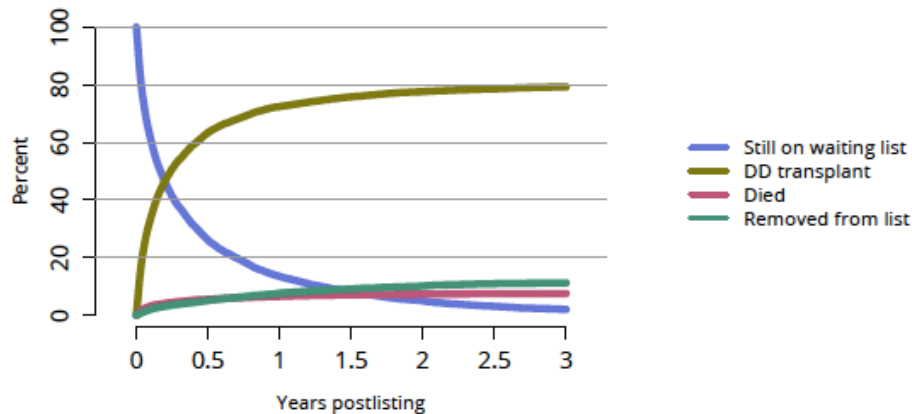
Lung Transplant Listing Criteria: Risk Factors

- Age 65-70 years
- GFR 40-60
- Mild to moderate CAD
- Severe CAD that can be revascularized via PCI prior to transplant
- Patients with prior CABG
- Reduced LVEF 40-50%
- Peripheral vascular disease
- Connective tissue diseases (scleroderma, lupus, inflammatory myopathies)
- Severe gastroesophageal reflux disease
- Esophageal dysmotility
- Thrombocytopenia, leukopenia, or anemia with high likelihood of persistence after transplant
- Osteoporosis
- BMI 16-17 or 30-34.9 kg/m²
- Frailty
- Hypoalbuminemia
- Diabetes that is poorly controlled
- Edible marijuana use
- *Scedosporium apiospermum* infection
- HIV infection with undetectable viral load
- Previous thoracic surgery
- Prior pleurodesis
- Mechanical ventilation
- Retransplant >1 year for obstructive CLAD

Leard LE, et al. *JHLT* 2021; 40(11): 1349-79.

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What Happens Once a Patient is Listed?



Valapour M, et al. OPTN/SRTR 2020 Annual Data Report: Lung. *Am J Transplant* 2022; 22(S2): 438-518.

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Lung Allocation Policy

- For candidates <12 years, access to lung transplant is based on:
 - Blood type compatibility
 - Distance from donor hospital
 - Age
 - Illness-based priority status
 - Waiting time as tiebreaker
- For candidates ≥ 12 years, access to lung transplant is based on:
 - Blood type compatibility
 - Distance from donor hospital
 - Age
 - Lung allocation score (LAS)
 - Waiting time as tiebreaker

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Lung Allocation Score (LAS)

- DOB (age)
- Height, weight (BMI)
- Lung diagnosis code
- Functional status
- Assisted ventilation
- Supplemental oxygen requirement
- Pulmonary artery pressure, systolic
- Pulmonary artery pressure, mean
- Cardiac index
- 6 minute walk distance
- Total bilirubin
- Serum creatinine
- pCO₂ (current, highest, lowest)

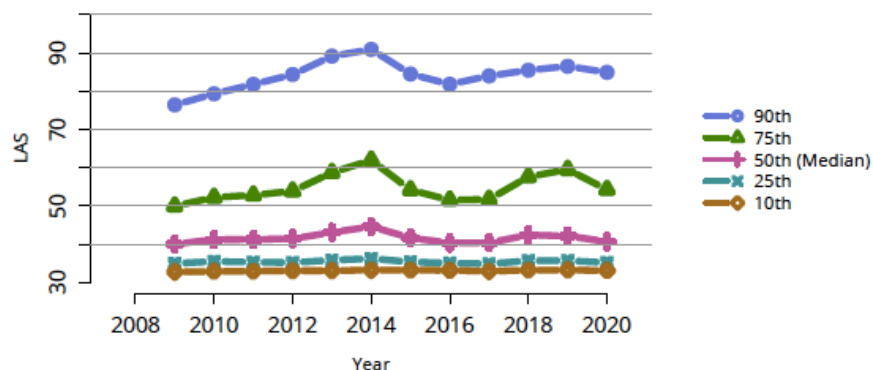
Score range: 0-100
 A higher score reflects a higher priority for transplant.

Eberlein M, et al. *Clin Chest Med* 2011; 213-22.

<https://optn.transplant.hrsa.gov/data/allocation-calculators/las-calculator/>

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Median LAS at Transplant



Valapour M, et al. OPTN/SRTR 2020 Annual Data Report: Lung. *Am J Transplant* 2022; 22(S2): 438-518.

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Single or Bilateral Lung Transplant?

Outcome parameter	Advantage Single Lung	Advantage Bilateral Lung
Duration of operation	+	-
ICU and hospital stay	-	-
Early mortality	-	-
Long-term survival	-	+
FEV1 improvement with lung transplant	-	+
Freedom from BOS	-	+
QOL measures	-	-
Cost effectiveness (individual perspective)	-	+
Maximum benefit (societal perspective)	+	-
High risk recipient	-	+

Puri V, et al. *Thorac Surg Clin* 2015; 25(1): 47-54.

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Question 2:

Which of the following statements is true?

- a) A higher LAS would indicate higher transplant priority for a 10 y/o girl with cystic fibrosis, on a lung transplant waitlist.
- b) A 60 y/o man with IPF, O blood type, PRA 85%, and LAS 32 may benefit from desensitization therapy since he is likely to receive organ offers.
- c) The LAS is a number that ranges from 6-40.
- d) The LAS considers both current illness as well as likelihood of post-transplant success, with a goal of reducing waitlist mortality while avoiding futile transplants.

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Question 2:

Which of the following statements is true?

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- c) The LAS is a number that ranges from 6-40.
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Medication Regimens for Lung Transplant Recipients



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Medication Regimens

- Immunosuppression
 - Induction is common; triple-drug maintenance regimens
- Antimicrobials
 - Prophylaxis for CMV (6-12 mos), PJP (indefinite), aspergillus (6 mos)
 - Empiric treatment for donor-derived infection (pneumonia)
- Other routine therapies
 - Mucous clearance
 - DVT prophylaxis
 - Afib prevention (K, Mag, heart rate control)
 - Osteoporosis prevention (calcium, vitamin D)
 - BOS prophylaxis (PPI, azithromycin, montelukast)

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Evaluating Allograft Function in Lung Transplant Recipients



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Evaluating Lung Allograft Function

- Laboratory testing:
 - Stains and cultures from sputum, bronchoalveolar lavage (BAL), or bronchial washing
- Pulmonary function tests:
 - Spirometry at routine visits and prn
- Imaging
 - Chest xray and/or high resolution CT
- Pleural fluid analysis
 - Ultrasound-guided thoracentesis
- Bronchoscopy
 - Bronchial evaluation, bronchoalveolar lavage (BAL), and transbronchial biopsy (TBB)

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Post-transplant survival and complications

	1 year	3 years	5 years
Patient survival	89.4%	74.8%	61.2%
Complications:			
Acute rejection episode	14.6%		
BOS	5.7%		40.2%
SCr >2.5	4.8%		12.5%
Chronic dialysis	1.9%		3.3%
Malignancy			24%
PTLD (EBV IgG neg)	7.6%		
PTLD (EBV IgG pos)	1.1%		

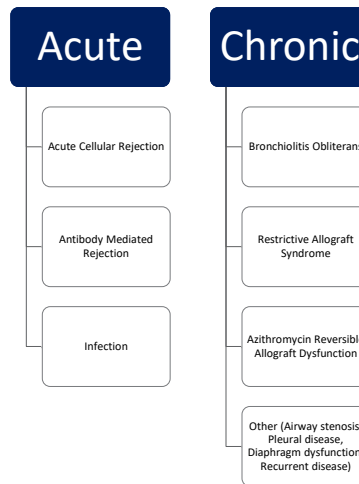
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Immunologic Complications After Lung Transplantation

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Causes of Lung Allograft Dysfunction




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Acute Cellular Rejection

- Occurs in over 50% of patients (lifetime incidence)
- Symptoms vary:
 - Cough, dyspnea, purulent sputum, severe hypoxemia
 - Asymptomatic (caught via protocol surveillance biopsies)
- Diagnosed via bronchoscopy pathology and allograft biopsy
- Associated with development of chronic rejection
- Most episodes respond to first line therapies


Stewart S, et al. *J Heart Lung Transplant* 2007; 26: 1229-42.

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Acute Cellular Rejection: Histologic Grading		
A: Acute rejection	General Management	
Grade 0 = none		
Grade 1 = minimal	Don't treat unless symptomatic	
Grade 2 = mild	Mixed; treat vs increased surveillance	
Grade 3 = moderate	Treat	
Grade 4 = severe	Treat	
B: Airway inflammation		
Grade 0 = none		
Grade 1R = low grade		
Grade 2R = high grade		
Grade X = ungradeable		
C: Chronic airway rejection		
0 = absent		
1 = present		
D: Chronic vascular rejection		

Stewart S, et al. *J Heart Lung Transplant* 2007; 26: 1229-42.

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Acute Cellular Rejection: Treatment		
<ul style="list-style-type: none"> First line: <ul style="list-style-type: none"> – Methylprednisolone 500-1000 mg (~15 mg/kg) IV daily x3 days – Upgrade maintenance regimen (e.g. correct nonadherence, optimize dosing, change cyclosporine to tacrolimus, change azathioprine to mycophenolate) For persistent or refractory rejection: <ul style="list-style-type: none"> – Repeat methylprednisolone – Upgrade maintenance regimen (e.g. add sirolimus or everolimus if >30 days post-transplant) – Consider antithymocyte globulin or alemtuzumab – Consider extracorporeal photophoresis or total lymphocytic radiation 		

Stewart S, et al. *J Heart Lung Transplant* 2007; 26: 1229-42.

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Antibody Mediated Rejection: Definition and Diagnostic Certainty

	Allograft dysfunction	Other causes excluded	Lung histology	Lung biopsy C4d	DSA
Definite	+	+	+	+	+
Probable	+	+	+	-	+
Probable	+	+	+	+	-
Probable	+	+	-	+	+
Probable	+	-	+	+	+
Possible	+	+	+	-	-
Possible	+	+	-	-	+
Possible	+	+	-	+	-
Possible	+	-	+	+	-
Possible	+	-	+	-	+
Possible	+	-	-	+	+

Levine DJ, et al. *J Heart Lung Transplant* 2016; 35: 397-406.

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Antibody Mediated Rejection: Treatment

- Corticosteroids (not as monotherapy)
- Plasmapheresis
- IVIG
- Rituximab
- Bortezomib or carfilzomib
- Eculizumab
- Extracorporeal photopheresis

Halverson LP, Hachem RR. *Semin Respir Crit Care Med* 2021; 42: 428-35.

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Question 3:

Which of the following appropriately matches a lung biopsy result with a treatment regimen?

- a) A surveillance biopsy at 3 months post-transplant was graded as A1,B0. The patient is asymptomatic. Do not treat.
- b) A surveillance biopsy at 9 months post-transplant was graded as A3,B0. The patient is symptomatic. Treat with alemtuzumab 30 mg IV x1.
- c) A for-cause biopsy at 2 weeks post-transplant was graded as A3,Bx. The patient is requiring oxygen. Treat with methylprednisolone 1000 mg IV daily x3 and add everolimus to the maintenance regimen.
- d) A for-cause follow-up biopsy 2 weeks after methylprednisolone treatment for cellular rejection was graded as A2,B0. Treat again with methylprednisolone 1000 mg IV daily x3 and change tacrolimus to cyclosporine.

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Question 4:

What is the diagnostic certainty for antibody mediated rejection in the following case:

AJ is a 48 y/o woman with FEV₁ reduced 30% from her post-transplant baseline. Her infectious workup is negative and chest x-ray is unrevealing. Lab testing reveals three class II DSA with C1q testing pending. Biopsy is A0,B0 with negative C4d staining and no abnormal histologic findings.

- a) Is not AMR
- b) Possible AMR
- c) Probable AMR
- d) Definite AMR

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Question 4:

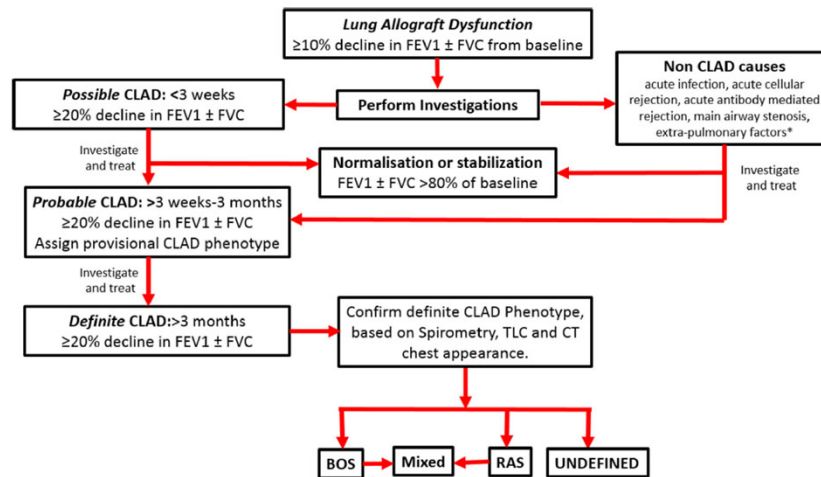
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- b) **Possible AMR**
- c) Probable AMR
- d) Definite AMR

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CLAD Evolution



(Reprinted with Permission) Verleden GM, et al. *JHLT* 2019; 38: 493.


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Chronic Loss of Allograft Function: Confounding Factors and Considerations

- Factors that warrant resetting the FEV₁ reference value:
 - Decreasing lung function due to normal aging
 - Surgical factors (e.g. transplant lung resection, chest-wall surgery)
 - Mechanical factors (e.g. pleural effusion, lung edema, airway stenosis)
 - Localized infection with chronic scarring (e.g. abscess, empyema, mycetoma)
- Confounding factors that do not warrant resetting the FEV1 reference value:
 - Any of the above without at least 6 months of stability
 - Infiltration with tumor or primary disease recurrence (e.g. LAM, sarcoidosis)
 - Drug or other pulmonary toxicity (e.g. sirolimus, amiodarone, methotrexate)
 - Pulmonary arterial strictures or emboli
 - Acute/subacute generalized infection
 - Acute/subacute cellular or antibody-mediated rejection
 - Acute/subacute effects of aspiration
- Failing to reach normal predicted lung function (e.g. donor/recip age difference, intra-op allograft reduction surgery)

Verleden GM, et al. *JHLT* 2019; 38: 493.

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CLAD Staging and Phenotypes

Stage	Spirometry
CLAD 0	Current FEV ₁ >80% FEV ₁ baseline
CLAD 1	Current FEV ₁ >65-80% FEV ₁ baseline
CLAD 2	Current FEV ₁ >50-65% FEV ₁ baseline
CLAD 3	Current FEV ₁ >35-50% FEV ₁ baseline
CLAD 4	Current FEV ₁ ≤35% FEV ₁ baseline

	Obstruction (FEV ₁ /FVC <0.7)	Restriction (TLC decline ≥10% from baseline)	CT Opacities
BOS	Yes	No	No
RAS	No	Yes	Yes
Mixed	Yes	Yes	Yes
Undefined	Yes	No	Yes
	Yes	Yes	No

Verleden GM, et al. *JHLT* 2019; 38: 493.

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Chronic Lung Allograft Dysfunction (CLAD): Bronchiolitis Obliterans Syndrome

- Definition:
 - Allograft dysfunction with delayed onset and persistent decline in FEV₁ (≥20% from baseline), without another known cause
- Findings:
 - Obstructive pulmonary function defect
 - Air trapping or mosaic attenuation on expiratory CT (support dx, lack sensitivity and sensitivity)
 - Obliterative bronchiolitis on pathology is histologic dx; BOS is clinical dx
- Risk factors:
 - PGD, acute rejection, lymphocytic bronchiolitis, AMR, GERD, CMV pneumonitis, symptomatic community-acquired respiratory virus infection, *Pseudomonas* colonization and infection of lung, *Aspergillus* colonization or fungal pneumonia, autoimmune sensitization to collagen V, increased BAL neutrophils
- Treatment:
 - Avoid sustained administration of high-dose corticosteroids
 - Consider converting cyclosporine to tacrolimus, montelukast (if stage 1), azithromycin, and/or fundoplication if documented GERD
- Prognosis:
 - Median survival after diagnosis is 3-5 years

Meyer KC, et al. *Eur Respir J* 2014; 44: 1479-1503.
 Verleden SE, et al. *J Thoracic Dis* 2017; 9: 2650.
 Ruttens D, et al. *PLoS One* 2018; 13(4): e0193564.

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Chronic Lung Allograft Dysfunction (CLAD): Restrictive Allograft Syndrome

- Definition:
 - Allograft dysfunction with delayed onset and persistent decline in FEV₁ ($\geq 20\%$ from baseline), TLC ($\geq 10\%$ from baseline), and persistent opacities on chest imaging
- Findings:
 - Restrictive pulmonary function
 - Persistent pleuro-parenchymal infiltrates on CT
 - Pleuroparenchymal fibro-elastosis on pathology
- Risk factors:
 - Acute rejection, lymphocytic bronchiolitis, *Pseudomonas* colonization, infection, blood eosinophilia, and BAL eosinophilia and neutrophilia
- Treatment:
 - Few effective options. Consider antifibrotics (pirfenidone/nintedanib), alemtuzumab, TLI, or ECP
- Prognosis:
 - Relentlessly progressive, with a stair step pattern of progression
 - Median survival after diagnosis is 0.5-1.5 years

Verleden SE, et al. *J Thoracic Dis* 2017; 9: 2650.

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Azithromycin for BOS Treatment

Outcome FEV ₁ (L)	Analysis	Mean difference in FEV1 (azithromycin minus placebo)	95% CI for population mean difference	p value
Mean difference, adjusted for baseline FEV1, randomization stratification variables (disease and transplant), and time since randomization	ITT (n=46)	0.035	-0.112 to 0.182	0.6
	As treated (n=46)	0.306	0.181 to 0.431	<0.001
	Completed treatment (n=33)	0.278	0.170 to 0.386	<0.001

Corris PA, et al. *Thorax* 2015; 70: 442.

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Azithromycin for BOS Prevention

7 year f/u	Azithromycin (n=40) 250 mg PO TIW	Placebo (n=43)	p value
75% CLAD-free survival	4.06 years	1.76 years	p=0.024
CLAD	11 (28%)	22 (51%)	p=0.043
Obstructive CLAD	8 (20%)	16 (37%)	p=0.10
Restrictive CLAD	3 (7.5%)	6 (14%)	p=0.49
Graft loss	16 (40%)	23 (53%)	p=0.27
Retransplantation for CLAD	3 (7.5%)	5 (11%)	p=0.71
All cause mortality	14 (35%)	21 (49%)	p=0.27
FEV ₁ , % predicted	84%	75%	p<0.0011
FVC, % predicted	102%	88%	p<0.0001
6-min walk distance, % predicted	80%	75%	p<0.0001

Rutten D, et al. *Am J Transplant* 2016; 16: 254-61.

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Question 5:

EL is 2 years post lung transplantation with a sudden 20% drop in FEV₁. Chest x-ray shows infiltrates and a BAL culture grew *Pseudomonas* which is pan-sensitive. Which of the following is the best treatment?

- a) Start azithromycin 250 mg three times a week indefinitely
- b) Start ciprofloxacin 750 mg twice a day for 10 days
- c) Start tobramycin 300 mg via nebulizer twice a day for 10 days
- d) Place a PICC line and start cefepime 1g q8h for 10 days

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Question 6:

Which of the following treatments may offer a benefit in restrictive allograft syndrome?

- a) Azithromycin
- b) Methylprednisolone
- c) Alemtuzumab
- d) Plasmapheresis + IVIG**

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Question 6:

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Non-Immunologic Complications After Lung Transplantation

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Post-Transplant Complications

Early

- Pain
- Hypotension/shock
- Respiratory failure / PGD
- Surgical complications
 - Airway, vascular, bleeding
 - Phrenic nerve injury
- Pleural complications
- Cardiac complications
 - Atrial fibrillation, ischemia
- VTE
- AKI
- Infections
- Rejection
- GI complications (N/V, gastroparesis)

Late

- Rejection
- Malignancy
- CKD
- Infection
- Other medical comorbidities

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30-day mortality

- 3.6% overall, in post-LAS era
- Etiology:
 - Primary non-function (72.5%)
- Risk factors:
 - Patient
 - Vascular diseases as the transplant indication
 - H/o non-transplant cardiac or lung surgery
 - Mean pulmonary pressures >35 mm Hg
 - Disabled functional status
 - Inpatient at the time of transplant
 - ECMO support
 - High LAS
 - Donor
 - Blunt injury as mechanism of donor death
 - Ischemic time >6h
 - Perioperative
 - Development of any major complication (e.g. airway dehiscence, stroke, need for dialysis)

Banga A, et al. *Clin Transplant* 2019; 33: e13468.

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Primary Graft Dysfunction (PGD)

- Definition:
the presence of diffuse pulmonary opacities on thoracic imaging and hypoxemia without other identifiable cause, developing within the first 72 hours after implantation
- Incidence is ~30%
- Evaluate at 4 time points:
upon reperfusion of the second lung, then q24h +/- 6 hours

Snell GI, et al. *J Heart Lung Transplant* 2017; 36: 1097

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Primary Graft Dysfunction (PGD)

Grade	Pulmonary edema on chest Xray	PaO ₂ /FiO ₂ ratio (alternate: O ₂ /FiO ₂)
PGD grade 0	no	any
PGD grade 1	yes	>300 (alternate: >315)
PGD grade 2	yes	200-300 (alternate: 235-315)
PGD grade 3	yes	<200 (alternate: <235)

- No adjustment for NO, epoprostenol, or other therapies that improve oxygenation
- ECLS with bilateral pulmonary edema is grade 3
ECLS for non-hypoxic indication without pulmonary edema is ungradable

Snell GI, et al. *J Heart Lung Transplant* 2017; 36: 1097

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Post-Transplant Complications: Renal Insufficiency

- Incidence:
 - Acute kidney injury 56-69%; required dialysis 8%
 - Chronic kidney disease (SCr >2.5) at 3 years 5%; at 6 years 15%
- Consequences:
 - Morbidity and mortality (AKI requiring RRT is 4-5 fold increased risk)
- Risk factors:
 - Acute: preop pulmonary hypertension, IPF, reduced baseline GFR, mechanical ventilation >24h, IV amphotericin
 - Chronic: age, smoking history, gender, early ARF, CNI and other nephrotoxic medications, HTN, sarcoidosis, diabetes
- What to do?
 - Be aware, minimize risks where possible

Wehbe E, et al. *JHLT* 2012; 31: 244. Fidalgo P, et al. *Nephrol Dial Transplant* 2014; 29: 1702. Ojo AO, et al. *NEJM* 2003; 349: 931. Rocha PN, et al. *AJT* 2005; 5: 1469. Yusef RD, et al. *JHLT* 2015; 34: 1264. Lyu DM, et al. *Proc Am Thorac Soc* 2009; 101-7.

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Post-Transplant Complications: Thromboembolic Disease

- Incidence:
 - Pulmonary embolism 5-15%
 - Venous thromboembolism 20-45%
- Onset:
 - Median time from transplant to VTE is 47-69 days
- Risk factors for developing VTE:
 - Older age, prior VTE, male sex, prolonged mechanical ventilation and ICU stay, diabetes, pneumonia, ECMO, CPB, mTORi
- What to do?
 - VTE prophylaxis
 - Maintain high index of suspicion
 - Beware of DDI when treating!

Izbicki G, et al. *Chest* 2006; 129: 412. Yegen HA, et al. *Chest* 2007; 132: 547. Kahan ES, et al. *JHLT* 2007; 26: 339. Evans CF, et al. *Ann Thorac Surg* 2015; 100: 2033. Saez-Gimenez B, et al. *Transpl Int* 2007; 30: 1266.

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Post-Transplant Complications: Cardiovascular Complications

- Atrial dysrhythmias (atrial fibrillation) 25-35%
 - Risk factors older age, male sex, left atrial enlargement, prior a fib, IPF, regurgitant valvulopathy, CAD, prior CABG, CPB, diastolic dysfunction
 - Medical therapy can be transient; stop 2-3 months post transplant
- Hemodynamic instability (hypotension) common
 - Responds well to volume, vasopressors, inotropes
- CAD
 - Among 5-year survivors, the prevalence of risk factors is very high
- Pericarditis
 - Several case reports; onset 6 mos to 9 years post-transplant

Lyu DM, et al. *Proc Am Thorac Soc* 2009; 101-7.

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Post-Transplant Complications: Diabetes

- Incidence:
 - New onset diabetes after transplant at 1 year 24%; at 5 years 34%
- Risk factors:
 - Glucocorticoid, CNI, older age, BMI >30, cystic fibrosis
- What to do?
 - Follow international consensus guidelines for PTDM

Hackman KL, et al. *Diabet Care* 2014; 37: 2919. Ollech JE, et al. *Eur J Cardiothorac Surg* 2008; 33: 844.
 Sharif A, et al. *AJT* 2014; 14: 1992.

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Post-Transplant Complications: Gastrointestinal Complications

- Nausea, vomiting, GERD, diarrhea constipation occur in >60% of patients
- Gastroparesis in ~24%
- GERD is prevalent in ESLD; lung tx increases likelihood; GERD and aspiration are linked with BOS
- What to do?
 - Evaluation via manometry, pH impedance studies, upper GI series
 - PPIs, anti-emetics and/or promotility agents
 - Nissen fundoplication

Lyu DM, et al. *Proc Am Thorac Soc* 2009; 101-7.

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Post-Transplant Complications: Osteoporosis

- Incidence in lung transplant candidates:
 - 32-54%
- Within the first year post-transplant:
 - 6-18% experience fracture; 4-12% loss in BMD
- Risk factors for developing osteoporosis:
 - Steroids, tobacco, limited mobility, malabsorption
- What to do?
 - Bone mineral density evaluation at baseline and q2 years
 - Calcium and vitamin D supplementation
 - Treatments for osteoporosis, where indicated

Lyu DM, et al. *Proc Am Thorac Soc* 2009; 101-7.

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Post-Transplant Complications: Malignancy

- Malignancy (e.g. skin ca, PTLD)
 - 4% at 1 year; 12% at 5 years; 25% at 10 years
- What to do?
 - Use just enough immunosuppression
 - Consider avoiding voriconazole
 - Keep up with routine surveillance

Lyu DM, et al. *Proc Am Thorac Soc* 2009; 101-7.

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Health-Related Quality of Life

- Lung transplant improves HRQL in all 5 measures:
 - SF12 physical component summary
 - SF12 mental component summary
 - Airway Questionnaire 20-revised
 - EuroQol-5D
 - EuroQol Visual Analog Scale
- Improvements are significant and durable
- Improvements in disability accounted for much of the improvement
- Recipients ≥ 65 years old enjoyed less improvement in SF12 PCS and SF12 MCS vs younger recipients

Singer JP, et al. *Am J Transplant* 2017; 17(5): 1334-5.

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Question 7:

Which of the following are risk factors for mortality within 30 days after lung transplant?

- a) Requirement for pre-operative mechanical ventilation and ECMO, younger recipient age, and esophageal dysfunction
- b) Requirement for pre-operative mechanical ventilation and ECMO, older recipient age, and gastroparesis
- c) Requirement for intra-operative ECMO, renal failure, and gastroparesis
- d) Requirement for intra-operative ECMO, renal failure, and esophageal dysfunction

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Question 7:

Which of the following are risk factors for mortality within 30 days after lung transplant?

- a) Requirement for pre-operative mechanical ventilation and ECMO, younger recipient age, and esophageal dysfunction
- b) Requirement for pre-operative mechanical ventilation and ECMO, older recipient age, and gastroparesis
- c) Requirement for intra-operative ECMO, renal failure, and gastroparesis
- d) Requirement for intra-operative ECMO, renal failure, and esophageal dysfunction

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Question 8:

Which of the following long-term complications occur in a majority of cases?

- a) Nausea, vomiting, and/or diarrhea
- b) Post-transplant diabetes mellitus
- c) Osteoporosis
- d) Venous thromboembolism

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Question 8:

Which of the following long-term complications occur in a majority of cases?

- a) Nausea, vomiting, and/or diarrhea
- b) Post-transplant diabetes mellitus
- c) Osteoporosis
- d) Venous thromboembolism

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Key Takeaways

- Lung transplantation carries substantial risk for short- and long-term complications, but offers life saving therapy to those in need
- The timeline from listing to transplant is much shorter in lung transplantation versus other organs; only a minority of patients will remain on the waitlist >1 year
- Medication regimens for lung transplant recipients generally include triple-drug maintenance immunosuppression, triple therapy for infectious prophylaxis (Aspergillus, CMV/HSV, and PJP), and treatments to prevent post-operative complications (e.g. airway clearance, GERD, VTE, osteoporosis)
- Allograft function is most frequently monitored through spirometry, chest imaging, and bronchoscopy
- Immunologic complications can be acute or chronic, cellular or antibody mediated, and chronic rejection can be obstructive or restrictive
- Non-immunologic complications are numerous and require careful prevention, surveillance, and treatment

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Lung Transplantation

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