Post Lung Transplant Complications: Emphasis on CT Imaging Findings

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Learning Objectives

- To identify the pulmonary complications and pathological processes which may occur after lung transplantation
- To describe the role of imaging in post transplant patients with emphasis on the CT imaging findings of the select relevant entities

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Introduction

- Lung transplantation has been widely accepted as a treatment of choice among patients with end stage lung disease.
- Past experiences have shown its efficacy in improving the longevity as well as quality of life in many patients. Nevertheless, it is not devoid of complications which may vary from trivial and treatable entities to life threatening conditions.
- The complications can be divided into plural, pulmonary and airway diseases such as; hyperacute, acute, and chronic rejection including bronchiolitis obliterans organizing pneumonia; pulmonary infections; bronchial anastomotic complications; pleural effusions; pneumothoraces, lung herniation, pulmonary thromboembolism; upper-lobe fibrosis; primary disease recurrence; posttransplantation lymphoproliferative disorder.
- Imaging, especially CT is crucial in early detection, evaluation and diagnosis of these complications, in order to decrease the morbidity and mortality associated with certain conditions. This educational exhibit addresses the pathological processes after lung transplantation and discusses the role of imaging, with emphasis on CT imaging findings.
Reperfusion Edema

Ischemia-reperfusion injury is a noncardiogenic pulmonary edema that typically occurs more than 24 hours after transplantation, peaks in severity on postoperative day 4, and generally improves by the end of the 1st week. The radiographic and CT features are nonspecific and may include perihilar groundglass opacities, peribronchial and perivascular thickening, and reticular interstitial or airspace opacities located predominantly in the middle and lower lung lobes.

26 year-old woman, status post LT for cystic fibrosis. Chest radiographs on day 1 and day 2 demonstrate bilateral alveolar opacities likely reperfusion edema.
Acute Rjection

Acute rejection due to a cell-mediated immune response commonly occurs in the 2nd postoperative week. Repeated episodes of acute rejection are considered a predisposing factor for chronic rejection or bronchiolitis obliterans syndrome.

High-resolution CT features may include ground-glass opacities (often with basal distribution), peribronchial cuffing, inter- and intralobular septal thickening, and new or increased pleural effusions. Absence of ground-glass opacities almost excludes acute rejection in a postoperative lung transplant.

41 year-woman with bilateral lung transplant, CT chest obtained 3 weeks after demonstrating bilateral patchy ground glass and consolidative opacities (arrows) and left pneumothorax. Transbronchial biopsy showed acute rejection, with a marked perivascular inflammatory infiltrate of mononuclear cells.
Acute Rejection

The clinical features of acute rejection are variable and non-specific: dyspnea, cough, fever, reduced FEV1 and even acute hypoxemia. The formal diagnosis requires histology from a trans-bronchial biopsy. Clinically, patients respond well with increasing immunosuppression.

61 year-man underwent single right lung transplant for chronic obstructive lung disease. 
(a): Patient developed acute rejection in early post operative period. CT showing diffuse ground glass opacities throughout the right lung. 
(b,c): The same patient over the time developed chronic rejection with patchy airspace opacities and peribronchial thickening
Chronic Rejection

Chronic rejection of a lung transplant is a clinicopathologic syndrome characterized by bronchiolitis obliterans, a dense development of eosinophilic fibrous scarring of the small airways. The term *bronchiolitis obliterans syndrome* is used to describe the less specific graft dysfunction with a physiologic airflow obstruction and a decline in forced expiratory volume in 1 second from the posttransplantation baseline.

![Chronic rejection in a patient with right lung transplants for COPD. (left) Inspiratory axial chest CT images show mosaic attenuation (regions of mixed hypo- and hyperattenuation). (right) Expiratory images show a hypoattenuating region (arrows) produced by air trapping, a hallmark of chronic rejection due to bronchiolitis obliterans.](image-url)
Chronic Rejection: Bronchiolitis Obliterans Syndrome

50 year-man, Right lung transplant. Bronchiolitis, bronchiectasis and collapse developed in the transplanted lung and finally required pneumonectomy. Later the patient underwent left side lung transplant.
CT findings of chronic rejection include bronchiectasis, bronchial wall thickening, nodular and linear branching opacities, air trapping, regional volume expansion or contraction, mosaic lung attenuation, interlobular septal thickening, and peribronchovascular infiltrates.

50 year-old woman with bilateral lung transplant developed bilateral bronchiolitis, bronchiectasis, bronchial wall thickening, peribronchial nodules and mosaic attenuation pattern. Transbronchial biopsy showed bronchiolitis obliterans and chronic rejection. Incidentally noted cavitary lesion in the right upper lobe from atypical mycobacterial infection.
Cryptogenic organizing pneumonia occurs in 10%–28% of patients after lung transplantation and is characterized by the presence of inflammation and fibromyxomatous granulation tissue within the alveoli, alveolar ducts, and small airways. Although bronchiolitis obliterans with organizing pneumonia has been reported to occur in conjunction with chronic rejection and with bacterial and CMV infections, the condition is most commonly associated with acute rejection, and it responds rapidly to high-dose corticosteroid therapy.

High-resolution CT often shows evidence of peripheral airspace consolidation, ground-glass opacities, nodular or masslike consolidation, and linear or reticular opacities. Additional findings include bronchiectasis, bronchiolectasis, fibrosis, lung volume loss, and air trapping.

52 year-man with left lung transplant, HRCT images showing peripheral consolidation, linear opacities and mild bronchiectasis consistent with COP. Right native lung shows diffuse fibrosis and honeycombing.
Bronchial anastomotic complications that are common after lung transplantation include stenosis, tissue degeneration, infection, and dehiscence. The overall prevalence of such complications is approximately 15%.

**Bronchial dehiscence** of the right main bronchus anastomosis in a 56 year woman with bilateral lung transplant for pulmonary fibrosis: Axial CT and axial minip images, obtained more than 4 weeks after lung transplantation, shows a crescent of air outside the airway (arrows), medial to the right main bronchus. This finding was due to an anastomotic leak from dehiscence which was confirmed on bronchoscopy.
Bronchial Anastomotic Complications: Bronchial Dehiscence

The presence of a bronchial wall defect, fixed or dynamic bronchial narrowing, bronchial wall irregularity, extraluminal air, or a combination of these features at CT is indicative of anastomotic dehiscence. Indirect findings that are suggestive of an air leak include pneumothorax, pneumomediastinum, and ipsilateral lung volume loss. Bronchial dehiscence may resolve without sequelae, may result in a stricture that requires stent placement.

61 year-man, status post right lung transplant for pulmonary fibrosis, axial and coronal CT images show right bronchial deiscence at the anastomotic site with formation of a small air pocket anterior and inferior to the suture line (arrows). The native left lung shows advanced fibrotic changes.
Bronchial Anastomotic Complications: Bronchial Stenosis

Donor bronchus ischemia caused by disruption of the native bronchial circulation is a key factor underlying airway related complications. Other risk factors include recurrent infection and rejection.

63 year-man with bilateral lung transplantation. There is severe narrowing of the right upper lobe bronchus, status post stent placement (arrow). There is occlusion of the bronchus intermedius (eclipse) on the coronal mini-p image. However, no right lower or middle lobe collapse seen, likely from the collateral air drift.
Bronchial Anastomotic Complications: Bronchial Stenosis

63 yo-man with bilateral lung transplantation. There is occlusion of the bronchus intermedius (eclipse). The 3D volume rendered (VR) image very well depicts the abrupt cut off of the bronchus intermedius (arrow).

50 year-woman, status post B/L lung transplant, axial CT and 3D VR images show severe narrowing of the left main bronchus with volume loss in the left lung. She underwent transbronchial fluoroscopic bronchial stent placement.
Pleural Complications

Pleural complications are seen in 22–34% of patients after transplantation. Bilateral-lung transplantations frequently result in a single communicating pleural space. Therefore, fluid and gas collections are often bilateral. Additionally, pleural space may communicate with the pericardium which may result in pneumopericardium or pericardial effusion.

Bilateral moderate pneumothoraces (blue arrows) and pneumopericardium (yellow arrow) in a patient with bilateral lung transplants for idiopathic pulmonary fibrosis. Axial chest CT images (lung window), obtained more than a week after lung transplantation. A thoracostomy tube also is visible.

Pneumothorax is the most common pleural complication; it usually resolves with the insertion of thoracostomy tube. New, persistent, or enlarging pneumothoraces should prompt further investigations to elucidate the cause of the air leak.
Pleural Complications: Hydropneumomediastium and hydropneumopericardium

59 year-old man with recent bilateral lung transplant. PA and Lateral chest radiographs demonstrate an air fluid level in the mediastinum obscuring the cardiac silhouette. Right sided small bore pleural catheter and subcutaneous emphysema are seen.
Pleural Complications: Hydropneumomediatium and hydropneumopericardium

59 year- man with recent bilateral lung transplant. Axial CT images in the mediastinal and lung window show right sided pneumothorax communicating with the pericardium (arrow) with air fluid level compatible with hydropneumopericardium (arrows). Right sided small bore pleural catheter and subcutaneous emphysema are seen.
Pleural Complications: Pleural fluid herniation through the right chest wall defect

55 yo-man with right single lung transplant. Right sided pleural effusion is seen herniating through the right chest wall defect into the infrascapular soft tissues (arrows)
Pleural and Pericardial Complications

Two different patients with pleural collections; (a) recurrent right chylothorax after lung transplant, note the low density of the fluid (b) left plural hematoma.

Constrictive pericarditis 6 months after bilateral lung transplantation. Note the pericardial thickening (arrows). Patient also has left pleural effusion.
Lung Herniation

Lung herniation after lung transplant is a rare but known entity. It is most commonly seen after unilateral lung transplantation through the posterior thoracotomy/rib defect but is also noted in bilateral lung transplant. The herniated lung can undergo necrosis or strangulation if the blood supply is obstructed.

Right lower lobe herniation through a chest wall defect after bilateral lung transplant (arrows). The herniated lung tissue is seen as a focal lucency within the right lateral chest wall mimicking subcutaneous emphysema. On HRCT, however, lung vascular markings are clearly seen within the distinguishing it from subcutaneous emphysema.
Lung Infections

Infection is the most common complication after transplantation and is a major cause of morbidity and mortality. Patients have increased susceptibility to infection because of immunosuppression, lung denervation and loss of the cough reflex, impaired mucociliary function, and lymphatic drainage.

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Time of Occurrence</th>
<th>Imaging Findings</th>
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<tbody>
<tr>
<td>Cytomegalovirus</td>
<td>2-4 months</td>
<td>Nodules, ground-glass opacities and consolidation</td>
</tr>
<tr>
<td>Aspergillus</td>
<td>2-4 months</td>
<td>Irregular nodules with surrounding halos, consolidation</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Within first 3 months</td>
<td>Multifocal consolidation, ground glass opacities (GGO)</td>
</tr>
<tr>
<td>Candida</td>
<td>Within first 3 months</td>
<td>Multifocal infiltrates, interstitial thickening, nodules</td>
</tr>
<tr>
<td>Other viruses</td>
<td>2 weeks to 2 years</td>
<td>GGO, peribronchial nodules, mass like consolidation</td>
</tr>
<tr>
<td>Mycobacterium</td>
<td>Late in the course, usually after 4 months</td>
<td>Tree in bud nodules, cavitation, consolidation, pleural effusions</td>
</tr>
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Lung Infections: Cytomegalovirus

Cytomegalovirus (CMV) is the most common cause of opportunistic infection. The rate of CMV infection in lung transplant recipients has been reported to be at least 50%. Seronegative recipients who receive seropositive donor lungs are at the highest risk for primary infection after transplantation. The most common CT manifestations include ground-glass opacities, airspace consolidation, nodules, interlobular septal thickening, pleural effusions, thickened and enhancing pleura, and bronchiectasis.

34 year-old woman 3 months post bilateral lung transplant. Axial HRCT images show diffuse ground glass and patchy nodular opacities (arrows). The transbronchial biopsy was positive for CMV.
Lung Infections: Adenovirus

In addition to CMV, a number of community-acquired viruses, particularly respiratory syncytial virus (RSV), parainfluenza virus, adenovirus, and influenza viruses may infect lung transplant recipients. Most such infections occur from 2 weeks to 2 years after transplantation. HRCT findings are non specific and may show ground glass opacities, peribronchial thickening, centrilobular opacities, air space consolidation.

43 year-man with bilateral lung transplant and progressive dyspnea. HRCT of the chest showing diffuse ground glass opacities. The bronchial lavage and biopsy was positive for adenovirus infection.
Lung Infections: Aspergillosis

Infection due to *Aspergillus* occurs 1–6 months after lung transplantation, with the peak incidence within the first 3 postoperative months. *Aspergillus* infections may manifest as ulcerative tracheobronchitis, bronchial anastomotic infection, aspergilloma, necrotizing pneumonia, invasive pulmonary disease, disseminated infection, or empyema.

66 year-man with right lung transplant for IPF. Axial HRCT images showing areas of mass like consolidations (arrow) with surrounding GGO (Halo sign) (arrow)

Typical features on chest radiographs and CT images include focal nodular and masslike regions of consolidation; cavitation; nodules (solitary or multiple) with a surrounding rim of ground-glass opacity, referred to as the “halo” sign; and pleural thickening.
Vascular complications include pulmonary artery anastomotic stenosis, pulmonary embolism, infarction. The risk of pulmonary infarction is greatest in the immediate postoperative period because the transplanted lung does not have an alternative bronchial blood supply. Perfusion scintigraphy may aid in making the diagnosis. The prognosis is usually dismal, but successful outcomes have recently been reported with angioplasty and stent insertion.

Post lung transplant right pulmonary artery stenosis at the anastomotic site (arrow) on the axial contrast enhanced CT chest. The digital subtraction angiogram confirms the findings (arrow).
52 year-old woman, status post bilateral lung transplantation (LT). Axial and coronal contrast enhanced CT images show hypodense filling defect in the left pulmonary artery (PA) (arrows). It appears crescentic on coronal image suggesting an in situ thrombus.

Two different patients of LT with thrombo-embolic phenomena; (a) thrombus in the left atrium (arrow), (b) left lower lobe PA thrombus (arrow). Also note the left lung herniation through the chest wall defect (eclipse) in (b).
Recurrent Disease in The Transplanted Lung

Recurrent disease in the transplanted lung is not very common, however may affect approximately 1% of recipients. Sarcoidosis, lymphangioleiomyomatosis, cystic fibrosis, pulmonary fibrosis and Langerhans cell histiocytosis have been reported to recur in the transplanted lung. The radiologic features of recurrent disease in the donor lung are similar to those of the original disease, but they may mimic other posttransplantation complications such as infection, rejection, and PTLD.

23 year-woman with lymphangioleiomyomatosis (LAM), pre transplant image(a) showing extensive cystic changes bilaterally. Post transplant images (b,c) showing recurrent cystic changes in the right lower lobe suggestive of disease recurrence.
Recurrent Disease in The Transplanted Lung: Cystic Fibrosis

Two different patients of cystic fibrosis (top and bottom HRCT Images) showing recurrence of the disease in the transplanted lungs with bronchiectasis, bronchial wall thickening and peribronchial nodules, especially in first patient
Post Transplant Lymphoproliferative Disorders (PTLD)

PTLD is a spectrum of diseases that vary from a histologically benign polyclonal lymphoid proliferation to aggressive high-grade lymphoma. It may manifest from 1 month to several years after transplantation but tends to occur within the first year, peaking at 3–4 months. The incidence is approximately 5% (range, 1.8–20%), and it is more common with lung transplantation than with other solid organ transplantations. Seronegative status for Epstein-Barr virus prior to transplantation is thought to be a major risk factor for the development of PTLD.

PTLD in a patient with a right lung transplant for IPF. Axial chest CT images, obtained at 5 months after lung transplantation, demonstrate multiple right middle lobe masses (arrows) and left lung fibrosis. Transbronchial biopsy specimen showed marked infiltration of the bronchiolar wall with destruction of the smooth-muscle layer by large atypical lymphocytes consistent with PTLD.
Post Transplant Lymphoproliferative Disorders (PTLD)

HRCT imaging findings of PTLD include multiple pulmonary nodules (with or without the “halo” sign), consolidation, interlobular septal thickening, pleural effusion, and mediastinal lymphadenopathy. Late disease, which is treated primarily with chemotherapy and irradiation, may develop more than 1 year after transplantation and is predominantly associated with extrathoracic involvement.

Biopsy proven high grade diffuse B cell lymphoma in a patient with one year post right lung transplant. Multiple enlarged right hilar lymph nodes are seen (arrows). Mass like consolidative opacities in the right lung, peribronchial thickening, nodularity and septal thickening are seen as well depicting lymphatic spread of the disease.
Post Lung-Transplant Primary Bronchogenic Carcinoma

Bronchogenic carcinoma after lung transplantation is rare and may occur late in the course. Emphysema and pulmonary fibrosis before transplantation are known risk factors. It usually manifests as a noncalcified solitary pulmonary nodule or mass with or without mediastinal lymphadenopathy.

62 year-man, post lung transplant, routine frontal chest radiograph showing abnormal convex paratacaracheal stripe (arrow). Contrast enhanced CT chest showing conglomerate lymph node mass in the pre and paratracheal region (arrow). Biopsy came positive for squamous cell carcinoma of lung origin.
Pneumatosis Cystodes Coli and Retropneumoperitoneum

Bilateral lung transplant recipients may develop benign pneumatos is coli (PC) or pneumoperitoneum after surgery. Benign PC in bilateral lung transplant recipients has a similar and specific linear and cystic appearance and is not due to ischemic bowel. No specific cause for the PC and pneumoperitoneum is found. The findings are incidental in otherwise asymptomatic patients.

Routine chest radiograph of a patient with bilateral lung transplant partially demonstrate ill defined linear lucency in the right upper abdomen. CT abdomen performed later showing extensive cystic pneumatos is coli throughout the ascending colonic wall and small retro-pneumoperitoneum. Patient was asymptomatic and no definite cause for pneumatos is was found. He was discharged without any intervention.
Progressive upper-lobe fibrosis occurs 1–4 years after transplantation. Radiographic and HRCT features include interlobular septal thickening and reticular or ground-glass opacities, traction bronchiectasis, honeycombing, architectural distortion, and loss of lung volume.

39 year-old woman underwent B/L LT for pulmonary fibrosis. Serial radiographs obtained after the surgery demonstrate development of fibrotic changes predominantly in bilateral upper lobes. HRCT image confirms the findings.
Conclusion

- Radiologists can guide clinicians through the broad spectrum of complications which occur after lung transplant from the radiological and computer tomography findings.
- Radiologists should be familiar with the imaging appearances of common surgical techniques as well as those of complications of lung transplantation.
- Because the radiologic pattern of disease may be nonspecific, it is critical to know the time course from lung transplantation and relevant postoperative history in order to narrow the differential diagnosis.
References


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