Trillium Gift of Life Network

Ontario's Referral and Listing Criteria for Adult Lung Transplantation

Version 3.0

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Adult Lung Transplantation Referral & Listing Criteria

PATIENT REFERRAL CRITERIA:

The patient referral criteria are guidelines which a Health Care Provider would utilize to refer a patient to a transplant center for assessment. In general, referral for lung transplantation assessment is advisable when patients have a less than 50%, 2- to 3-year predicted survival or New York Heart Association (NYHA) class III or IV level of function, or both.

The criteria identified below are the agreed upon conditions for which a patient should be referred for lung transplant assessment.

1) **Chronic Obstructive Pulmonary Disease (COPD):** Referral for lung transplantation should be considered for patients with chronic obstructive pulmonary disease (COPD). Such patients would meet the following criteria:
    - Progressive disease despite maximal treatment including medication, pulmonary rehabilitation, and oxygen therapy;
    - Patient is not a candidate for endoscopic or surgical lung volume reduction surgery (LVRS). Simultaneous referral of patients with COPD for both lung transplant and LVRS evaluation is appropriate;
    - Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise (BODE) index of 5-6;
    - Partial pressure of carbon dioxide [$PaCO_2$] >50mmHg or 6.6 kPa and/or partial pressure of oxygen [PaO_2] <60mmHg or 8 kPa; or,
    - Forced Expiratory Volume (FEV1) <25% predicted.

2) **Cystic Fibrosis and Other Causes of Bronchiectasis:** Referral for lung transplantation should be considered for patients with cystic fibrosis and other causes of bronchiectasis. Such patients would have one or more of the following:
    - FEV1 below 30% predicted or a patient with advanced disease with a rapidly falling FEV1 despite optimal therapy (particularly in young female patients), infected with non-tuberculous mycobacterial (NTM) disease or *B cepacia* complex and/or diabetes;
    - 6-minute walk distance <400 m;
    - Development of pulmonary hypertension in the absence of hypoxic exacerbation (as defined by a systolic pulmonary arterial pressure (PAP) >35 mmHg on echocardiography or mean PAP >25 mmHg measured by right heart catheterization); or,
    - Clinical decline characterized by increasing frequency of exacerbations associated with any of the following:
        - An episode of acute respiratory failure requiring non-invasive ventilation
        - Increasing antibiotic resistance and poor clinical recovery from exacerbations
        - Worsening nutritional status despite supplementation
        - Pneumothorax
        - Life-threatening hemoptysis despite bronchial embolization

3) **Interstitial Lung Disease:** Referral for lung transplantation should be considered for patients with histologic or radiographic evidence of Usual Interstitial Pneumonia (UIP) or fibrosing Non-Specific Interstitial Pneumonitis (NSIP), regardless of lung function. Such patients would have:
    - 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; or,
- For inflammatory interstitial lung disease (ILD), failure to improve dyspnea, oxygen requirement, and/or lung function after a clinically indicated trial of medical therapy.

4) **Pulmonary Vascular Disease:** Referral for lung transplantation should be considered for patients with pulmonary vascular diseases. Such patients would have one of the following:
    - NYHA functional class of III or IV symptoms during escalating therapy;
    - Rapidly progressive disease (assuming weight and rehabilitation concerns not present);
    - Use of parenteral targeted pulmonary arterial hypertension (PAH) therapy regardless of symptoms or NYHA functional class; or,
    - Known or suspected pulmonary veno-occlusive disease (PVOD) or pulmonary capillary hemangiomatosis.

5) **Sarcoidosis:** Referral for lung transplantation should be considered for patients with sarcoidosis if they are NYHA functional class III or IV.

6) **Lymphangioleio-myomatosis:** Referral for lung transplantation should be considered for patients with lymphangioleio-myomatosis if they are NYHA functional class III or IV.

7) **Pulmonary Langerhans Cell Histiocytosis (Eosinophilic Granuloma):** Referral for lung transplantation should be considered for patients with pulmonary Langerhans cell histiocytosis if they are NYHA functional class III or IV.

PATIENT LISTING INDICATIONS:

Each patient is assessed individually for their suitability for transplantation by the transplant program. The criteria identified below are the conditions for which a patient may be eligible to be waitlisted for lung transplantation in Ontario.

1) **Chronic Obstructive Pulmonary Disease (COPD):** Listing for lung transplantation may be considered for patients with COPD. Such patients would meet the following criteria:
    - BODE index $\geq$7;
    - FEV1 <15%-20% predicted;
    - $\geq$3 severe exacerbations during preceding year;
    - One severe exacerbation with acute hypercapnic respiratory failure; or,
    - Moderate to severe pulmonary hypertension.

2) **Cystic Fibrosis and Other Causes of Bronchiectasis:** Listing for lung transplantation may be considered for patients with cystic fibrosis or other causes of bronchiectasis. Such patients would have one of the following:
    - Chronic respiratory failure;
        - With hypoxia alone (PaO2 <8 kPa or <60 mmHg)
        - With hypercapnia (PaCO2 >6.6 kPa or >50 mmHg)
    - Long-term non-invasive ventilation therapy;
    - Pulmonary hypertension;
    - Frequent hospitalization;
    - Rapid lung function decline; or,
    - World Health Organization functional Class IV.

3) **Interstitial Lung Disease:** Listing for lung transplantation may be considered for patients with interstitial lung disease (ILD). Such patients would have:
    - Decline in FVC $\geq$10% during 6 months of follow-up (note: 5% decline is associated with poorer prognosis and may warrant listing);
    - Decline in DLCO $\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; or,
    - Hospitalization because of respiratory decline, pneumothorax, or acute exacerbation.

    Note: ILD severe enough to warrant consideration of lung transplantation may be associated with collagen vascular diseases such as scleroderma and rheumatoid arthritis. If the lung disease has not responded to appropriate treatment and there are no extrapulmonary contraindications to transplantation, it is reasonable to use similar guidelines to those proposed for idiopathic ILD.

4) **Pulmonary Vascular Diseases:** Listing for lung transplantation may be considered for patients with pulmonary vascular diseases. Such patients would have one of the following:
    - NYHA class III or IV despite a trial of at least 3 months of combination therapy including prostanoids;
    - Cardiac index of < 2 liters/min/m^2;
    - Mean right atrial pressure of >15 mm Hg;
    - 6-minute walk test of <350 m; or,
    - Development of significant hemoptysis, pericardial effusion, or signs of progressive right heart failure (renal insufficiency, increasing bilirubin, brain natriuretic peptide, or recurrent ascites).

5) **Sarcoidosis**: Listing for lung transplantation may be considered for patients with sarcoidosis. Such patients would meet the following criteria:
   - Impairment of exercise tolerance (NYHA functional class III or IV) and any of the following:
     - Hypoxemia at rest;
     - Pulmonary hypertension; or,
     - Elevated right atrial pressure exceeding 15 mm Hg.

6) **Lymphangioleio-myomatosis**: Patients with lymphangioleio-myomatosis may be considered for lung transplantation. Such patients would have one of the following:
   - Severe impairment in lung function and exercise capacity (e.g., VO_2 max < 50% predicted); or,
   - Hypoxemia at rest.

7) **Pulmonary Langerhans Cell Histiocytosis (Eosinophilic Granuloma):** Patients with pulmonary Langerhans cell histiocytosis may be considered for lung transplantation. Such patients would have one of the following:
   - Severe impairment in lung function and exercise capacity; or,
   - Hypoxemia at rest.

8) **General:** Patients not included in the preceding categories but have a poor quality of life (based on the clinical judgment of the care team at the time of assessment) may be considered for lung transplantation. Listing for lung transplantation may also be considered for patients if the following requirements are met:
   - The absence of obvious contraindications for transplant; and,
   - The potential to undergo rehabilitation after transplantation.

9) **Lack of Alternative Medical Options:** Patients who fail to respond to maximal medical therapy or the absence of alternative/conventional surgical options may be considered for lung transplantation.

ABSOLUTE LISTING CONTRAINDICATIONS:

The following are conditions relating to the lung transplant candidate that constitute absolute contraindications to lung transplantation. As such, they prevent a transplant from being done until the condition is resolved.

1) **Psychosocial Issues:** Patients must undergo a complete psychosocial evaluation prior to listing for transplantation. Patients who display the following are not candidates for lung transplantation:
   - Current non-adherence to medical therapy or a history of repeated or prolonged episodes of non-adherence to medical therapy that are perceived to increase the risk of non-adherence after transplantation;
   - Psychiatric or psychologic conditions associated with the inability to cooperate with the medical/allied healthcare team and/or adhere with complex medical therapy;
   - Absence of adequate/reliable social support system; or,
   - Substance abuse or dependence (e.g. alcohol, tobacco, marijuana, or other illicit substances). In many cases, convincing evidence of risk reduction behaviours, 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.

2) **Bleeding Diathesis:** Patients with uncorrectable bleeding diathesis are not candidates for lung transplantation.

3) **Obesity:** Patients with class II or III obesity [body mass index (BMI) $\geq$35.0/m^2] are not candidates for lung transplantation.

4) **Infections:** Patients with a chronic infection with highly virulent and/or resistant microbes that are poorly controlled pre-transplant or patients with evidence of active tuberculosis (TB) infection are not candidates for transplantation.

RELATIVE LISTING CONTRAINDICATIONS:

The following are conditions relating to the lung transplant candidate that constitute relative contraindications to lung transplantation. While each patient is evaluated on an individual basis, the presence of one or more of the following may preclude a candidate from being listed on the lung transplantation wait list.

1) **Age:** Patients older than 65 years with low physiologic reserve and/or other relative contraindications may not be eligible for lung transplantation. Older patients have less optimal survival, likely due to comorbidities, and therefore recipient age should be a factor in candidate selection. Although there cannot be endorsement of an upper age limit as an absolute contraindication, the presence of several relative contraindications can combine to increase the risks of transplantation above a safe threshold.

2) **Medical Stability:** Patients with acute medical instability, including, but not limited to acute sepsis, myocardial infarction, and liver failure may not be eligible for lung transplantation.

3) **Functional Status:** Patients with severely limited functional status with poor rehabilitation potential may not be eligible for lung transplantation.

4) **Infection:** Patients with the following infections may not be eligible for lung transplantation:
   - Colonization or infection with highly virulent bacteria, fungi, and certain strains of mycobacteria (e.g. chronic extra-pulmonary infection expected to worsen post-transplantation);
   - Non-tuberculous mycobacterium (NTM) and progressive pulmonary or extra-pulmonary disease secondary to NTM despite optimal medical therapy or inability to tolerate optimal medical therapy;
   - Hepatitis B and/or C infections with significant clinical, radiologic or biochemical signs of cirrhosis or portal hypertension, and do not achieve stability on appropriate therapy; or,
   - *Burkholderia cenocepacia, Burkholderia gladioli*, and multi-drug-resistant *Mycobacterium absecessus* that is not sufficiently treated pre-operatively, and an expectation of inadequate control in the post-operative period, should be considered as having relative contraindications to transplant.

   Note: HIV infections may be considered for lung transplantation if their disease is controlled with undetectable HIV-RNA and patient is compliant with antiretroviral therapy. Patients should not have any current acquired immunodeficiency syndrome-defining illnesses.

5) **Obesity:** Patients with class I obesity (BMI 30-34.9 kg/m^2), particularly truncal (central obesity), may not be eligible for lung transplantation.

6) **Osteoporosis:** Patients with severe or symptomatic osteoporosis may not be eligible for lung transplantation.

7) **Mechanical Ventilation:** Patients with mechanical ventilation and/or extracorporeal life support (ECLS) may not be eligible for lung transplantation.

8) **Disease:** Patients with untreatable advanced dysfunction of another major organ system (e.g. heart, liver, or kidney) may not be eligible for lung transplantation unless combined organ transplantation can be performed. Patients with uncorrected atherosclerotic disease with suspected or confirmed end-organ ischemia or dysfunction and/or coronary artery disease not amenable to revascularization may not be eligible for lung transplantation. Patients who may have atherosclerotic disease burden sufficient to put the patient at risk for end-organ disease after lung transplantation may not be eligible for lung transplantation

   Other medical conditions that have not resulted in end-stage organ damage, such as diabetes mellitus, systemic hypertension, epilepsy, central venous obstruction, peptic ulcer disease, or gastroesophageal reflux, should be optimally treated before transplantation. With regard to coronary artery disease, some patients will be candidates for percutaneous coronary intervention or coronary artery bypass graft (CABG) preoperatively or, in some instances, combined lung transplant and CABG.

9) **Malignancy:** Patients with a recent history of malignancy may not be eligible for lung transplantation. Patients with a 2-year disease-free interval combined with a low predicted risk of recurrence after lung transplantation may be reasonable, for instance, in non-melanoma localized skin cancer that has been treated appropriately. A 5- year disease-free interval is prudent in most cases, particularly for patients with a history of hematologic malignancy, sarcoma, melanoma, or cancers of the breast, bladder, or kidney.

   In the case of adenocarcinoma in situ and minimally invasive adenocarcinoma, patients with the following may be considered for referral and listing:
   - Diffuse parenchymal tumor involvement causing lung restriction and significant respiratory compromise;
   - Significantly reduced quality of life; or,
   - Failure of conventional medical therapies.

10) **Deformity:** Patients with significant chest wall/spinal deformity may not be eligible for lung transplantation.

11) **Malnutrition:** Patients with progressive or severe malnutrition may not be eligible for lung transplantation.

12) **Chest surgery:** Patients with extensive prior chest surgery with lung resection may not be eligible for lung transplantation.

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