Lung and Lobar Lung Transplant

Policy Number: MM.07.024
Original Effective Date: 05/21/1999
Line(s) of Business: HMO; PPO
Current Effective Date: 09/23/2011
Section: Transplants
Place(s) of Service: Inpatient

I. Description

A lung transplant consists of replacing all or part of diseased lungs with healthy lung(s). Transplantation is an option for patients with end-stage lung disease.

End-stage lung disease may be the consequence of a number of different etiologies. The most common indications for lung transplantation are chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), cystic fibrosis (CF), alpha-1 antitrypsin deficiency, and idiopathic pulmonary arterial hypertension (IPAH). Prior to the consideration for transplant, patients should be receiving maximal medical therapy including oxygen supplementation or surgical options such as lung-volume reduction surgery for COPD. Lung or lobar lung transplantation is an option for patients with end-stage lung disease despite these measures.

A lung transplant refers to single-lung or double-lung replacement. In a single-lung transplant, only one lung from a deceased donor is provided to the recipient. In a double-lung transplant, both the recipient's lungs are removed and replaced by the donor's lungs. In a lobar transplant, a lobe of the donor's lung is excised, sized appropriately for the recipient’s thoracic dimensions, and transplanted. Donors for lobar transplant have been primarily living-related donors, with one lobe obtained from each of two donors (e.g., mother and father) in cases for which a bilateral transplantation is required. There are also cases of cadaver lobe transplants. Combined lung-pancreatic islet cell transplant is being studied for patients with cystic fibrosis. (1)

Since 2005, potential recipients have been ranked according to the Lung Allocation Score (LAS). Patients 12 years of age and older receive a score between 1 and 100 based on predicted survival after transplantation reduced by predicted survival on the waiting list; the LAS takes into consideration the patient’s disease and clinical parameters. Children under the age of 12 are prioritized based on length of time on the waiting list. A Lung Review Board (LRB) has authority to adjust scores upon appeal. In 2009, 1,660 patients received lung transplants in the United States.
all but one from deceased donors. There were 1,089 patients on the waiting list at the end of 2008. (2) The 1-, 5-, and 10-year patient survival rate is 79%, 52%, and 29%, respectively. (3)

II. Policy

A. Lung transplantation is covered (subject to Administrative Guidelines) for carefully selected patients with irreversible, progressively disabling, end-stage pulmonary disease including but not limited to 1 of the conditions listed below.

B. A lobar lung transplant from a living or deceased donor is covered (subject to Administrative Guidelines) for children and adolescents with end-stage pulmonary disease including but not limited to one of the conditions listed below.

- Bilateral bronchiectasis
- Congenital bronchiectasis
- Alpha-1 antitrypsin deficiency
- Primary pulmonary hypertension
- Cystic fibrosis (both lungs to be transplanted)
- Bronchopulmonary dysplasia
- Postinflammatory pulmonary fibrosis
- Idiopathic/interstitial pulmonary fibrosis
- Sarcoidosis
- Scleroderma
- Lymphangiomyomatosis
- Emphysema
- Eosinophilic granuloma
- Bronchiolitis obliterans
- Recurrent pulmonary embolism
- Pulmonary hypertension due to cardiac disease
- Chronic obstructive pulmonary disease
- Eisenmenger’s syndrome

C. Lung transplantation is not medically necessary in patients with the following absolute contraindications:

1. Known current malignancy, including metastatic cancer;
2. Recent malignancy with a high incidence of recurrence;
3. Untreated systemic infection making immunosuppression unsafe, including chronic infection; or
4. Other irreversible end-stage disease not attributed to lung disease
III. Policy Guidelines

General:

Patients must meet UNOS guidelines for lung allocation score (LAS) greater than zero.

Lung Specific

A. Bilateral lung transplantation is typically required when chronic lung infection disease is present, i.e., associated with cystic fibrosis and bronchiectasis. Some, but not all, cases of pulmonary hypertension will require bilateral lung transplantation.

B. Bronchiolitis obliterans is associated with chronic lung transplant rejection, and thus may be the etiology of a request for lung retransplantation.

C. Relative contraindications to lung transplantation:

1. History of cancer with a moderate risk of recurrence;
2. Systemic disease that could be exacerbated by immunosuppression;
3. Psychosocial conditions or chemical dependence affecting the ability to adhere to therapy;
4. Coronary artery disease not amenable to percutaneous intervention or bypass grafting, or associated with significant impairment of left ventricular function*; or
5. Colonization with highly resistant or highly virulent bacteria, fungi, or mycobacteria

IV. Administrative Guidelines

Precertification is required. To precertify, complete HMSA's Precertification Request and mail or fax the form as indicated along with the required documentation.

<table>
<thead>
<tr>
<th>Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>32850</td>
<td>Donor pneumonectomy(ies) (including cold preservation), from cadaver donor</td>
</tr>
<tr>
<td>32851</td>
<td>Lung transplant, single; without cardiopulmonary bypass</td>
</tr>
<tr>
<td>32852</td>
<td>with cardiopulmonary bypass</td>
</tr>
<tr>
<td>32853</td>
<td>Lung transplant, double (bilateral, sequential, or en bloc); without cardiopulmonary bypass</td>
</tr>
<tr>
<td>32854</td>
<td>with cardiopulmonary bypass</td>
</tr>
<tr>
<td>32855</td>
<td>Backbench standard preparation of cadaver donor lung allograft prior to transplantation, including dissection of allograft from surrounding tissues to prepare pulmonary venous/atrial cuff, pulmonary artery, and bronchus, unilateral</td>
</tr>
</tbody>
</table>
V. Scientific Background

Literature Review

This policy was originally created in 1996 and updated regularly with searches of the MEDLINE database. The most recent literature search was performed for the period of June 2009 to October 2010. Due to the nature of the population, there are no randomized controlled trials (RCTs) that compare lung transplantation with alternatives. Systematic reviews are based on case series and registry data. The extant RCTs compare surgical technique, infection prophylaxis, or immunosuppressive therapy and are not germane to this policy. The following is a summary of the evidence based on registries, case series, and expert opinion.

Survival

Authors of a recent review of the current status of lung transplantation observe that while transplantation can prolong survival, survival statistics for lung transplantation are not as favorable as in patients receiving other solid organ transplants; lung transplants having a half life of approximately 5 years versus 10 years for heart, kidney, and liver transplants. (4) Yusen notes that the literature provides conflicting data on survival and quality of life outcomes. (5) He encourages development and reporting of valid measures of outcomes such as symptom control and function, as well as survival, which will assist patients in weighing the potential costs and benefits of lung transplantation.

In 2009, Thabut and colleagues reported on a comparison of patients undergoing single- and double-lung transplantation for idiopathic pulmonary fibrosis (IPF). (6) A retrospective review was conducted of 3,327 patients with data in the UNOS registry. More patients underwent single-lung as compared to double-lung transplant (64.5 vs. 35.5%, respectively). Median survival time was greater for the double lung group at 5.2 years (95% confidence interval [CI], 4.3 to 6.7 years) versus 3.8 years (95% CI, 3.6 to 4.1 years; p<0.001). After adjustment for baseline differences, however, survival times were not statistically different. The authors concluded that overall survival did not differ between the 2 groups: single-lung transplants offered improved short-term survival but long-term harm, whereas double-lung transplant increased short-term harm but was associated with a long-term survival benefit.

Patient Selection
In 2008, Kozower and colleagues performed a retrospective cohort study using data from 5 academic medical centers to evaluate the impact of a new lung allocation score on short-term outcomes after lung transplantation. (7) This lung allocation score was implemented in May 2005 by the Organ Procurement and Transplantation Network [OPTN]. This new score changed lung allocation from a system based on waiting time to an algorithm based on the probability of survival for 1 year on the transplant list and survival 1-year post-transplantation. Results were compared for 170 patients who received transplants on the basis of the new lung allocation scores (May 4, 2005 to May 3, 2006) with those of 171 patients who underwent transplants the preceding year before implementation of the scoring system. Waiting time decreased from 681 to 445.6 days (p<0.001). Recipient diagnoses changed, with an increase (15% to 25%) in idiopathic pulmonary fibrosis cases and decreases in emphysema (46% to 34%) and cystic fibrosis (CF) (23% to 13%). Hospital mortality and 1-year survival were the same between groups (5.3% vs. 5.3% and 90% vs. 89%, respectively). Presumably due to increased severity of illness, the incidence of primary graft dysfunction and postoperative intensive care unit length of stay increased in the year after implementation of the scoring system; graft dysfunction grew from 14.8% (24/170) to 22.9% (39/171); (p=0.04) and length of stay rose from 5.7 to 7.8 days.

In 2010, Yusen and colleagues reviewed the effect of the Lung Allocation Score (LAS) on lung transplantation by comparing statistics for the period before and after its implementation in 2005. (8) Other independent changes in clinical practice, which may affect outcomes over the same period of time, include variation in immunosuppressive regimens, an increased supply of donor lungs, changes in diagnostic mix, and increased consideration of older recipients. Deaths on the waiting list declined following implementation of the LAS system, from approximately 500 per 5,000 patients to 300 per 5,000 patients. However, it is expected that implementation of the LAS affected patient characteristics of transplant applicants. One-year survival post-transplantation did not improve after implementation of the LAS system: patient survival data before and after is approximately 83%. Long-term survival data are not yet available for comparison.

**Pediatric Considerations**

In October 2010, Aurora and colleagues reviewed pediatric lung transplants which have been reported to the international registry. (9) Pediatric patients are defined as those younger than 18 years of age. The authors note a steady increase in the number of pediatric lung transplants in recent years; 102 transplants were completed internationally in 2008. In contrast to adult patients, the most common indication for pediatric patients was CF, accounting for 70% of lung transplants worldwide. Survival has improved in the recent era and 5-year survival is equivalent to adult recipients (52% in both cases). Patients 11 years and younger have tended to have better survival rates than those older than 11 years of age.

**Contraindications**

Absolute contraindications to lung transplant have been an evolving concern. Individual transplant centers may differ in their guidelines, and individual patient characteristics may vary within a specific condition. In general, lung transplantation is contraindicated in patients who are not
expected to survive the procedure or in whom patient-oriented outcomes, such as morbidity and mortality, are not expected to change due to comorbid conditions unaffected by the transplantation e.g., imminently terminal cancer or other disease. Further, consideration is given to conditions in which the necessary immunosuppression would lead to hastened demise, such as active untreated infection. However, stable chronic infections have not always been shown to reduce life expectancy in lung transplant patients.

Malignancy

Concerns regarding a potential recipient’s history of cancer have been based on the observation of significantly increased incidence of cancer in kidney transplant patients. (10) In fact, carcinogenesis is 2 to 4 times more common in lung transplant patients, likely due to the higher doses of immunosuppression necessary for the prevention of allograft rejection. Initially, lymphomas are the predominant malignancies that develop in lung transplant patients; as the term of survival increases, skin cancers become more common. Up to 28% patients will develop de novo malignancy if they survive 10 years. (3) For renal transplant patients who had a malignancy treated prior to transplant, the incidence of recurrence ranged from zero to more than 25%, depending on the tumor type. (11, 12) However, it should be noted that the availability of alternative treatment strategies informs recommendations for a waiting period following high-risk malignancies: in renal transplant, a delay in transplantation is possible due to dialysis; end-stage lung disease patients may not have an option to defer.

HIV

Solid organ transplant for patients who are human immunodeficiency virus (HIV)-positive has been controversial, due to the long-term prognosis for HIV positivity and the impact of immunosuppression on HIV disease. Although HIV-positive transplant recipients may be of research interest at some transplant centers, the minimal data regarding long-term outcome in these patients primarily consist of case reports and abstract presentations of liver and kidney recipients. Nevertheless, some transplant surgeons would argue that HIV positivity is no longer an absolute contraindication to transplant due to the advent of highly active antiretroviral therapy (HAART), which has markedly changed the natural history of the disease.

In March 2009, the Organ Procurement Transplantation Network (OPTN) revised its policies on HIV status in recipients. It reiterates an earlier position that: “A potential candidate for organ transplantation whose test for HIV is positive but who is in an asymptomatic state should not necessarily be excluded from candidacy for organ transplantation, but should be advised that he or she may be at increased risk of morbidity and mortality because of immunosuppressive therapy.” (13)

In 2006, the British HIV Association and the British Transplantation Society Standards Committee published guidelines for kidney transplantation in patients with HIV disease. (14) These criteria may be extrapolated to other organs:
- CD4 count >200 cells/ml for at least 6 months
- Undetectable HIV viremia (less than 50 HIV RNA copies/ml) for at least 6 months
- Demonstrable adherence and a stable HAART regimen for at least 6 months
- Absence of AIDS defining illness following successful immune reconstitution after HAART

Other Infections

In 2008, two papers evaluated the impact of infection with various species of Burkholderia on outcomes for lung transplantation for cystic fibrosis. Murray and colleagues sought to quantify the risks of infection with Burkholderia species on survival before and after transplantation. (15) Multivariate Cox survival models assessing hazard ratios (HRs) were applied to 1,026 lung transplant candidates and 528 transplant recipients. Of the transplant recipients, 88 were infected with Burkholderia. Among transplant recipients infected with Burkholderia cenocepacia, only those infected with non-epidemic strains (n=11) had significantly greater post-transplant mortality than uninfected patients (HR, 2.52; 95% confidence interval [CI, 1.04-6.12; p=0.04). Transplant recipients infected with Burkholderia gladioli (n=14) also had significantly greater post-transplant mortality than uninfected patients (HR, 2.23; 95% CI, 1.05-4.74; p=0.04). Hazard ratios for patients infected with Burkholderia multivorans (n=32) were similar to those for uninfected transplant recipients (HR, 0.66). When adjustments for specific species/strains were included, lung allocation scores of B multivorans-infected transplant candidates were comparable to uninfected candidate scores, and scores for patients infected with non-epidemic B cenocepacia or B gladioli were lower. In a smaller study of 22 patients colonized with Burkholderia cepacia complex who underwent lung transplantation in two French centers, the risk of death by univariate analysis was significantly higher for the 8 patients infected with B cenocepacia than for the other 14 colonized patients (11 of whom had B multivorans). (16)

In patients with CF, there are no absolute contraindications based on either the type of the organism or the pattern of resistance. (17) Infection with B cenocepacia is associated with increased mortality in some transplant centers, a factor that may be taken into account when evaluating overall risk for transplant survival. (18) Patients colonized with pan-resistant bacteria other than B cepacia appear to have slightly decreased survival relative to patients harboring sensitive bacteria. In 1 retrospective report with 103 patients, survival with pan-resistant bacteria was 91% at 1 year, 89% at 2 years, 63% at 3 years, and 58% at 5 years; this was compared to survival rates of patients with sensitive bacteria (98%, 97%, 91%, and 85%, respectively) from the same centers, and to survival rates for patients with CF from the UNOS registry (1 year, 86%; 3 years, 65%; 5 years, 50%). (19)

Summary

The literature, consisting of case series and registry data, demonstrates that lung transplantation provides a survival benefit in appropriately selected patients and thus may be considered medically necessary. It may be the only option for some patients with end-stage lung disease. Lung transplantation is not medically necessary in patients in whom the procedure is expected to be
futile due to comorbid disease or in whom post-transplantation care is expected to significantly worsen comorbid conditions.

**Technology Assessments, Guidelines, and Position Statements**

A key publication is the 2006 guidelines from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. (17) The consensus-based guidelines state that, “Lung transplantation is now a generally accepted therapy for the management of a wide range of severe lung disorders, with evidence supporting quality of life and survival benefit for lung transplant recipients. However, the number of donor organs available remains far fewer than the number of patients with end-stage lung disease who might potentially benefit from the procedure. It is of primary importance, therefore, to optimize the use of this resource, such that the selection of patients who receive a transplant represents those with realistic prospects of favorable long-term outcomes. There is a clear ethical responsibility to respect these altruistic gifts from all donor families and to balance the medical resource requirement of one potential recipient against those of others in their society. These concepts apply equally to listing a candidate with the intention to transplant and potentially de-listing (perhaps only temporarily) a candidate whose health condition changes such that a successful outcome is no longer predicted.”

**Medicare National Coverage**

Lung transplantation is covered under Medicare when performed in a facility that is approved by Medicare as meeting institutional coverage criteria—approximately 57 programs in the U.S. (20) The Centers for Medicare and Medicaid Services have stated that under certain limited cases, exceptions to the facility-related criteria may be warranted if there is justification and the facility ensures safety and efficacy objectives.

**VI. Important Reminder**

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with
HMSA’s determination as to medical necessity in a given case, the physician may request that
HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any
supporting documentation.

VII. References

2. Lichtenstein DR, Jagannath S, Baron TH et al. Sedation and anesthesia in GI endoscopy.
Heart and Lung Transplantation: twenty-seventh official adult lung and heart-lung transplant
2009; 6(1):128-36
6. Thabut G, Christie JD, Kremers WK et al. Survival differences following lung transplantation
7. Kozower BD, Meyers BF, Smith MA et al. The impact of the lung allocation score on short-term
and Lung Transplantation: thirteenth official pediatric lung and heart-lung transplantation
Transplant 2005; 5(9):2079-84.
November 2010.
patients with cystic fibrosis colonised with Burkholderia cepacia complex: results from two
for Heart and Lung Transplantation. International guidelines for the selection of lung transplant
candidates: 2006 update--a consensus report from the Pulmonary Scientific Council of the

