Lung and Lobar Lung Transplant*

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DESCRIPTION

A lung transplant consists of replacing all or part of diseased lungs with healthy lung(s) or lobes. For most individuals a lung transplant is a palliative rather than curative treatment intended for end-stage lung disease which has failed to respond to alternative medical or surgical treatment. The primary goal of lung transplantation is extended survival.

Solid organ transplantation offers a treatment option for patients with different types of end stage organ failure that can be lifesaving or provide significant improvements to a patient's quality of life. Many advances have been made in the last several decades to reduce perioperative complications. Available data supports improvement in long-term survival as well as improved quality of life particularly for liver, kidney, pancreas, heart, and lung transplants. Allograft rejection remains a key early and late complication risk for any organ transplantation. Transplant recipients require life-long immunosuppression to prevent rejection. Patients are prioritized for transplant by mortality risk and severity

of illness criteria developed by the Organ Procurement and Transplantation Network (OPTN) and United Network of Organ Sharing.

Lung Transplantation
Lung transplantation involves either single-lung or double-lung replacement. One or both lungs are transplanted from a donor with pronounced brain death into the chest cavity of the recipient.

In 2021, 41,354 transplants were performed in the United States procured from 13,861 deceased donors and 6,541 living donors. Lung transplants were the fourth most common procedure with 2,524 transplants performed from both deceased and living donors in 2021.

End-stage lung disease may derive from different etiologies. The most common indications for lung transplantation are chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, cystic fibrosis, a1-antitrypsin deficiency, and idiopathic pulmonary arterial hypertension. Before consideration for transplant, patients should be receiving maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for chronic obstructive pulmonary disease. 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 1 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 primarily been living-related donors, with 1 lobe obtained from each of 2 donors (generally friends or family members) in cases for which bilateral transplantation is required. There are also cases of cadaver lobe transplants.

Lung Allocation Score
Potential recipients who are 12 years of age and older are ranked according to the Lung Allocation Score. A score may range between 0 and 100 and incorporates predicted survival after transplantation and predicted survival on the waiting list; the Lung Allocation Score takes into consideration the patient's disease and clinical parameters. The waiting list incorporates the Lung Allocation Score, geography, and blood type classifications. Children younger than 12 years old receive a priority for lung allocation. Under this system, children younger than 12 years old with respiratory lung failure and/or pulmonary hypertension who meet criteria are considered "priority 1", and all other candidates in the age group are considered "priority 2". A lung review board has the authority to adjust scores on appeal for adults and children

Potential Contraindications to Transplantation
Malignancy

Malignancies are common after lung transplantation, with 21% and 40% of patients reporting one or more malignancies at 5 and 10 years posttransplantation, respectively. Skin cancer occurred most frequently, and lymphoproliferative disorders were the malignancies most associated with morbidity posttransplantation.

Human Immunodeficiency Virus (HIV) Infection
Current Organ Procurement and Transplantation Network (OPTN) policy permits human immunodeficiency virus (HIV)-positive transplant candidates. The 2020 US Public Health Service guideline also allows for transplantations in HIV-positive recipients with proper screenings and effective regimens for HIV infections.

The British HIV Association and the British Transplantation Society (2017) updated their guidelines on kidney transplantation in patients with HIV disease. These criteria for adding a patient to the waitlist may be extrapolated to other organs:

- Adherent with treatment, particularly antiretroviral therapy
- Cluster of Differentiation 4 count greater than 100 cells/mL (ideally >200 cells/mL) for at least 3 months
- Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least 6 months
- No opportunistic infections for at least 6 months
- No history of progressive multifocal leukoencephalopathy, chronic intestinal cryptosporidiosis, or lymphoma.

Other Infections
Infection with Burkholderia cenocepacia is associated with increased mortality in some transplant centers, a factor that may be considered when evaluating the overall risk of transplant survival. Two articles have evaluated the impact of infection with various species of Burkholderia on outcomes for lung transplantation for cystic fibrosis. In a study by Murray et al (2008), multivariate Cox survival models were applied to 1026 lung transplant candidates and 528 transplant recipients. Of the transplant recipients, 88 were infected with Burkholderia. Among transplant recipients infected with B. cenocepacia, only those infected with nonepidemic strains (n=11) had significantly greater posttransplant mortality than uninfected patients (HR , 2.52; 95% CI, 1.04 to 6.12; p=.04). Transplant recipients infected with Burkholderia gladioli (n=14) also had significantly greater posttransplant mortality than uninfected patients (HR , 2.23; 95% CI, 1.05 to 4.74; p=.04). When adjustments for specific species or strains were included, the Lung Allocation Scores of Burkholderia multivorans-infected transplant candidates were comparable with uninfected candidate scores, and scores for patients infected with nonepidemic B. cenocepacia or B. gladioli were lower. In a smaller study of 22 patients colonized with Burkholderia cepacia complex who underwent lung transplantation in 2 French centers, Boussaud et al (2008) reported that 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).

An analysis of international registry data by Yusen et al (2016) found that non-cytomegalovirus (CMV) infection is a major cause of mortality within 30 days of a lung

transplant in adults. A total of 655 (19%) of 3424 deaths after transplants between 1990 and 2015 were due to non-CMV infection. Only 3 (0.1%) of the deaths were due to CMV infection.

Lung Transplantation for End-Stage Pulmonary Disease

Clinical Context and Therapy Purpose

The purpose of lung transplantation in patients who have end-stage pulmonary disease is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does lung transplantation improve the net health outcome in patients with end-stage pulmonary disease?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with end-stage pulmonary disease.

Before consideration for transplant, patients should be receiving maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for chronic obstructive pulmonary disease (COPD).

Interventions

The therapy being considered is a lung transplant.

Comparators

The following practice is currently being used to make decisions about reducing the risk of end-stage pulmonary disease: medical management, such as maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for COPD.

Outcomes

The general outcomes of interest are overall survival (OS), change in disease status, treatment-related mortality, and treatment-related morbidity (e.g., immunosuppression, graft failure, surgical complications, infections, cardiovascular complications, malignancies). Short-term follow-up ranges from immediate post-surgery to 30 days post-transplantation; lifelong follow-up (10 years or more given current survival data) is necessary due to immunosuppression drugs and risk of graft failure.

Study Selection Criteria

- Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Review of Evidence

Registry Studies
Paraskeva et al. (2018) analyzed survival rates of adolescent lung transplant recipients using data from the International Society for Heart and Lung Transplantation Registry. Patients between 10 and 24 years old represented 9% of the registry data (n=2319) and they were compared with both old and young cohorts. Overall survival in the adolescent cohort was 65% at 3 years, which was similar to that observed in adults between 50 and 65 years of age, but significantly lower in comparison to the pediatric subgroup (73%; p=.006) and adults 25 to 34 years old (75%; p<.001) and 35 to 49 years old (71%; p<.001). Within the adolescent group, patients between 15 and 19 years of age had the poorest survival rates at 3 years (59%) compared with 10- to 14-year-old patients (73%; p<.001) and 20- to 24-year-old year patients (66%; p<.001). The registry study was biased toward the inclusion of North American data and potential data entry errors or missing data. There were no data reported on the cause of mortality, differences in regimens, or rates of graft dysfunction between the groups.

In 2015, one of the International Society for Heart and Lung Transplantation registries contained data from 49,453 adult recipients who received lung transplantation (including lung retransplantation) through June 30, 2015, at 134 transplant centers. A total of 55,795 lung transplants were performed, of which 53,522 (95.9%) were primary transplants and 2273 (4.1%) were retransplants. The overall median survival of patients who underwent lung transplantation was 5.8 years. Estimated unadjusted survival rates were 89% at 3 months, 80% at 1 year, 65% at 5 years, and 32% at 10 years. Patients who survived a year after primary transplantation had a median survival of 8 years. In the first 30 days after transplantation, the major reported causes of mortality were graft failure (24.5%) and non-cytomegalovirus (CMV) infections (19.1%); however non-CMV infections became the major cause of death for the remainder of the first year. Beyond the first year, the most commonly reported causes of mortality were obstructive bronchiolitis/bronchiolitis obliterans syndrome, graft failure, and non-CMV infections. Beyond 10 years posttransplant, the major causes of mortality were obstructive bronchiolitis/bronchiolitis obliterans syndrome (21.5%), non-CMV infection (16.5%), and nonlymphoma malignancy (13.7%).

Through 2014, another International Society for Heart and Lung Transplantation registry contained a total of 2,229 pediatric lung transplants. Most transplants (73%) were done in children between the ages of 11 and 17 years. Median survival in children who underwent lung transplantation was 5.4 years, similar to survival in adults (mean

survival, 5.7 years). However, median survival in children was lower (2.2 years) than in adults (5.6 years) for single-lung transplants.

Thabut et al. (2010) reported on a comparison between patients undergoing single- and double-lung transplantation for idiopathic pulmonary fibrosis. A retrospective review was conducted of 3,327 patients with data in the United Network for Organ Sharing (UNOS) registry. More patients underwent single-lung transplant (64.5%) compared with double-lung transplant (35.5%). Median survival time was greater for the double-lung group at 5.2 years (95% confidence interval [CI[, 4.3 to 6.7 years) than the single-lung group at 3.8 years (95% CI, 3.6 to 4.1 years; p<.001). After adjusting for baseline differences, however, survival times did not differ statistically. The authors concluded that OS did not differ between the groups. Single-lung transplants offered improved short-term survival but a reduced long-term benefit, whereas double-lung transplant increased short-term harm but was associated with a long-term survival benefit.

Black et al. (2014) reported on Lung Allocation Score and single- versus double-lung transplant in 8778 patients (8050 had a Lung Allocation Score <75 vs. 728 had a Lung Allocation Score ≥75).14, A significant decrease in survival was seen in single-lung transplant patients with a high Lung Allocation Score compared with double-lung transplant patients with a high Lung Allocation Score (p<.001).

Yu et al. (2019) compared double-lung with single-lung transplantations for outcomes of survival, pulmonary function, surgical indicators, and complications in a meta-analysis of 30 studies (n=1980 recipients of single-lung transplants and n=2112 recipients of double-lung transplants).15, Overall survival, in-hospital mortality, and postoperative complications besides bronchiolitis obliterans syndrome were similar between the 2 groups. Recipients of double-lung transplants had lower rates of bronchiolitis obliterans syndrome, better postoperative lung function, and improved long-term survival, while recipients of single-lung transplants spent less time in surgery, the postoperative intensive care unit, and the postoperative hospital stay.

Yusen et al. (2010) reviewed the effect of the Lung Allocation Score on lung transplantation by comparing statistics for the period before and after its implementation in 2005.16, 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 the implementation of the Lung Allocation Score system, from approximately 500 per 5,000 patients to 300 per 5,000 patients. However, it is expected that the implementation of the Lung Allocation Score affected patient characteristics of transplant applicants. One-year survival posttransplantation did not improve after implementation of the Lung Allocation Score system: patient survival data before and after were approximately 83%. Long-term survival data are not yet available. Shafii et al. (2014) reported on a retrospective evaluation of the Lung Allocation Score and mortality in 537 adults wait-listed for lung transplantation and 426 who underwent primary lung transplantation between 2005 and

2010.17, Patients on the waitlist who had a higher Lung Allocation Score had a higher mortality rate (p<.001). In the highest quartile of Lung Allocation Score (range, 47-95), within 1 year of listing, there was a 75% mortality rate. A higher Lung Allocation Score was also associated with early posttransplant survival (p=.05) but not late posttransplant survival (p=.4). When other predictive factors of early mortality were taken into account, pretransplant Lung Allocation Score was not independently related to posttransplant mortality (p=.12).

Section Summary: Lung Transplant for End-Stage Pulmonary Disease
International registry data on a large number of patients receiving lung transplantation (>50,000) found relatively high patient survival rates (89% at 3 months, 80% at 1 year, 65% at 5 years, 32% at 10 years). In patients who survived 1-year, median survival was 8 years. After adjusting for potential confounding factors, survival did not differ significantly after single- or double-lung transplant. A subgroup analysis of an international registry study found decreased survival for adolescent patients, especially between 15 and 19 years of age, who received lung transplantation, but the study was limited by inclusion bias, lack of data on mortality, differences in treatment regimens, and rates of graft dysfunction.

Lobar Lung Transplantation for End-Stage Pulmonary Disease

Clinical Context and Therapy Purpose
The purpose of lobar lung transplantation in patients who have end-stage pulmonary disease is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does lobar lung transplantation improve the net health outcome in patients with end-stage pulmonary disease?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with end-stage pulmonary disease.

Before consideration for transplant, patients should be receiving maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for COPD.

Interventions
The therapy being considered is a lobar lung transplant.

Date (2011) published that, as of 2011, approximately 400 living-donor lobar lung transplants had been performed worldwide. Procedures in the U.S. decreased after 2005 due to changes in the lung allocation system. Date also reported that size matching

between donor and recipient is important and that, to some extent, size mismatching (oversized or undersized grafts) can be overcome by adjusting the surgical technique.

Comparators
The following practice is currently being used to make decisions about end-stage pulmonary disease: medical management, such as maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for COPD.

Outcomes
The general outcomes of interest are OS, change in disease status, treatment-related mortality, and treatment-related morbidity (e.g., immunosuppression, graft failure, surgical complications, infections, cardiovascular complications, malignancies). Short-term follow-up ranges from immediate post-surgery to 30 days post-transplantation; lifelong follow-up (10 years or more given current survival data) is necessary due to immunosuppression drugs and risk of graft failure.

Study Selection Criteria
- Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Review of Evidence

Systematic Reviews
Eberlein et al. (2017) reported a systematic review of studies on lobar lung transplantation from deceased donors. Reviewers identified 9 studies comparing outcomes after lobar lung or lung transplant, all of which were single-center retrospective cohort studies. Seven studies were conducted in Europe, 1 in Australia, and 1 in North America. One-year survival reported in individual studies ranged from 50% to 100% after lobar lung transplant and from 72% to 88% after conventional lung transplant. In a pooled analysis of data from 8 studies, lobar lung transplant recipients (n=284) had a significantly higher risk of 1-year mortality than lung transplant recipients (n=2,777) (relative risk [RR], 1.85; 95% CI, 1.52 to 2.25; p<.001; I2=0%).

Retrospective Studies
Several studies have reported on lobar lung transplantation from living donors. For example, Barr et al. (2005) reported on living-donor lobar lung transplants in the U.S. Ninety patients were adults and 43 were children. The primary indication for transplantation (86%) was cystic fibrosis. At the time of transplantation, 67% of patients were hospitalized, and 20% were ventilator dependent. Overall recipient survival rates at

1, 3, and 5 years were 70%, 54%, and 45%, respectively. There was no statistically significant difference in survival between adults and children who underwent transplantation. Moreover, survival rates were similar to the general population of lung transplant recipients. The authors also reported that rates of postoperative pulmonary function in patients surviving more than 3 months posttransplant were comparable with rates in cadaveric lung transplant recipients.

Date et al (2015) reported a retrospective study comparing 42 living-donor lobar lung transplants with 37 cadaveric lung transplants. Survival rates at 1 and 3 years did not differ significantly between groups (89.7% and 86.1% vs. 88.3% and 83.1%, respectively, p=.55), despite living-donor lobar lung transplant patients having poorer health status preoperatively. For a program in Japan, Date et al (2012) reported on 14 critically ill patients (10 children, 4 adults) who had undergone single living-donor lobar lung transplants. Patients were followed for a mean 45 months. The 3-year survival rate was 70%, and the 5-year survival was 56%. Severe graft dysfunction occurred in 4 patients. Mean forced vital capacity was lower in patients experiencing severe graft dysfunction (54.5%) than in the other patients (66.5%). The authors postulated that this suggested size mismatching in patients with severe graft dysfunction.

Slama et al. (2014) compared outcomes in 138 cadaveric lobar lung transplants (for size discrepancies) with 778 patients who received cadaveric whole-lung transplants, 239 of whom had downsizing by wedge resection of the right middle lobe and/or the left lingula.23, Survival rates in the lobar lung transplant group at 1 and 5 years were 65.1% and 54.9% versus 84.8% and 65.1% in the whole-lung and downsized by wedge resection group (p<.001). The lobar lung transplantation group experienced significantly inferior early postoperative outcomes, but in patients who were successfully discharged, survival rates were similar to standard lung transplantation (p=.168).

Section Summary: Lung Lobar Transplant for End-Stage Pulmonary Disease
There is less data on lung lobar transplants than on whole-lung transplants. The available data reported in case series have suggested reasonably similar survival outcomes, and lung lobar transplants may be the only option for patients unable to wait for a whole-lung. A 2017 systematic review found 1-year survival rates ranging from 50% to 100%.

Lung or Lobar Retransplantation When Meeting Criteria for a Lung Transplant

Clinical Context and Therapy Purpose
The purpose of lung retransplantation in patients who have had a prior lung or lobar transplant and who meet criteria for a lung transplant is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does lung or lobar retransplantation improve the net health outcome in patients with a failed prior lung or lobar transplant?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with a prior lung or lobar transplant who meet criteria for a lung transplant.

Interventions
The therapy being considered is lung or lobar retransplantation.

Comparators
The following practice is currently being used to make decisions about treating those whose lung or lobar transplant has failed and would still be considered as meeting eligibility criteria for an initial transplant: medical management, such as maximal medical therapy, including oxygen supplementation, or surgical options, such as lung volume reduction surgery for COPD.

Outcomes
The general outcomes of interest are OS, change in disease status, treatment-related mortality, and treatment-related morbidity (e.g., immunosuppression, graft failure, surgical complications, infections, cardiovascular complications, malignancies). Short-term follow-up ranges from immediate post-surgery to 30 days post-transplantation; lifelong follow-up.

Study Selection Criteria
- Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Review of Evidence

Case Series
Registry data and case series have demonstrated favorable outcomes with lung retransplantation in certain populations, such as in patients who meet criteria for initial lung transplantation.

Biswas Roy et al. (2018) published a single-center retrospective study comparing survival outcomes in 29 patients who received retransplantation for chronic lung allograft dysfunction with 390 patients receiving a primary lung transplant at the same center. Patients receiving retransplantation had significantly higher use of extracorporeal membrane oxygenation support for severe primary graft dysfunction (p=.019) and underwent cardiopulmonary bypass and re-exploration for bleeding (p=.019) more frequently than patients receiving primary transplantation (p=.029). At 1-year follow-up,

89.7% of primary transplant patients were living compared with 89.2% of retransplantation patients. At 5-year follow-up, a greater percentage of the retransplantation group had survived, compared with the primary transplantation group (64.3% vs. 58.2%), although the difference was not statistically significant. While high Lung Allocation Score and extended hospital length of stay were both identified as independent mortality risk factors, retransplantation was not (hazard ratio [HR], 1.58; 95% CI, 0.31 to 8.08; p=.58). Study limitations included its single-center, retrospective design, the potential selection bias for younger patients, and the small size of the retransplantation group. Further, follow-up data at 3 and 5 years were incomplete for some patients, and patients who were refused retransplantation were not considered in the analyses. However, for appropriately selected patients, retransplantation after chronic lung allograft dysfunction resulted in 1- and 5-year survival rates comparable to those seen after primary lung transplantation.

Registry Studies

The Organ Procurement and Transplantation Network (OPTN) has reported data on lung transplants performed between 2008 and 2015. Patient survival rates after repeat transplants were lower than primary transplants, but a substantial number of patients survived. For example, 1-year patient survival was 87.2% (95% CI, 86.4% to 87.9%) after a primary lung transplant and 76% (95% CI, 71.0% to 80.2%) after a repeat transplant. Five-year patient survival rates were 53.4% (95% CI, 52.2% to 54.7%) after a primary lung transplant and 32.9% (95% CI, 27.7% to 38.2%) after repeat transplant.

The International Society for Heart and Lung Transplantation Registry contained data on 2273 retransplantation patients performed through June 2015 (4.4% of lung transplantations). The major causes of death in the first 30 days after retransplantation were graft failure and non-CMV infection, followed by multiorgan failure, cardiovascular causes, and technical factors related to the transplant procedure. Beyond the first year, the most commonly reported causes of mortality were obstructive bronchiolitis/bronchiolitis obliterans, graft failure, and non-CMV infections.

Section Summary: Lung or Lobar Retransplant When Meeting Criteria for a Lung Transplant

Data from registries and case series have found favorable outcomes with lung retransplantation in patients who meet criteria for initial lung transplantation. Given the exceedingly poor survival without retransplantation of patients who have exhausted other treatments, evidence of a moderate level of posttransplant survival is sufficient to suggest treatment efficacy in this patient population.

Summary of Evidence

For individuals who have end-stage pulmonary disease who receive a lung transplant, the evidence includes case series and registry studies. Relevant outcomes are OS, change in disease status, and treatment-related mortality and morbidity. International registry data on a large number of patients receiving lung transplantation (>50,000) found relatively high patient survival rates, especially among those who survived the first year

posttransplant. After adjusting for potential confounding factors, survival did not differ significantly after single- or double-lung transplant. Lung transplantation may be the only option for some patients with end-stage lung disease. The evidence is sufficient to determine that the technology results in an improvement in the net health outcomes.

For individuals who have end-stage pulmonary disease who receive a lobar lung transplant, the evidence includes case series and systematic reviews. Relevant outcomes are OS, change in disease status, and treatment-related mortality and morbidity. There are less data on lung lobar transplants than on whole-lung transplants, but several case series have reported reasonably similar survival outcomes between the procedures, and lung lobar transplants may be the only option for patients unable to wait for a whole-lung transplant. A 2017 systematic review found 1-year survival rates in available published studies ranging from 50% to 100%. The evidence is sufficient to determine that the technology results in an improvement in the net health outcomes.

For individuals with a prior lung or lobar transplant who meet criteria for a lung transplant and receive a lung or lobar lung retransplant, the evidence includes case series and registry studies. Relevant outcomes are OS, change in disease status, and treatment-related mortality and morbidity. Data from registries and case series have found favorable outcomes with lung retransplantation in patients who meet criteria for initial lung transplantation. Given the exceedingly poor survival prognosis without retransplantation of patients who have exhausted other treatments, the evidence of a moderate level of posttransplant survival may be considered sufficient in this patient population. The evidence is sufficient to determine that the technology results in an improvement in the net health outcomes.

Professional Guidelines and Position Statements

American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA)
(2018) The ACC/AHA guideline for the management of adults with congenital heart disease (ACHD) stated in patients with ACHD and Eisenmenger syndrome exhibiting deteriorating functional ability, mechanical circulatory and pulmonary support, lung transplantation with concomitant repair of anatomic cardiovascular defects, and heart–lung transplantation has been applied.

International Society for Heart and Lung Transplantation

Initial Transplant

In 2021, the International Society for Heart and Lung Transplantation published updated consensus-based guidelines on the selection of lung transplant candidates. The guidelines states that:

- "Lung transplantation should be considered for adults with chronic, end-stage lung disease who meet all the following general criteria:
    1. High (>50%) risk of death from lung disease within 2 years if lung transplantation is not performed.

2. High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function."

The guideline also notes risk factors to be considered in the evaluation of transplant candidates, along with pediatric and disease-specific considerations.

Retransplant
The 2021 guideline update briefly addressed lung retransplantation, with the consensus statement noting that "The outcomes after re-transplants are inferior compared to first lung transplants, particularly if the re-transplant is done within the first year after the original transplant or for patients with restrictive allograft syndrome (RAS) [...] In the pre-transplant evaluation of such patients, particular emphasis should be focused on understanding the possible reasons for the graft failure, such as alloimmunization, poor adherence, gastroesophageal reflux, or repeated infections".

American Thoracic Society et al.

Bronchiolitis Obliterans Syndrome in Lung Transplant
(2014) The American Thoracic Society published guidelines on the management of bronchiolitis obliterans syndrome in lung transplant recipients in conjunction with the International Society for Heart and Lung Transplantation and the European Respiratory Society. The guideline recommends referral to a transplant surgeon to be evaluated for retransplantation for end-stage bronchial obliterans syndrome that is refractory to other therapies.

Diagnosis and Management of Patients with Idiopathic Fibrosis
(2011) Evidence-based recommendations from the American Thoracic Society and three international cardiac societies were published for the diagnosis and management of patients with idiopathic fibrosis. For appropriately selected patients with idiopathic pulmonary fibrosis, the international guideline panel recommended lung transplantation (strong recommendation, low-quality evidence).

Regulatory Status
Solid organ transplants are a surgical procedure and, as such, are not subject to regulation by the U.S. Food and Drug Administration (FDA).

The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation Title 21, parts 1270 and 1271. Lung transplants are subject to these regulations.

PRIOR APPROVAL

Prior approval is required.

POLICY

Related Policy

- 07.03.08 Heart-Lung Transplant

Initial Transplant

Lung or lobar (living or deceased) lung transplantation may be considered **medically necessary** in individuals with irreversible, progressively disabling, end-stage pulmonary disease that is unresponsive to maximum alternative medical therapies with, but not limited to, **one of the following** indications:

- Alpha-1 antitrypsin deficiency; **or**
- Asbestosis; **or**
- Bronchiectasis; **or**
- Bronchiolitis obliterans; **or**
- Chronic bronchitis; **or**
- Chronic obstructive pulmonary disease (COPD); **or**
- Cystic fibrosis; **or**
- Eisenmenger syndrome; **or**
- Emphysema; **or**
- Idiopathic pulmonary fibrosis; **or**
- Interstitial lung disease; **or**
- Lymphangioleiomyomatosis; **or**
- Pulmonary fibrosis from other causes; **or**
- Pulmonary hypertension; **or**
- Recurrent pulmonary embolism; **or**
- Sarcoidosis

Retransplantation

Retransplantation after a failed lung or lobar lung (living or deceased) transplant may be considered **medically necessary** in individuals who meet criteria for lung or lobar lung transplantation.

Investigational

Lung and lobar lung (living or deceased) transplant and retransplant is considered **investigational** when the above criteria are not met and for all other indications because the evidence is insufficient to determine that the technology results in an improvement on net health outcomes..

Policy Guidelines

Solid Organ Potential Contraindications

The following potential contraindications to solid organ transplants are *subject to the judgment of the transplant center*:

- Known current malignancy, including metastatic cancer

- Recent malignancy with high risk of recurrence
- Untreated systemic infection making immunosuppression unsafe, including chronic infection
- Other irreversible end-stage diseases not attributed to heart or lung disease
- History of cancer with a moderate risk of recurrence
- Systemic disease that could be exacerbated by immunosuppression
- Psychosocial conditions or chemical dependency affecting ability to adhere to therapy

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 32851 Lung transplant, single; without cardiopulmonary bypass
- 32852 Lung transplant, single; with cardiopulmonary bypass
- 32853 Lung transplant, double (bilateral sequential or en bloc); without cardiopulmonary bypass
- 32854 Lung transplant, double (bilateral sequential or en bloc); with cardiopulmonary bypass
- S2060 Lobar lung transplant
- S2061 Donor lobectomy (lung) for transplantation, living donor

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POLICY HISTORY

Date	Reason	Action
November 2022	Annual Review	Policy Revised
November 2021	Annual Review	Policy Revised
November 2020	Annual Review	Policy Revised
November 2019	Annual Review	Policy Renewed
November 2018	Annual Review	Policy Renewed
November 2017	Annual Review	Policy Renewed
November 2016	Annual Review	Policy Renewed
November 2015	Annual Review	Policy Revised
December 2014	Annual Review	Policy Revised
February 2014	Annual Review	Policy Revised
March 2013	Annual Review	Policy Renewed
March 2012	Annual Review	Policy Renewed

April 2011	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
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