Heart/Lung Transplant

Policy Number: MM.07.006
Original Effective Date: 05/21/1996
Line(s) of Business: HMO; PPO
Current Effective Date: 01/22/2016
Section: Transplants
Place(s) of Service: Inpatient

Precertification is required for this service

I. Description

The heart/lung transplantation involves a coordinated triple operative procedure consisting of procurement of a donor heart-lung block, excision of the heart and lungs of the recipient, and implantation of the heart and lungs into the recipient. A heart/lung transplantation refers to the transplantation of one or both lungs and heart from a single cadaver donor.

The evidence for combined heart/lung transplant in patients who have end-stage cardiac and pulmonary disease includes case series and registry data. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related morbidity and mortality. The available literature describes outcomes after heart/lung transplantation. Given the exceedingly poor expected survival without transplantation, this evidence is sufficient to demonstrate that heart/lung transplantation provides a survival benefit in appropriately selected patients. It may be the only option for some patients with end-stage cardiopulmonary disease. Heart/lung transplant is contraindicated 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. Based on this evidence and established guidelines, heart/lung transplant may be considered likely to improve outcomes for those who meet clinical criteria and do not have contraindications to the procedure. A very limited amount of data suggest that, after controlling for confounding variables, survival rates after primary and repeat heart/lung transplants is similar. Findings are not conclusive due to the small number of cases of repeat heart/lung transplants reported in the published literature. Repeat heart/lung transplantation may be likely to improve outcomes in patients with a failed prior transplant who meet the clinical criteria for heart/lung transplantation.

Background

Combined heart/lung transplantation is intended to prolong survival and improve function in patients with end-stage cardiac and pulmonary diseases. The majority of recipients have Eisenmenger syndrome (37%), followed by idiopathic pulmonary artery hypertension (28%) and
cystic fibrosis (14%). Eisenmenger syndrome is a form of congenital heart disease in which systemic-to-pulmonary shunting leads to pulmonary vascular resistance. Eventually, pulmonary hypertension may lead to a reversal of the intracardiac shunting and inadequate peripheral oxygenation, or cyanosis.

However, the total number of patients with Eisenmenger syndrome has been declining in recent years, as a result of corrective surgical techniques and improved medical management of pulmonary hypertension. Heart/lung transplants have not increased appreciably for other indications either, as it has become more common to transplant a single or double lung and maximize medical therapy for heart failure, rather than perform a combined transplant. In these, patient survival rates are similar to lung transplant rates. Bronchiolitis obliterans syndrome is a major complication; 1-, 5-, and 10-year patient survival rates are 68%, 50%, and 40%, respectively.

In 2014, 24 individuals received heart/lung transplants in the United States. As of the end of October 2015, there were 49 patients on the waiting list for heart/lung transplants.

II. Policy

A. Heart/lung transplantation is covered (subject to Administrative Guidelines) for carefully selected patients with end-stage cardiac and pulmonary disease including, but not limited to, one of the following diagnoses:
   1. Irreversible primary pulmonary hypertension with heart failure;
   2. Nonspecific severe pulmonary fibrosis, with severe heart failure;
   3. Eisenmenger complex with irreversible pulmonary hypertension and heart failure;
   4. Cystic fibrosis with severe heart failure;
   5. Chronic obstructive pulmonary disease with heart failure;
   6. Emphysema with severe heart failure;
   7. Pulmonary fibrosis with uncontrollable pulmonary hypertension or heart failure.

B. Heart/lung retransplantation after a failed primary heart/lung transplant is covered (subject to Administrative Guidelines) in patients who meet criteria for heart/lung transplantation.

Heart/lung retransplantation in all other situations is not covered as it is not known to be effective in improving health outcomes.

III. Policy Guidelines

When the candidate is eligible to receive a heart in accordance with United Network for Organ Sharing (UNOS) guidelines for cardiac transplantation, the lung(s) shall be allocated to the heart-lung candidate from the same donor. When the candidate is eligible to receive a lung in accordance with the UNOS Lung Allocation System (LAS), the heart shall be allocated to the heart-lung candidate from the same donor if no suitable Status 1A isolated heart candidates are eligible to receive the heart. Status 1A is described below.

Specific criteria for prioritizing donor thoracic organs for transplant are provided by the Organ Procurement and Transplantation Network (OPTN) and implemented through a contract with
UNOS. Donor thoracic organs are prioritized by UNOS on the basis of recipient medical urgency, distance from donor hospital, and pediatric status. Patients who are most severely ill (status 1A) are given highest priority. Criteria from OPTN for listing status are as follows (Organ Procurement and Transplantation Network, 2015).

**Adult Patients (18 years of age or older)**

**Status 1A**
A patient is admitted to the listing transplant center hospital and has at least one of the following devices or therapies in place:

A. Mechanical circulatory support that includes at least one of the following:
   1. Total artificial heart
   2. Intra-aortic balloon pump, or
   3. Extracorporeal membrane oxygenator (ECMO)

B. Continuous mechanical ventilation

C. Requires continuous infusion of a single high-dose intravenous inotrope or multiple intravenous inotropes, and requires continuous hemodynamic monitoring of left ventricular filling pressures.

A patient has one of the following devices or therapies in place (with or without being admitted to the listing transplant center hospital):

1. Mechanical circulatory support that includes at least one of the following:
   a. Left ventricular assist device (LVAD)
   b. Right ventricular assist device (RVAD)
   c. Left and right ventricular assist devices (BiVAD)

2. Mechanical circulatory support and there is medical evidence of significant device-related complications including, but not limited to, thromboembolism, device infection, mechanical failure, or life-threatening ventricular arrhythmias.

**Status 1B**
A patient has at least one of the following devices or therapies in place:

1. Left ventricular assist device (LVAD)
2. Right ventricular assist device (RVAD)
3. Left and right ventricular assist devices (BiVAD)
4. Continuous infusion of intravenous inotropes

A patient who does not meet Status 1A or 1B is listed as Status 2.
**Pediatric Patients**
A candidate listed as status 1A meets at least one of the following criteria:

1. Requires assistance with a mechanical ventilator;
2. Requires assistance with a mechanical assist device (eg, ECMO);
3. Requires assistance with a balloon pump;
4. Is younger than 6 months old with congenital or acquired heart disease exhibiting reactive pulmonary hypertension at greater than 50% of systemic level. Such a candidate may be treated with prostaglandin E (PGE) to maintain patency of the ductus arteriosus;
5. Requires infusion of a single high dose of an intravenous inotrope or multiple intravenous inotropes. or multiple inotropes (e.g., addition of dopamine at >5.0 mcg/kg/min); or
6. Has a life expectancy without a heart transplant of less than 14 days.

A candidate listed as status 1B meets at least one of the following criteria:

1. Requires infusion of low-dose single inotropes;
2. Is younger than 6 months old and does not meet the criteria for status 1A; or
3. Is in the less than 5th percentile for the candidates expected height and/or weight according to most recent Centers for Disease Control and Prevention’s (CDC) National Center for Health Statistics pediatric clinical growth chart;
4. Is 1.5 or more standard deviations below the candidate’s expected height growth or weight growth according to the most recent CDC National Center for Health Statistics pediatric clinical growth chart.

Status 7 patients are considered temporarily unsuitable to receive a thoracic organ transplant.

Potential contraindications subject to the judgment of the transplant center:

1. Known current malignancy, including metastatic cancer
2. Recent malignancy with high risk of recurrence
3. Untreated systemic infection making immunosuppression unsafe, including chronic infection
4. Other irreversible end-stage disease not attributed to heart or lung disease
5. History of cancer with a moderate risk of recurrence
6. Systemic disease that could be exacerbated by immunosuppression
7. Psychosocial conditions or chemical dependency affecting ability to adhere to therapy

**IV. Administrative Guidelines**

Precertification is required for a transplant evaluation and for the transplant itself and should be submitted by the proposed treating facility. To precertify, please complete HMSA's Precertification Request and mail or fax the form as indicated along with the required documentation.
<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>33930</td>
<td>Donor cardiectomy-pneumonectomy (including cold preservation)</td>
</tr>
<tr>
<td>33933</td>
<td>Backbench standard preparation of cadaver donor heart/lung allograft prior to transplantation, including dissection of allograft from surrounding soft tissues to prepare aorta, superior vena cava, inferior vena cava, and trachea for implantation</td>
</tr>
<tr>
<td>33935</td>
<td>Heart-lung transplant with recipient cardiectomy-pneumonectomy</td>
</tr>
<tr>
<td>33960-33961</td>
<td>Prolonged extracorporeal circulation code range</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10-PCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>02YA0Z0</td>
<td>Surgical, heart and great vessels, transplantation, heart, open, allogeneic</td>
</tr>
<tr>
<td>OBYK0Z0, OBYL0Z0, OBYM0Z0</td>
<td>Surgical, respiratory system, transplantation, open, allogeneic, code by bilateral, left or right lung(s)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 CM</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E84.0, E84.8-E.84.9</td>
<td>Cystic fibrosis code range</td>
</tr>
<tr>
<td>I27.0</td>
<td>Primary pulmonary hypertension</td>
</tr>
<tr>
<td>I27.1-I27.9</td>
<td>Other pulmonary heart diseases (includes Eisenmenger’s complex)</td>
</tr>
<tr>
<td>I50.1-I50.9</td>
<td>Heart failure code range</td>
</tr>
<tr>
<td>J43.0-J43.9</td>
<td>Emphysema code range</td>
</tr>
<tr>
<td>J44.0-J44.9</td>
<td>Other chronic obstructive pulmonary disease code range</td>
</tr>
<tr>
<td>J84.1</td>
<td>Other interstitial pulmonary diseases with fibrosis</td>
</tr>
</tbody>
</table>

V. Scientific Background

This policy has been updated regularly with searches of the MEDLINE database. Most recently, the literature was reviewed through October 6, 2015. Due to the nature of the population, there were no randomized controlled trials (RCTs) comparing heart/lung transplant to alternatives. Systematic reviews are based on case series and registry data. The extant RCTs compare surgical technique, infection prophylaxis, and immunosuppressive therapy and are not germane to this policy. The following is a summary of evidence based on registry data, case series, and expert opinion.
**Patient Selection**

Patients who are eligible for heart/lung transplantation can be listed under both the heart and lung allocation systems in the United States. In 2005, United Network for Organ Sharing (UNOS) changed the method by which lungs were allocated, from one based on length of time on the waiting list, to a system that incorporates the severity of the patient’s underlying disease, as well as likelihood of survival. However, it has been noted that the individual systems underestimate the severity of illness in patients with both end-stage heart and lung failure, and modification of the lung allocation score can be appealed for patients who meet the following criteria:

- Deterioration on optimal therapy
- Right arterial pressure greater than 15 mm Hg
- Cardiac index less than 1.8L/min/m²

Specific criteria for prioritizing donor thoracic organs for transplant are provided by the Organ Procurement and Transplantation Network (OPTN) and implemented through a contract with UNOS.

**Pediatric Considerations**

A 2014 analysis of data from the Organ Procurement and Transplantation Network (OPTN) reported on indications for pediatric heart/lung transplantation. The number of pediatric heart/lung transplants has decreased in recent years, i.e., 56 cases in 1993-1997; 21 cases in 2008-2013. The 3 most common indications for pediatric heart/lung transplant were primary pulmonary hypertension (n=55), congenital heart disease (n=37), and Eisenmenger syndrome (n=30). However, while 30 children received a heart/lung transplant for Eisenmenger syndrome through 2002, none have been performed for this indication since then. Pediatric heart/lung transplants have also been performed for other indications including alpha1 antitrypsin deficiency, pulmonary vascular disease, cystic fibrosis, and dilated cardiomyopathy.

In 2012, the Registry of the International Society for Heart and Lung Transplantation (ISHLT) reported on pediatric heart/lung transplant data collected through June 2011. Overall, survival rates after heart/lung transplants are comparable in children and adults (median half-life of 4.7 and 5.3 years, respectively). For pediatric heart/lung transplants that occurred between January 1990 and June 2010, the 5-year survival rate was 49%. The 2 leading causes of death in the first year after transplantation were noncytomegalovirus infection and graft failure. Beyond 3 years post-transplant, the major cause of death was bronchiolitis obliterans syndrome. An updated 2014 report on pediatric lung and heart/lung transplant from the same registry did not include updated data on pediatric heart/lung transplants due to the small number of patients available.

**Retransplantation**

Repeat heart-lung transplant procedures have been performed a study, published by Shuhaiber and colleagues in 2008 involved a review of data from the UNOS registry. The authors identified 799 primary heart-lung and 19 repeat heart-lung transplants. According to Kaplan-Meier survival
analysis, the observed median survival times were 2.08 years after primary transplant and 0.34 years after repeat transplants. In addition, the authors analyzed survival data in matched pairs of primary and repeat transplant patients, who were matched on a number of potentially confounding demographic and clinical characteristics. Matches were not available for 4 repeat transplant patients. For the 15 repeat transplant patients with primary transplant matches, survival time did not differ significantly in the 2 groups. Being on a ventilator was statistically significantly associated with decreased survival time. The main limitation of this analysis is the small number of repeat transplant procedures performed.

In 2014, Yusen et al reported outcomes for adult heart/lung transplants, with a focus on retransplantation, using data from the Registry of the International Society for Heart and Lung Transplantation. Thirty-three participating centers reported 75 adult heart/lung transplants in 2012, a decline from the peak year for heart/lung transplants (1989) during which 226 heart/lung transplants were performed. From 1982 to 2012, 90 adults had a first heart/lung retransplant after a previous heart/lung transplant. These 90 patients had a median survival of 0.3 year, with an unadjusted survival rate of 52%, 43%, 36%, and 27% at 3 months, 1 year, 3 years, and 5 years, respectively. Those who survived to 1 year had a conditional mean survival of 7.9 years.

Potential Contraindications

Individual transplant centers may differ in their guidelines, and individual patient characteristics may vary within a specific condition. In general, heart transplantation is contraindicated in patients who are not expected to survive the procedure, or in whom patient-oriented outcomes, such as morbidity or mortality, are not expected to change due to comorbid conditions unaffected by 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 heart transplant patients.

Malignancy

Concerns regarding a potential recipient’s history of cancer were based on the observation of significantly increased incidence of cancer in kidney transplant patients. In fact, carcinogenesis is 2 to 4 times more common, primarily skin cancers, in both heart transplant and lung transplant patients, likely due to the higher doses of immunosuppression necessary for the prevention of allograft rejection. The incidence of de novo cancer in heart transplant patients approaches 26% at 8 years post-transplant, the rate for lung transplant is 28% at 10 years. 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. However, it should be noted that the availability of alternate 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 cardiopulmonary failure patients may not have an option. A small study (n=33) of survivors of lymphoproliferative cancers who subsequently received cardiac transplant had 1-, 5-, and 10-year survival rates of 77%, 64%, and 50%, respectively. By comparison, overall 1-, 5-, and 10-year survival rates are expected to be 88%, 74%, and 55%, respectively for the general transplant candidate. The evaluation of a candidate who has a history of cancer must consider the prognosis...
and risk of recurrence from available information including tumor type and stage, response to therapy, and time since therapy was completed. Although evidence is limited, patients in whom cancer is thought to be cured should not be excluded from consideration for transplant. United Network for Organ Sharing (UNOS) has not addressed malignancy in current policies.

HIV

Solid organ transplant for patients who are HIV-positive (HIV+) was historically controversial, due to the long-term prognosis for human immunodeficiency virus (HIV) positivity and the impact of immunosuppression on HIV disease. The availability of highly active antiretroviral therapy (HAART) has markedly changed the natural history of the disease. A 2009 retrospective case series reported favorable outcomes for 7 patients with HIV who received a heart transplant. There are few data directly comparing outcomes for patients with and without HIV or for combined heart/lung transplants.

As of February 2013, the United Network for Organ Sharing (UNOS) policy on HIV-positive transplant candidates states: “A potential candidate for organ transplantation whose test for HIV is positive should not be excluded from candidacy for organ transplantation unless there is a documented contraindication to transplantation based on local policy.” (Policy 4, Identification of Transmissible Diseases in Organ Recipients).

In 2006, the British HIV Association and the British Transplantation Society Standards Committee published guidelines for kidney transplantation in patients with HIV disease. These criteria may be extrapolated to other organs:

- CD4 count greater than 200 cells/mm for at least 6 months
- Undetectable HIV viremia (less than 50 HIV-1 RNA copies/ml) for at least 6 months
- Demonstrable adherence and a stable HAART regimen for at least 6 months
- Absence of AIDS-defining (acquired immunodeficiency syndrome) illness following successful immune reconstitution after HAART

Other

Considerations for heart transplantation and lung transplantation alone may also pertain to combined heart-lung transplantation. For example, cystic fibrosis accounts for the most pediatric candidates for heart-lung transplantation, and infection with Burkholderia species is associated with higher mortality in these patients. And, experience with kidney transplantation in patients infected with HIV in the era of HAART has opened discussion of transplantation of other solid organs in these patients.

Summary

The evidence for combined heart/lung transplant in patients who have end-stage cardiac and pulmonary disease includes case series and registry data. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related morbidity and mortality. The available literature
describes outcomes after heart/lung transplantation. Given the exceedingly poor expected survival without transplantation, this evidence is sufficient to demonstrate that heart/lung transplantation provides a survival benefit in appropriately selected patients. It may be the only option for some patients with end-stage cardiopulmonary disease. Heart/lung transplant is contraindicated 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. Based on this evidence and established guidelines, heart–lung transplant may be considered medically necessary for those who meet clinical criteria and do not have contraindications to the procedure. A very limited amount of data suggest that, after controlling for confounding variables, survival rates after primary and repeat heart/lung transplants is similar. Findings are not conclusive due to the small number of cases of repeat heart-lung transplants reported in the published literature. Repeat heart-lung transplantation may be considered medically necessary in patients with a failed prior transplant who meet the clinical criteria for heart-lung transplantation.

Practice Guidelines and Position Statements

The Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation issued consensus-based guidelines on the selection of lung transplant recipients in 1998, 2006, and most recently updated in 2014. These guidelines make the following statements about lung transplantation: “Lung transplantation should be considered for adults with chronic, end-stage lung disease who meet all the following general criteria:

- High (>50%) risk of death from lung disease within 2 years if lung transplantation is not preformed.
- High (>80%) likelihood of surviving at least 90 days after lung transplantation.
- High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function.”

For combined heart/lung transplant, the guidelines state:

- Most commonly, patients with irreversible myocardial dysfunction or congenital defects with irreparable defects of the valves or chambers in conjunction with intrinsic lung disease or severe PAH [pulmonary arterial hypertension] are considered for heart-lung transplantation.
- “PAH and elevated PVR [pulmonary vascular resistance], defined as a PVR > 5 Woods units, a PVR index > 6, or a transpulmonary pressure gradient 16 to 20 mm Hg, should be considered as relative contraindications to isolated cardiac transplantation. If the pulmonary artery systolic pressure is >60 mm Hg in conjunction with any of these 3 variables, the risk of right heart failure and early death is increased.
- “If the PVR can be reduced to <2.5 with a vasodilator but the systolic blood pressure falls to <85 mm Hg, the patient remains at high risk of right heart failure and mortality after isolated cardiac transplantation. Mechanical circulatory support may be considered to improve these indices and still enable cardiac transplantation and obviate the need for heart-lung transplantation.
• “In most patients with pulmonary hypertension associated with right ventricular failure, isolated bilateral lung transplantation is associated with comparable or better results than heart-lung transplantation.”

**Medicare National Coverage**

Heart/lung transplantation is covered under Medicare when performed in a facility that is approved by Medicare as meeting institutional coverage criteria. The Centers for Medicare and Medicaid Services (CMS) has stated that under certain limited cases, exceptions to the criteria may be warranted if there is justification and if 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 Hawai‘i’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**


