Protocol

Heart Transplant

(70309)

Medical Benefit		**Effective Date**: 04/01/14	**Next Review Date**: 01/21
Preauthorization	Yes	**Review Dates**: 01/10, 01/11, 01/12, 01/13, 01/14, 01/15, 01/16, 01/17, 01/18, 01/19, 01/20	

Preauthorization is required and must be obtained through Case Management.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With end-stage heart failure	Interventions of interest are: • Heart transplant	Comparators of interest are: • Medical management • Cardiac device-based management (e.g., left ventricular assist device, total artificial heart)	Relevant outcomes include: • Overall survival • Symptoms • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With a prior heart transplant complicated by graft failure or severe dysfunction of the heart	Interventions of interest are: • Heart retransplant	Comparators of interest are: • Medical management • Cardiac device-based management (e.g., left ventricular assist device, total artificial heart)	Relevant outcomes include: • Overall survival • Symptoms • Morbid events • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

A heart transplant and a retransplant consist of replacing a diseased heart with a healthy donor heart. Transplantation is used for patients with refractory end-stage cardiac disease.

SUMMARY OF EVIDENCE

For individuals who have end-stage heart failure who receive a heart transplant, the evidence includes case series and registry data. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related morbidity and mortality. Heart transplant remains a viable treatment for those with severe heart dysfunction despite appropriate medical management with medication, surgery, or medical devices. Given the exceedingly poor survival rates without transplantation for these patients, evidence of posttransplant survival is sufficient to demonstrate that heart transplantation provides a survival benefit. Heart transplantation is contraindicated for patients for whom the procedure is expected to be futile due to comorbid disease or for whom posttransplantation care is expected to worsen comorbid conditions significantly. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have had a prior heart transplant complicated by graft failure or severe dysfunction of the heart who receive a heart retransplant, the evidence includes case series and registry data. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related morbidity and mortality. Despite improvements in the prognosis for many patients with graft failure, cardiac allograft vasculopathy, and severe dysfunction of the transplanted heart, heart retransplant remains a viable treatment for those whose severe symptoms persist despite treatment with other medical or surgical remedies. Given the exceedingly poor survival rates without retransplantation for patients who have exhausted other treatments, evidence of posttransplant survival is sufficient to demonstrate that heart retransplantation provides a survival benefit in appropriately selected patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

POLICY

Human heart transplantation may be considered **medically necessary** for select adults and children with end-stage heart failure when the following patient selection criteria are met.

ADULT PATIENTS

I. Accepted Indications for Cardiac Transplantation

1. Hemodynamic compromise due to heart failure demonstrated by any of the following three bulleted items,

   - Maximal oxygen consumption ($V0_2$) less than 10 mL/kg/min with achievement of anaerobic metabolism;
   - Refractory cardiogenic shock;
   - Documented dependence on intravenous inotropic support to maintain adequate organ perfusion;

   OR

2. Severe ischemia consistently limiting routine activity not amenable to bypass surgery or angioplasty; OR
3. Recurrent symptomatic ventricular arrhythmias refractory to all accepted therapeutic modalities.

II. Probable Indications for Cardiac Transplantation

1. Maximal VO_2 less than 14 mL/kg/min and major limitation of the patient's activities; OR
2. Recurrent unstable ischemia not amenable to bypass surgery or angioplasty; OR
3. Instability of fluid balance/renal function not due to patient noncompliance with regimen of weight monitoring, flexible use of diuretic drugs, and salt restriction.

III. The following conditions are inadequate indications for cardiac transplantation unless other factors as listed above are present.

1. Ejection fraction less than 20%;
2. History of functional class III or IV symptoms of heart failure;
3. Previous ventricular arrhythmias;
4. Maximal VO_2 greater than 15 mL/kg/min.

PEDIATRIC PATIENTS

1. Patients with heart failure and persistent symptoms at rest who require one or more of the following:

- Continuous infusion of intravenous inotropic agents; OR
- Mechanical ventilatory support; OR
- Mechanical circulatory support.

2. Patients with heart disease and symptoms of heart failure who do not meet the above criteria but who have:
   - Severe limitation of exercise and activity (if measurable, such patients would have a maximum Vo_2 less than 50% predicted for age and sex); OR
   - Cardiomyopathies or previously repaired or palliated congenital heart disease and significant growth failure attributable to the heart disease; OR
   - Near sudden death and/or life-threatening arrhythmias untreatable with medications or an implantable defibrillator; OR
   - Restrictive cardiomyopathy with reactive pulmonary hypertension; OR
   - Reactive pulmonary hypertension and risk of developing fixed, irreversible elevation of pulmonary vascular resistance that could preclude orthotopic heart transplantation in the future; OR
   - Anatomic and physiologic conditions likely to worsen the natural history of congenital heart disease in infants with a functional single ventricle; OR
   - Anatomic and physiologic conditions that may lead to consideration for heart transplantation without systemic ventricular dysfunction.

Heart retransplantation after a failed primary heart transplant may be considered **medically necessary** in patients who meet criteria for heart transplantation.

Heart transplantation is considered **investigational** in all other situations.

POLICY GUIDELINES

Individual transplant facilities may have their own additional requirements or protocols that must be met in order for the patient to be eligible for a transplant at their facility.

GENERAL CRITERIA

Potential contraindications for solid organ transplant subject to the judgment of the transplant center include the following:

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 diseases 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.

Policy-specific potential contraindications include:

1. Pulmonary hypertension that is fixed as evidenced by pulmonary vascular resistance greater than five Wood units, or transpulmonary gradient 16 mm/Hg or more despite treatment*
2. Severe pulmonary disease despite optimal medical therapy, not expected to improve with heart transplantation.*

*Some patients may be candidates for combined heart and lung transplantation (See the Heart/Lung Transplant Protocol).

Patients must meet the United Network for Organ Sharing (UNOS) guidelines for status 1A, 1B, or s 2 (and not currently be Status 7).

CARDIAC SPECIFIC CRITERIA

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 the 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 IA) are given highest priority. The following factors are considered in assessing the severity of illness: reliance on continuous mechanical ventilation, infusion of intravenous inotropes, and/or dependency on mechanical circulatory support (i.e., total artificial heart, intra-aortic balloon pump, extracorporeal membrane oxygenator, ventricular assist device).

Additional criteria, which are considered in pediatric patients, include diagnosis of an OPTN-approved congenital heart disease diagnosis, presence of ductal dependent pulmonary or systemic circulation, and diagnosis of hypertrophic or restrictive cardiomyopathy while less than one year old. Of note, pediatric heart transplant candidates who remain on the waiting list at the time of their 18th birthday without receiving a transplant continue to qualify for medical urgency status based on the pediatric criteria.

Specific criteria for prioritizing donor thoracic organs for retransplant include severe coronary allograft vasculopathy, mild or moderate coronary allograft vasculopathy with a left ventricular ejection fraction less than 45%, coronary allograft vasculopathy with restrictive physiology, or symptomatic graft dysfunction without evidence of active rejection.

MEDICARE ADVANTAGE

If a transplant is needed, we arrange to have the Medicare–approved transplant center review and decide whether the patient is an appropriate candidate for the transplant.

BACKGROUND

HEART FAILURE

In the U.S., approximately 6.5 million people 20 years of age and older have heart failure and 309,000 die each year from this condition.[1] The reduction of cardiac output is considered to be severe when systemic circulation cannot meet the body's needs under minimal exertion.

Heart failure may be due to a number of differing etiologies, including ischemic heart disease, cardiomyopathy, or congenital heart defects. The leading indication for a heart transplant has shifted over time from ischemic to nonischemic cardiomyopathy. From 2009 to 2014, nonischemic cardiomyopathy was the dominant underlying primary diagnosis among patients 18 to 39 years (64%) and 40 to 59 years (51%) undergoing transplant operations.[2] Ischemic cardiomyopathy was the dominant underlying primary diagnosis among the heart transplant recipients 60 to 69 years (50%) and 70 years and older (55%). Overall, ischemic cardiomyopathy is the underlying

heart failure diagnosis in approximately 40% of men and 20% of women who receive a transplant. Approximately 3% of the heart transplants during this time period were in adults with congenital heart disease.

Treatment

Innovations in medical and device therapy for patients with advanced heart failure have improved the survival of patients awaiting heart transplantation. The demand for heart transplants far exceeds the availability of donor organs, and the length of time patients are on the waiting list for transplants has increased. According to data from the Organ Procurement and Transplantation Network, in 2017, a total of 3,244 heart transplants were performed in the U.S.[3] As of July 2018, there were 4,003 patients on the waiting list for a heart transplant. The chronic shortage of donor hearts has led to the prioritization of patients awaiting transplantation to ensure greater access for patients most likely to derive benefit. Prioritization criteria are issued by the Organ Procurement and Transplantation Network and fulfilled through a contract with the United Network for Organ Sharing.[4]

From 2008 to 2015, approximately 4% of heart transplants were repeated transplantations. Heart retransplantation raises ethical issues due to the lack of sufficient donor hearts for initial transplants. The United Network for Organ Sharing does not have separate organ allocation criteria for repeat heart transplant recipients.

Prioritization of Candidates

Most heart transplant recipients now are hospitalized as status 1 patients at the time of transplant. This shift has occurred due to the increasing demand for the scarce resource of donor organs resulting in increased waiting time for recipients. Patients initially listed as status 2 candidates may deteriorate to a status 1 candidate before a donor organ becomes available. Alternatively, as medical and device therapy for advanced heart failure improves, some patients on the transplant list will recover enough function to be delisted. Lietz and Miller (2007) reported on survival for patients on the heart transplant waiting list, comparing the era between 1990 and 1994 with the era of 2000 to 2005.[5] One-year survival for United Network for Organ Sharing status 1 candidate improved from 49.5% to 69.0%. Status 2 candidates fared even better, with 89.4% surviving one year compared with 81.8% in the earlier time period.

Johnson et al (2010) reported on waiting list trends in the U.S. between 1999 and 2008.[6] The proportion of patients listed as status 1 increased, even as the waiting list and posttransplant mortality for this group have decreased. Meanwhile, status 2 patients have decreased as a proportion of all candidates. Completed transplants have trended toward the extremes of age, with more infants and patients older than age 65 years having transplants in recent years.

As a consequence, aggressive treatment of heart failure has been emphasized in recent guidelines. Prognostic criteria have been investigated to identify patients who have truly exhausted medical therapy and thus are likely to derive the maximum benefit for heart transplantation. Maximal oxygen consumption (Vo2max), which is measured during maximal exercise, is a measure suggested as a critical objective criterion of the functional reserve of the heart. The American College of Cardiology and American Heart Association have adopted Vo2max as a criterion for patient selection.[7] Studies have suggested that transplantation can be safely deferred in those patients with a Vo2max of greater than 14 mL/kg/min. The importance of the Vo2max has also been emphasized by the American Heart Association when addressing heart transplant candidacy.[8] In past years, a left ventricular ejection fraction of less than 20% or a New York Heart Association class III or IV status might have been used to determine transplant candidacy. However, as indicated by the American College of Cardiology criteria, these measurements are no longer considered adequate to identify transplant candidates. These measurements may be used to identify patients for further cardiovascular workup but should not be the sole criteria for transplant.

Methods other than Vo2max have been proposed as predictive models in adults.[9-12] The Heart Failure Survival Scale and the Seattle Heart Failure Model (SHFM) are examples. In particular, the SHFM provides an estimate of one-, two-, and three-year survival with the use of routinely obtained clinical and laboratory data. Information on pharmacologic and device usage is incorporated into the model, permitting some estimation on the effects of

current, more aggressive heart failure treatment strategies. Levy et al (2006) introduced the model using a multivariate analysis of data from the Prospective Randomized Amlodipine Survival Evaluation-1 heart failure trial (n=1125).[13] Applied to the data of five other heart failure trials, SHFM correlated well with actual survival (r=0.98). SHFM has been validated in both ambulatory and hospitalized heart failure populations,[14-16] but with a noted underestimation of mortality risk, particularly in blacks and device recipients.[17,18] None of these models has been universally adopted by transplant centers.

REGULATORY STATUS

Heart transplantation is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration.

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. Heart transplants are included in these regulations.

RELATED PROTOCOLS

Heart/Lung Transplant

Immune Cell Function Assay

Laboratory Tests for Heart and Kidney Transplant Rejection

Total Artificial Hearts and Implantable Ventricular Assist Devices

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Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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