Clinical Policy Title: Heart transplants

Clinical Policy Number: CCP.1034

Effective Date: January 1, 2016
Initial Review Date: June 16, 2013
Most Recent Review Date: November 6, 2018
Next Review Date: November 2019

Related policies:

CCP.1210 Heart valve transplant

ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas considers the use of heart transplantation to be clinically proven and, therefore, medically necessary when the following criteria are met (Yancy, 2017; Kirk, 2014; Yancy, 2013):

- Adults with end-stage, irreversible, refractory, symptomatic heart failure requiring maximal continuous medical or mechanical support.
- Children with end-stage heart disease characterized by intractable symptoms and heart failure that cannot be treated with conventional medical or surgical methods.

Heart failure of irreversible underlying etiology in children (age newborn to 12 years), adolescents (age 12 years to 18 years), and adults (age >18 years) is treatable with heart transplantation and includes, but is not limited to:

- Cardiac arrhythmia.
- Cardiac retransplantation due to graft failure.
- Cardiomyopathy due to nutritional, metabolic, hypertrophic, or restrictive etiologies.
- Congenital heart disease.
  - Severe stenosis or atresia in proximal coronary arteries.
  - Moderate to severe stenosis or insufficiency of the atrioventricular or systemic semilunar valve(s).
  - Severe ventricular dysfunction.
  - Pulmonary hypertension and a potential risk of developing fixed, irreversible elevated pulmonary vascular resistance that may preclude future orthotopic heart transplant.
  - Severe aortic insufficiency not amenable to surgical correction.
  - Severe arterial oxygen desaturation.
- End-stage ventricular failure.
- Idiopathic dilated cardiomyopathy.
- Inability to be weaned from temporary cardiac-assist devices after myocardial infarction or nontransplant cardiac surgery.
- Intractable coronary artery disease.
- Myocarditis.
- Postpartum cardiomyopathy.
- Right ventricular dysplasia/cardiomyopathy.
- Valvular heart disease.

Assessment of heart failure severity requires a minimum of the following examinations and tests:

- Electrocardiogram.
- Echocardiogram.
- Right heart catheterization.
- VO$_2$ max.
- HbA1C for diabetics.
- Serum creatinine <2.5 mg/dL (≤1.5 mg/dL in children) or glomerular filtration rate >35 mL/min.
- Carotid Doppler ultrasound when indicated or age >50 years.

Retransplantation in individuals with graft failure of an initial heart transplant, due to either technical reasons or hyperacute rejection, is considered medically necessary.

Retransplantation in individuals with chronic rejection, cardiac allograft vasculopathy, or recurrent disease is considered medically necessary.

**Limitations:**

All other uses of heart transplantation are not medically necessary. Relative contraindications for transplant recipients include, but are not limited to, the following:

- Pulmonary hypertension as evidenced by:
o Pulmonary vascular resistance greater than 5 Wood units.
o Transpulmonary gradient greater than or equal to 16 mm/Hg.

Absolute contraindications for transplant recipients include, but are not limited to:

- Metastatic cancer.
- Ongoing or recurring infections that are not effectively treated.
- Serious cardiac or other ongoing insufficiencies that create an inability to tolerate transplant surgery.
- Serious conditions that are unlikely to be improved by transplantation as life expectancy can be finitely measured.
- Active, systemic lupus erythematosus or sarcoid with multisystem involvement.
- Any systemic condition with a high probability of recurrence in the transplanted heart.
- Demonstrated patient noncompliance, which places the organ at risk by not adhering to medical recommendations.
- Potential complications from immunosuppressive medications are unacceptable to the patient.
- Acquired immune deficiency syndrome (diagnosis based on Centers for Disease Control and Prevention definition of CD4 count, 200 cells/mm3) unless the following are noted:
  • CD4 count greater than 200 cells/mm3 for greater than six months.
  • Human immunodeficiency virus-1 undetectable.
  • On stable antiretroviral therapy greater than three months.
  • Meeting all other criteria for heart transplantation.

Alternative covered services:

None.

Background

Heart transplants, the first of which was conducted on a human in 1967 (Moosdorf, 2012), have become more widespread over time. It has become a viable option for patients with end-stage heart disease who are not amenable to other medical and surgical treatments. Currently, from 2,200 to 2,400 transplants are performed annually in the United States (Mehra, 2017). About 13 percent of heart transplants involve pediatric patients under 21 years of age (Peterson, 2017).

Despite strides made in medical therapy for patients with an advanced stage of heart failure, more than 3,000 patients in the United States await heart transplants at any given time. The International Society for Heart Lung Transplantation lists criteria for heart transplantation that are used in setting priorities for who on the waiting list for the procedure should be treated first (Mehra, 2016).
The most important criterion for selecting patients for heart transplants is prognosis, or factors that predict the need for transplant, both from the recipient and the donor. Such factors include:

**Recipients**
- Need for artificial breathing support.
- If the transplant is a repeat.
- Heart conditions other than coronary artery disease or cardiomyopathy.
- Preoperative need for assistance with a ventricular device.
- Being obese.
- Being female.

**Donors**
- Female donors.
- Age over 40 (associated with narrowing of coronary arteries).
- Significant thickening of the left ventricle (Eisen, 2017).

Various interventions are now used before or after heart transplantation to improve survival and quality of life. For example, use of left ventricular assist device is often used as a bridge to transplant (Seco, 2017). Drugs such as amiodarone (an antiarrhythmic), immunosuppressive agents, and post-transplant statins are given to many patients.

A large number of cardiac transplant patients lead a relatively normal lifestyle after surgery, having no limitations in their activity. One study of 66 Japanese heart transplant patients operated on from 2006 to 2015 assessed how many were working by 2016. After excluding deaths, those in school or before school, or retired patients, 42 of 55 (76 percent) have returned to work. An additional 16 percent (n=9) are capable of working but are housewives (Nawata, 2017).

**Searches**

AmeriHealth Caritas searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.

We conducted searches on September 21, 2018. Search terms were: "transplantation," "heart transplant," and "immunosuppression."

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use
predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.

- **Guidelines based on systematic reviews.**
- **Economic analyses,** such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

The principal guidelines governing criteria for heart transplants are periodically issued by a team from the American College of Cardiology, American Heart Association, and the Heart Failure Society of America (Yancy, 2017; Yancy, 2013). A guideline governing pediatric heart transplant criteria was issued by the International Society for Heart and Lung Transplantation (Kirk, 2014). Criteria for setting priorities for which patients have the greatest need for heart transplantation and management during and after the procedure are covered.

Long-term trends in survival after heart transplantation are not necessarily rising. One review reports worsening survival because many patients are transplanted due to complications of assist device support such as device infections or stroke, which are high risk factors for the transplantation. Patients are now waiting a longer time in intensive care before surgery, during which they gradually deteriorate. Donor age has significantly increased because of organ shortage (Hetzer, 2013).

A systematic review/meta-analysis of 55 studies (n=47,901) assessed risk factors for sudden cardiac death after heart transplant. Cardiac allograft vasculopathy was associated with an elevated risk of sudden death, while independent predictors included older donor age, younger recipient age, non-Caucasian race, reduced left ventricular ejection fraction, rejection, infection, and cancer (Alba, 2018).

A systematic review/meta-analysis of 29 studies compared 1,470 heart transplant patients who underwent percutaneous coronary interventions to 50 patients who underwent coronary artery bypass graft, to prevent or minimize transplant coronary artery vasculopathy, a major cause of death after transplants. Demographics and comorbidities among the two groups were similar. Bypass patients had a significantly higher early mortality (36.4 versus 4.3 percent, \( P <0.001 \)) and overall mortality (42.3 versus 21.4 percent, \( P = 0.049 \)). Patients with drug-eluting stents had similar mortality rates to those with bare-metal stents (Luc, 2017).

Use of a left ventricular assist device as a bridge to transplantation is frequently done in patients before a heart transplantation. In a review of 20 studies (n=4,575), patients with left ventricular assist device had a nonsignificantly different long-term survival (odds ratio 1.24), acute rejection (1.10), chronic rejection (0.99), 30-day post-operative mortality (0.91), stroke (1.64), renal failure (1.43), bleeding (1.56), or infection (2.44) than those patients undergoing orthotopic heart transplant without a bridge. In a subset of five studies (n=837), total cost for the bridge group ranged from $316,078 to $1,025,500, while the non-bridge group ranged from $179,051 to $802,200 (Seco, 2017).
A review of 2,152 patients by The International Society for Heart and Lung Transplantation Registry focused on risk factors for 30-day mortality (total 4.5 percent) for patients with left ventricular assist devices. Risk factors included ventilator support at transplant (hazard ratio 5.00), female recipient/male donor (3.29), history of hemodialysis (2.51), history of coronary bypass (1.89), increasing recipient age ($P = 0.002$), body mass index ($P = 0.002$), creatinine ($P = 0.004$), and total bilirubin ($P < 0.001$) (Healy, 2016).

A meta-analysis of nine studies (n=16,509) assessed outcomes of amiodarone, an antiarrhythmic drug favored for heart transplant patients, as several studies had indicated mixed results. Pre-transplant amiodarone was not associated with an increase in postoperative mortality versus control (Odds Ratio 1.38), and no association was observed between a longer duration of follow-up for those taking the drug and higher odds of mortality ($P = .91$) (Jennings, 2017).

A review of 17,857 adult heart transplant patients from 2001 to 2011 looked at those who received no antibody-based induction or contemporary immunosuppression agents, for a minimum of 12 months. Overall, immunosuppression agents did not significantly affect survival (Whitson, 2015).

A Cochrane review of 10 randomized controlled trials (n=300) studied effects of cardiac rehabilitation, which is often recommended to prevent adverse effects after heart transplantation. After 12 weeks, exercise capacity ($\text{VO}_{2\text{peak}}$) for those undergoing cardiac rehabilitation was compared to those with no exercise control. Exercise was not found to have impact on health-related quality of life (Anderson, 2017).

A meta-analysis of 10 studies (four randomized and controlled) was conducted on effects of statins after heart transplant. Use of statins was linked with a significant reduction in all-cause mortality ($P <0.0001$); in hemodynamically significant/fatal rejection ($P = 0.0005$); in incidence of coronary vasculopathy ($P = 0.003$), and in terminal cancer ($P = 0.002$) (Vallakati, 2016).

A systematic review/meta-analysis found a significantly higher mortality in patients with a high body mass index (hazard ratio of 1.10 for >30 kg/m$^2$ and 1.24 for >35 kg/m$^2$). Underweight (body mass index <18.5 kg/m$^2$) transplant candidates also had elevated mortality (1.24 for ages 40–65, 1.70 for ages <65). Weight loss before heart transplantation is advised for obese and overweight patients (Foroutan, 2018).

The 10-year survival rate for pediatric heart transplants is over 60 percent, even though the literature on this patient population is limited (Peterson, 2017). One study of 322 patients under age 1 who received a heart transplant had an actuarial graft survival of 59 percent at 25 years (Chinnock, 2011).

A systematic review/meta-analysis of adult heart transplant patients documented that 30-day mortality was significantly higher in those patients who had congenital heart disease (risk ratio 2.18). Mortality at one and five years was higher in the congenital heart disease cohort, but the difference was not significant; and 10-year mortality was significantly lower in congenital heart disease patients (risk ratio 0.75). Deaths caused by malignancy, infection, rejection, and cardiac allograft vasculopathy were
decreased in congenital heart disease patients, significant only for malignancy. Reoperation and dialysis risk were not statistically different between the two groups (Doumouras, 2016).

A systematic review of 14 studies addressing quality of life up to 10 years after heart transplantation found that demoralization, depression, pain, gastrointestinal symptoms, sexual dysfunction, and poor oral health negatively influence health-related quality of life, while social and family support have a positive impact (Tackmann, 2018).

A systematic review (Conway, 2013) considered psychosocial and psychological health post-heart transplant. The most consistent findings across all the studies (seven) were related to the importance of social support. Faith, optimism, and sense of control were also perceived as positive influences on outcome. The authors opined that the act of facilitation for support socially permits heart transplant recipients to progress more successfully back to full lifestyle independence.

Policy updates:

A total of two guidelines/other and 16 peer-reviewed references were added to and four peer-reviewed references removed from this policy in September 2018.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alba (2018)</td>
<td><strong>Key points:</strong>&lt;br&gt;• Systematic review/meta-analysis of 55 studies (n=47,901).&lt;br&gt;• Assessment of various risk factors for sudden cardiac death after heart transplant.&lt;br&gt;• Cardiac allograft vasculopathy was associated with an elevated risk of sudden death.&lt;br&gt;• Independent predictors included older donor age, younger recipient age, non-Caucasian race, reduced left ventricular ejection fraction, rejection, infection, and cancer.</td>
</tr>
<tr>
<td>Anderson (2017)</td>
<td><strong>Key points:</strong>&lt;br&gt;• Cochrane review of 10 randomized controlled trials (n=300).&lt;br&gt;• Study focused on effects of cardiac rehabilitation, which is often recommended to prevent adverse effects after heart transplantation.&lt;br&gt;• After 12 weeks, exercise capacity (VO_{peak}) for those undergoing cardiac rehabilitation was found to have no benefit compared to those with no exercise control. Exercise was not found to have impact on health-related quality of life within 12 weeks.</td>
</tr>
<tr>
<td>Luc (2017)</td>
<td><strong>Key points:</strong>&lt;br&gt;• Systematic review/meta-analysis of 29 studies (n=1,520) heart transplant patients.&lt;br&gt;• A comparison of 1,470 heart transplant patients who underwent percutaneous coronary interventions to 50 patients who underwent coronary artery bypass graft to prevent or minimize transplant coronary artery vasculopathy, a major cause of death after transplants.&lt;br&gt;• Demographics and comorbidities among the two groups were similar.&lt;br&gt;• Bypass patients had a significantly higher early mortality (36.4% versus 4.3%, (P &lt;0.001))</td>
</tr>
</tbody>
</table>
and overall mortality (42.3% versus 21.4%, \( P = 0.049 \)).

- Patients with drug-eluting stents had similar mortality rates to those with bare-metal stents.

<table>
<thead>
<tr>
<th>Seco (2017)</th>
<th>Key points:</th>
</tr>
</thead>
</table>
| Left ventricular assist devices as a bridge to transplant | - A review of 20 studies (n=4,575) of heart transplant patients.  
- Left ventricular assist device patients had a nonsignificantly different long-term survival (odds ratio 1.24), acute rejection (1.10), chronic rejection (0.99), 30-day post-operative mortality (0.91), stroke (1.64), renal failure (1.43), bleeding (1.56), or infection (2.44) than those patients undergoing orthotopic heart transplant without a bridge.  
- In a subset of five studies (n=837), total cost for the bridge group ranged from $316,078 to $1,025,500, while the non-bridge group ranged from $179,051 to $802,200. |

<table>
<thead>
<tr>
<th>Vallakati (2016)</th>
<th>Key points:</th>
</tr>
</thead>
</table>
| Statins after heart transplant | - A meta-analysis of 10 studies (four randomized and controlled).  
- Analysis was conducted on effects of statins after heart transplant.  
- Use of statins was linked with a significant reduction in all-cause mortality (\( P <0.001 \)); in hemodynamically significant/fatal rejection (\( P = 0.0005 \)), in incidence of coronary vasculopathy (\( P = 0.003 \)), and in terminal cancer (\( P = 0.002 \)). |

References

Professional society guidelines/other:


Peer-reviewed references:


**Centers for Medicare & Medicaid National Coverage Determination:**


**Local Coverage Determinations:**

No Local Coverage Determinations identified as of the writing of this policy.
**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>33945</td>
<td>Heart transplant, with or without recipient cardiectomy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD 10 Codes</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>I11.0</td>
<td>Hypertensive heart disease with heart failure</td>
<td></td>
</tr>
<tr>
<td>I42.0-I42.9</td>
<td>Cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>I43</td>
<td>Cardiomyopathy in diseases classified elsewhere</td>
<td></td>
</tr>
<tr>
<td>I50.1-I50.9</td>
<td>Heart failure</td>
<td></td>
</tr>
<tr>
<td>I51.0-I51.7</td>
<td>Complications and ill-defined descriptions of heart disease</td>
<td></td>
</tr>
<tr>
<td>Q20.0-Q20.9</td>
<td>Congenital malformations of cardiac chambers and connections</td>
<td></td>
</tr>
<tr>
<td>Q21.0-Q21.9</td>
<td>Congenital malformations of cardiac septa</td>
<td></td>
</tr>
<tr>
<td>Q22.0-Q22.9</td>
<td>Congenital malformations of pulmonary and tricuspid valves</td>
<td></td>
</tr>
<tr>
<td>Q23.0-Q23.9</td>
<td>Congenital malformations of aortic and mitral valves</td>
<td></td>
</tr>
<tr>
<td>Q24.0-Q24.9</td>
<td>Other congenital malformations of heart</td>
<td></td>
</tr>
<tr>
<td>T86.20-T86.298</td>
<td>Complications of heart transplant</td>
<td></td>
</tr>
<tr>
<td>Z94.1</td>
<td>Heart transplant status</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Code Level II</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
</table>