Clinical Policy Title: Heart valve transplant

Clinical Policy Number: 04.02.06

Effective Date: January 1, 2016
Initial Review Date: November 18, 2015
Most Recent Review Date: November 16, 2016
Next Review Date: November 2017

Related policies:

CP#04.02.05  Heart transplants

ABOUT THIS POLICY: Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’s 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 Prestige Health Choice 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. Prestige Health Choice’s 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. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Coverage policy

Prestige Health Choice considers the use of heart valve transplants to be clinically proven and, therefore, medically necessary when the following indications are present:

- Aortic valvular incompetence.
- Pulmonary valvular incompetence.
- Aortic valvular stenosis.
- Pulmonary valvular stenosis.
- Complex left ventricular outflow tract obstruction.
- Complex right ventricular outflow tract obstruction.
- Congenital lesions associated with valvular derangement.

Prestige Health Choice considers the use of heart valve tissue engineering based on decellularized xenogenic or allogeneic starter matrices to be investigational and, therefore, not medically necessary.
Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website can be accessed at http://ahca.myflorida.com/Medicaid/.

All other uses of heart valve transplants are not medically necessary.

Absolute contraindications for heart valve transplant recipients include, but are not limited to, individuals with the following:

- Metastatic cancer.
- Ongoing or recurring infections not effectively treated.
- Serious cardiac or other ongoing insufficiencies that create an inability to tolerate transplant surgery.
- Serious conditions 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 that are unacceptable to the patient.
- Acquired immune deficiency syndrome (AIDS) (diagnosis based on Centers for Disease Control and Prevention [CDC] definition of CD4 count, 200 cells/mm3) unless the following are noted:
  - CD4 count greater than 200 cells/mm3 for greater than six months.
  - HIV-1 RNA undetectable.
  - Stable antiretroviral therapy longer than three months.
  - No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioidomycosis, resistant fungal infections, Kaposi's sarcoma or other neoplasm).

Alternative covered services:

Prosthetic cardiac valve implantation.

Background

The most common treatment for end-stage valvular heart diseases is surgical replacement by either mechanical or bioprosthetic heart valves. Bioprosthetic heart valve replacements are either of animal origin (xenografts) or taken from human donors (homografts). Cryopreserved donor valves are the heart
valve replacements closest to the natural valve, being non-thrombogenic and having a low risk of infection.

An emerging trend in treatment of aortic stenosis by transcatheter approaches (transfemoral, transapical) has created a body of evidence regarding the efficacy and safety of minimally invasive implantation of a mechanical prosthetic versus open-surgical transplantation of tissue. In general, patients who are younger (i.e., <60 years of age) and who can tolerate lifetime anticoagulation may benefit more from a minimally invasive mechanical device implantation than a bioprosthetic.

**Searches**

Prestige Health Choice searched PubMed and the databases of:
- UK National Health Services Center 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 (CMS).

We conducted searches on October 21, 2016. Search terms were: "heart valve transplant (MeSH)," "valve allograft (MeSH)" and "prosthetic heart valve."

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**

Over the last thirty years, there has been a significant change in clinical demand for allografts from aortic valves to pulmonary valves. The reasons for this change include an increase in pediatric cardiac surgery, the adoption of the Ross procedure and improved durability of aortic porcine valves. Various reports have also associated the use of allogeneic aortic valves with more rapid failure than that observed with allogeneic pulmonary valves. These factors have contributed to a growing interest in stimulating the growth of natural valve tissue in the laboratory, to create replacements that might then be implanted into patients with valvular heart disease. A similar approach is also being used with biodegradable synthetic materials to build a valve-replacement for these indications.
The Ross procedure was first devised in 1967 and sought to provide a permanent aortic valve substitution, which would not degenerate like a homograft valve and would not require chronic anticoagulation therapy like a prosthetic valve. Ross sought to attain a balance between a more complicated surgical procedure (essentially a double valve replacement) and a potentially more durable and physiologic aortic valve replacement. It is thought that the autografted pulmonary valve will grow with the young patient, thus obviating the need for re-operation. Studies have also shown that the Ross procedure resulted in significant improvement in left ventricular wall thickness and outflow tract velocity not observed in allograft aortic valve replacements in children. For these reasons, the Ross procedure is considered most appropriate for young adults.

Takkenberg (2009), in a systematic review of 39 randomized controlled trials (RCTs), compared the results of the Ross procedure in children and adults (≤50 years of age). The authors concluded that the Ross procedure provides satisfactory results for both children and young adults, but durability limitations become apparent by the end of the first postoperative decade. David (2009) noted that the Ross procedure is preferred to prosthetic valvular replacement due to the excellent hemodynamic performance and growing capacity of the autograft, the long-term expected durability of the homograft, and a very low thrombogenicity obviating the need for chronic anticoagulation therapy. The authors concluded that young adults with aortic stenosis and a normal-size aortic root are the best candidates for the Ross procedure.

Despite the many advantages of an aortic allograft valve (AAV) over a prosthetic aortic valve, its durability is suboptimal (Palka 2002). An RCT inclusive of 570 patients studied long-term results with a cryopreserved AAV by conducting follow-up echocardiographic study at an average of seven years postoperatively. There was significant AAV regurgitation present in 14.7 percent of the patients studied, and AAV stenosis was present in 3.2 percent.

Heart valve tissue engineering based on decellularized xenogenic or allogeneic starter matrices is feasible today; however, availability of healthy homologous donor valves is limited, and xenogenic materials are associated with infectious and immunologic risks. To address such limitations, biodegradable synthetic materials have been pursued as a means for the creation of living autologous tissue-engineered heart valves (TEHVs) in vitro. The host repopulation capacity of such technology in a non-human primate model with up to eight weeks’ follow-up revealed mobile and thin leaflets after eight weeks, with mild-to-moderate valvular insufficiency and relative leaflet shortening. These results suggest that human cell-derived bioengineered decellularized materials are a promising start for heart valve tissue engineering.

**Policy updates:**

Foroutan (2016) performed a systematic review and meta-analysis of observational studies on the topic of frequency of survival, stroke, atrial fibrillation, structural valve deterioration, and length of hospital stay after surgical aortic valve replacement (SAVR) with a bioprosthetic valve in patients with severe symptomatic aortic stenosis. The authors used the GRADE system to quantify absolute effects and
quality of evidence. Published survival curves provided data for survival and freedom from structural valve deterioration, and random effect models provided the framework for estimates of pooled incidence rates of stroke, atrial fibrillation, and length of hospital stay. In patients undergoing SAVR with a bioprosthetic valve, median survival was 16 years in those aged 65 or less, 12 years in those aged 65 to 75, seven years in those aged 75 to 85, and six years in those aged more than 85. The incidence rate of stroke was 0.25 per 100 patient years (95 percent confidence interval 0.06 to 0.54) and atrial fibrillation 2.90 per 100 patient years (1.78 to 4.79). Post-SAVR, freedom from structural valve deterioration was 94.0 percent at 10 years, 81.7 percent at 15 years, and 52 percent at 20 years, and mean length of hospital stay was 12 days (95 percent confidence interval 9 to 15). The authors concluded that patients with severe symptomatic aortic stenosis undergoing SAVR with a bioprosthetic valve can expect only slightly lower survival than those without aortic stenosis, and a low incidence of stroke and, up to 10 years, of structural valve deterioration. The rate of deterioration increases rapidly after 10 years, and particularly after 15 years.

Vandvik (2016) created a systematic review and meta-analysis combining the available published data from 3128 patients with symptomatic severe aortic stenosis at low or moderate risk of perioperative death. Compared with SAVR, transfemoral transcatheter aortic valve implantation (TAVI) reduced mortality and stroke, life-threatening bleeds, atrial fibrillation, and acute kidney injury at two years, but increased heart failure, major vascular complications, pacemaker insertion, and need for aortic valve reintervention within two years. In contrast, transapical TAVI may increase mortality and stroke compared with the surgical approach. The results for mortality, stroke, and acute kidney injury were based on a subgroup analysis for transfemoral versus transapical approach, deemed credible by the review authors according to specific criteria. Estimates of baseline risk for most outcomes came from a linked systematic review on prognosis for patients undergoing SAVR. The panel was reasonably confident that the absolute effect sizes for the short-term benefit and harm of TAVI and SAVR were true and accurate estimates (that is, overall moderate certainty according to GRADE). But the panel was very uncertain about the long-term durability of the valves used in TAVI, particularly with respect to their recommendations in younger patients with a longer predicted life expectancy. The low certainty in the estimated long term re-intervention rate after TAVI of approximately 27 in 100 people reflects an absence of published follow-up studies beyond five years. There are no studies on patients deciding between TAVI and SAVR, although one study evaluated patient preferences and values when deciding whether to undergo SAVR (versus no surgery). One study identified multiple biomedical, functional, social, and environmental factors influencing patients’ decisions to undergo assessment for TAVI. Overall, there is evidence of variability in individual values and preferences, highlighting the need for shared decision making, particularly for patients aged between 65 and 85 years.

Siemieniuk (2016) examined in a systematic review of 3,179 patients with a mean perioperative risk of death <8% the effect of TAVI versus SAVR. The authors used the GRADE system to quantify absolute effects and quality of evidence. SAVR compared with transfemoral TAVI was associated with reduced mortality (risk difference per 1000 patients: −30, 95 percent confidence interval −49 to −8, moderate certainty), stroke (−20, −37 to 1, moderate certainty), life-threatening bleeding (−252, −293 to −190, high certainty), atrial fibrillation (−178, −150 to −203, moderate certainty), and acute kidney injury (−53,
−39 to −62, high certainty) but increased short-term aortic valve reintervention (7, 1 to 21, moderate certainty), permanent pacemaker insertion (134, 16 to 382, moderate certainty), and moderate or severe symptoms of heart failure (18, 5 to 34, moderate certainty). Compared with SAVR, transapical TAVI was associated higher mortality (57, −16 to 153, moderate certainty, P=0.015 for interaction between transfemoral versus transapical TAVI) and stroke (45, −2 to 125, moderate certainty, interaction P=0.012). No study reported long term follow-up, which is particularly important for structural valve deterioration. The authors concluded that for many patients, particularly those who have a shorter life expectancy or place a lower value on the risk of long term valve degeneration, there is likely net benefit with transfemoral TAVI versus SAVR. SAVR, however, performs better than transapical TAVI, which is of interest to patients who are not candidates for transfemoral TAVI.

Lytvyn (2016) conducted a systematic review of adults with aortic stenosis considering or recently post-valve replacement, either TAVI or via surgery (i.e., SAVR). One study of patients with severe aortic stenosis used a standard gamble study to ascertain that the median hypothetical mortality risk patients were willing to tolerate to achieve full health was 25 percent (IQR 25 – 50 percent). However, there was considerable variability; for mortality risk levels defined by current guidelines, 130 participants (30 percent) were willing to accept low-to-intermediate risk (≤8 percent), 224 (51 percent) high risk (>8–50 percent) and 85 (19 percent) a risk that guidelines would consider prohibitive (>50 percent). Study authors did not, however, assess participants’ understanding of the exercise, resulting in a potential risk of bias. A second qualitative study of 15 patients identified the following factors that influence patients to undergo assessment for TAVI: symptom burden; expectations; information support; logistical barriers; facilitators; obligations and responsibilities. The study was limited by serious risk of bias due to authors' conflict of interest in that five of the nine authors were industry-funded.

Leon (2016) in a randomized controlled trial (RCT) studied 2,032 intermediate-risk patients with severe aortic stenosis, at 57 centers, undergoing either TAVR or surgical replacement. The primary end point was death from any cause or disabling stroke at two years. The primary hypothesis was that TAVR would not be inferior to surgical replacement. Before randomization, patients were entered into one of two cohorts on the basis of clinical and imaging findings; 76.3 percent of the patients were included in the transfemoral-access cohort and 23.7 percent in the transthoracic-access cohort. The rate of death from any cause or disabling stroke was similar in the TAVR group and the surgery group (P=0.001 for noninferiority). At 2 years, the Kaplan–Meier event rates were 19.3 percent in the TAVR group and 21.1 percent in the surgery group (hazard ratio in the TAVR group, 0.89; 95 percent confidence interval [CI], 0.73 to 1.09; P=0.25). In the transfemoral-access cohort, TAVR resulted in a lower rate of death or disabling stroke than surgery (hazard ratio, 0.79; 95 percent CI, 0.62 to 1.00; P=0.05), whereas in the transthoracic-access cohort, outcomes were similar in the two groups. TAVR resulted in larger aortic-valve areas than did surgery and also resulted in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation; surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation. In intermediate-risk patients, TAVR was similar to surgical aortic-valve replacement with respect to the primary end point of death or disabling stroke.
An American College of Cardiology (ACC)/American Heart Association (AHA) task force (2014) published guidelines for the management of patients with valvular heart disease that are summarized in Appendix A.

### Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content</th>
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<tbody>
<tr>
<td>Foroutan (2016).</td>
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</table>
### patients with severe aortic stenosis at low and intermediate risk: systematic review and meta-analysis

- to −190, high certainty), atrial fibrillation (−178, −150 to −203, moderate certainty), and acute kidney injury (−53, −39 to −62, high certainty).
- On the other hand TAVI was associated with short term aortic valve reintervention (7, 1 to 21, moderate certainty), permanent pacemaker insertion (134, 16 to 382, moderate certainty), and moderate or severe symptoms of heart failure (18, 5 to 34, moderate certainty).
- Compared with SAVR, transapical TAVI was associated higher mortality (57, −16 to 153, moderate certainty, P=0.015 for interaction between transfemoral versus transapical TAVI) and stroke (45, −2 to 125, moderate certainty, interaction P=0.012).
- No study reported on long term follow-up important for assessment of structural valve durability.
- The authors concluded that for selected patients there is net benefit with transfemoral TAVI versus SAVR.
- SAVR, however, performs better than transapical TAVI, which is of interest to patients who are not candidates for transfemoral TAVI.

### Lytvyn (2016)

**Patient values and preferences on transcatheter or surgical aortic valve replacement therapy for aortic stenosis: a systematic review**

**Key points:**

- Systematic review of adults with aortic stenosis and valve replacement with either TAVI or SAVR.
- Found that the median hypothetical mortality risk patients were willing to tolerate to achieve full health was 25 percent (IQR 25–50 percent).
- There was considerable variability; for mortality risk levels defined by current guidelines:
  - 130 participants (30 percent) were willing to accept low-to-intermediate risk (≤8%)
  - 224 (51 percent) high risk (>8–50 percent)
  - 85 (19 percent) a risk that guidelines would consider prohibitive (>50 percent).
- Side study of 15 patients identified the following factors that influence patients to undergo assessment for TAVI:
  - Symptom burden
  - Expectations
  - Information support
  - Logistical barriers
  - Facilitators
  - Obligations and responsibilities.
- The study was limited by serious risk of bias due to authors’ conflict of interest in that five of the nine authors were industry-funded.

### Vandvik (2016)

**Transcatheter or surgical aortic valve replacement for patients with severe, symptomatic, aortic stenosis at low to intermediate surgical risk: a clinical practice guideline**

**Key points:**

- Systematic review and meta-analysis of 3128 patients with symptomatic severe aortic stenosis at low or moderate risk of perioperative death.
- Compared with SAVR, TAVI reduced mortality and stroke, life threatening bleeds, atrial fibrillation, and acute kidney injury at two years, but increased heart failure, major vascular complications, pacemaker insertion, and need for aortic valve reintervention within 2 years.
- In contrast, transapical TAVI may increase mortality and stroke compared with the surgical approach.
- The results for mortality, stroke, and acute kidney injury were based on a subgroup analysis for transfemoral versus transapical approach, deemed credible by the review authors.
according to specific criteria.

- Estimates of baseline risk for most outcomes came from a linked systematic review on prognosis for patients undergoing SAVR.
- The panel were reasonably confident that the absolute effect sizes for the short term benefit and harm of TAVI and SAVR were true and accurate estimates (that is, overall moderate certainty according to GRADE).
- The panel was very uncertain about the long term durability of the valves used in TAVI, particularly with respect to their recommendations in younger patients with a longer predicted life expectancy.
- The low certainty in the estimated long term re-intervention rate after TAVI of approximately 27 in 100 people reflects an absence of published follow-up studies beyond five years.
- There are no studies on patients deciding between TAVI and SAVR, although one study evaluated patient preferences and values when deciding whether to undergo SAVR (versus no surgery).
- One study identified multiple biomedical, functional, social, and environmental factors influencing patients’ decisions to undergo assessment for TAVI.
- Overall, there is evidence of variability in individual values and preferences, highlighting the need for shared decision making, particularly for patients aged between 65 and 85 years.

ACC/ AHA (2014).

**Guidelines for the management of patients with valvular heart disease**

**Key points:**

**Summary of Recommendations for Prosthetic Valve Choice**

- **Class I**
  - 1. The choice of valve intervention, that is, repair or replacement, as well as type of prosthetic heart valve, should be a shared decision-making process that accounts for the patient’s values and preferences, with full disclosure of the indications for and risks of anticoagulant therapy and the potential need for and risk of reoperation.
  - 2. A bioprosthesis is recommended in patients of any age for whom anticoagulant therapy is contraindicated, cannot be managed appropriately, or is not desired.
- **Class IIa**
  - 1. A mechanical prosthesis is reasonable for AVR or MVR in patients less than 60 years of age who do not have a contraindication to anticoagulation.
  - 2. A bioprosthesis is reasonable in patients more than 70 years of age.
  - 3. Either a bioprosthetic or mechanical valve is reasonable in patients between 60 and 70 years of age.
- **Class IIb**
  - 1. Replacement of the aortic valve by a pulmonary autograft (the Ross procedure), when performed by an experienced surgeon, may be considered in young patients when VKA anticoagulation is contraindicated or undesirable.

**Summary of Recommendations for Prosthetic Valve Stenosis**

- **Class I**
  - 1. Repeat valve replacement is indicated for severe symptomatic prosthetic valve stenosis.

**Summary of Recommendations for Prosthetic Valve Regurgitation**

- **Class I**
  - 1. Surgery is recommended for operable patients with mechanical heart valves with intractable hemolysis or HF due to severe prosthetic or paraprosthetic regurgitation.
  - Class IIa
1. Surgery is reasonable for operable patients with severe symptomatic or asymptomatic bioprosthetic regurgitation.
2. Percutaneous repair of paravalvular regurgitation is reasonable in patients with prosthetic heart valves and intractable hemolysis or NYHA class III/IV HF who are at high risk for surgery and have anatomic features suitable for catheter-based therapy when performed in centers with expertise in the procedure.

**Weber (2013).**

**Key points:**
- Decellularized TEHVs (dTEHVs), based on biodegradable synthetic materials and vascular-derived cells, have potential to create an off-the-shelf starter matrix for guided tissue regeneration.
- In an animal model, the authors used a minimally invasive technique to introduce into the orthotopic pulmonary position just such a device.
- At eight weeks of follow-up, the dTEHV revealed mobile and thin leaflets with mild-to-moderate valvular insufficiency and relative leaflet shortening.
- The authors opined that these biomaterials may ultimately overcome the limitations of currently used valve replacements by providing homologous, non-immunogenic, off-the-shelf replacement constructs.

**Svensson (2013)**

**Key points:**
- Guidelines for management and quality measures for aortic valve and ascending aorta.
- The Ross procedure is not recommended for middle-aged or older adults when suitable alternatives to autograft replacement of the aortic valve are available.
- With comparable results and without the need for replacement of the right ventricular outflow tract (RVOT), the latter adds the additional risk of pulmonary valve dysfunction and subsequent replacement.
- The Ross procedure is not recommended for patients with bicuspid valves and aortic regurgitation or aortic dilation if other alternatives are available.

**David (2009)**

**Key points:**
- Ross procedure is preferred to prosthetic valvular replacement due to the excellent hemodynamic performance and growing capacity of the autograft, the long-term expected durability of the homograft, and a very low thrombogenicity obviating the need for chronic anticoagulation therapy.
- Complications include autograft or homograft failure and progressive dilatation of the neo-aortic root.
- A Ross operation is appropriate where replacement of the aortic valve is indicated, especially in younger patients, and contraindicated in primary or iatrogenic lesions of the pulmonary valve, in Marfan syndrome, and in autoimmune tissue diseases.

**Takkenberg (2009).**

**Key points:**
- Takkenberg (2009) stated that the Ross procedure provides satisfactory results for both children and young adults (≤ 50 years of age).
- Early mortality for consecutive, adult and pediatric patients series was 3.0%, 3.2% and 4.2%.
- Autograft deterioration rates were 1.15%, 0.78% and 1.38%/patient-year respectively, and for right ventricular outflow tract conduit were 0.91, 0.55% and 1.60%/patient-year respectively.
- For studies with mean patient age > 18 years versus mean patient age < or = 18 years, pooled autograft and right ventricular outflow tract deterioration rates were 1.14% versus 1.69% and 0.65% versus 1.66%/patient-year respectively.
- The authors concluded that the Ross procedure provides satisfactory results for both children and young adults; but durability limitations become apparent by the end of the first postoperative decade.

<table>
<thead>
<tr>
<th>Palka (2002)</th>
<th>Key points:</th>
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| - An RCT inclusive of 570 patients with allograft aortic valve transplant underwent a follow-up echocardiographic study at seven years post-operation that revealed significant AAV regurgitation was present in 14.7% of patients, and AAV stenosis was present in 3.2%.
- The root replacement subgroup had the smallest number of patients with significant AAV regurgitation (5.0%) compared with the subcoronary (23.0%) or the inclusion cylinder technique subgroup (14.7%).
- After 10 to 15 years after AAV replacement, grade 2 AAV dysfunction was present in 40% of patients in the subcoronary subgroup, but no significant dysfunction was observed in patients in the root replacement subgroup (P>0.001).
- The authors concluded that the root replacement technique is associated with less frequent AAV degeneration, suggesting more strict selection criteria for surgical replacement procedure type and patient/donor factors for AAV replacement.

**Glossary**

**Allograft** — The transplant of an organ or tissue from one individual to another of the same species with a different genotype.

**Aortic valve** — The heart valve between the left ventricle and the aorta (leading from the heart to the body).

**Congenital** — A condition existing at birth.

**Donor** — A person who gives an organ to be used in another person.

**Immunosuppression** — The process of preventing the body's immune system from rejecting an organ or tissue transplant.

**Mitral valve** — The largest of the four heart valves; allows blood to flow on the left side of the heart.
**Pulmonary valve** — The structure between the right ventricle and pulmonary artery; regulates movement of blood into the pulmonary artery.

**Rejection** — The condition in which a transplant recipient's body rejects the tissue or organ transferred from a donor.

**Ross procedure** — The Ross pulmonary autograft refers to a double valve replacement in which the native pulmonic valve is substituted for the diseased aortic valve, while a homograft prosthetic valve replaces the pulmonic valve.

**Transplantation** — The transfer of living tissue or organs from one person to another.

**Tricuspid valve** — The heart valve between the right atrium and the right ventricle.

**Valvulopathy** — The general category of valvular heart diseases associated with the specific or systemic deterioration of the valves within and providing competent outflow of blood from the heart.

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


CMS National Coverage Determination (NCDs):

No NCDs identified as of the writing of this policy.

Local Coverage Determinations (LCDs):

No NCDs 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>Comment</th>
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<tr>
<td>33406</td>
<td>Replacement, aortic valve, with cardiopulmonary bypass; with allograft valve (freehand)</td>
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<tr>
<td>33410</td>
<td>Replacement, aortic valve, with cardiopulmonary bypass; with stentless tissue valve</td>
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<tr>
<td>33411</td>
<td>Replacement, aortic valve; with aortic annulus enlargement, noncoronary sinus</td>
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<td>33412</td>
<td>Replacement, aortic valve; with transventricular aortic annulus enlargement (Konno procedure)</td>
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<tr>
<td>33413</td>
<td>Replacement, aortic valve; by translocation of autologous pulmonary valve with allograft replacement of pulmonary valve (Ross procedure)</td>
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<tr>
<td>33475</td>
<td>Replacement, pulmonary valve</td>
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<th>ICD-10 Code</th>
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### Appendix A

ACC/ AHA (2014) Guidelines for the management of patients with valvular heart disease

Evaluation and Selection of Prosthetic Valves

10.1.1. Diagnosis and Follow-Up

Class I
1. An initial TTE study is recommended in patients after prosthetic valve implantation for evaluation of valve hemodynamics. (Level of Evidence: B)

2. Repeat TTE is recommended in patients with prosthetic heart valves if there is a change in clinical symptoms or signs suggesting valve dysfunction. (Level of Evidence: C)

3. TEE is recommended when clinical symptoms or signs suggest prosthetic valve dysfunction. (Level of Evidence: C)

Class IIa
1. Annual TTE is reasonable in patients with a bioprosthetic valve after the first 10 years, even in the absence of a change in clinical status. (Level of Evidence: C)

10.1.2. Intervention

Class I
1. The choice of valve intervention, that is, repair or replacement, as well as type of prosthetic heart valve, should be a shared decision-making process that accounts for the patient's values and preferences, with full disclosure of the indications for and risks of anticoagulant therapy and the potential need for and risk of reoperation. (Level of Evidence: C)

2. A bioprosthesis is recommended in patients of any age for whom anticoagulant therapy is contraindicated, cannot be managed appropriately, or is not desired. (Level of Evidence: C)

Class IIa
1. A mechanical prosthesis is reasonable for AVR or MVR in patients less than 60 years of age who do not have a contraindication to anticoagulation. (Level of Evidence: B)

2. A bioprosthesis is reasonable in patients more than 70 years of age. (Level of Evidence: B)
3. Either a bioprosthetic or mechanical valve is reasonable in patients between 60 and 70 years of age. (Level of Evidence: B)

Class IIb
1. Replacement of the aortic valve by a pulmonary autograft (the Ross procedure), when performed by an experienced surgeon, may be considered in young patients when VKA anticoagulation is contraindicated or undesirable. (Level of Evidence: C)

10.2. Antithrombotic Therapy for Prosthetic Valves
Class I
1. Anticoagulation with a VKA and international normalized ratio (INR) monitoring is recommended in patients with a mechanical prosthetic valve. (Level of Evidence: A)

2. Anticoagulation with a VKA to achieve an INR of 2.5 is recommended in patients with a mechanical AVR (bileaflet or current-generation single tilting disc) and no risk factors for thromboembolism. (Level of Evidence: B)

3. Anticoagulation with a VKA is indicated to achieve an INR of 3.0 in patients with a mechanical AVR and additional risk factors for thromboembolic events (AF, previous thromboembolism, LV dysfunction, or hypercoagulable conditions) or an older-generation mechanical AVR (such as ball-in-cage). (Level of Evidence: B)

4. Anticoagulation with a VKA is indicated to achieve an INR of 3.0 in patients with a mechanical MVR. (Level of Evidence: B)

5. Aspirin 75 mg to 100 mg daily is recommended in addition to anticoagulation with a VKA in patients with a mechanical valve prosthesis. (Level of Evidence: A)

Class IIa
1. Aspirin 75 mg to 100 mg per day is reasonable in all patients with a bioprosthetic aortic or mitral valve. (Level of Evidence: B)

2. Anticoagulation with a VKA is reasonable for the first 3 months after bioprosthetic MVR or repair to achieve an INR of 2.5. (Level of Evidence: C)

Class IIb
1. Anticoagulation, with a VKA, to achieve an INR of 2.5 may be reasonable for the first 3 months after bioprosthetic AVR. (Level of Evidence: B)

2. Clopidogrel 75 mg daily may be reasonable for the first 6 months after TAVR in addition to life-long aspirin 75 mg to 100 mg daily. (Level of Evidence: C)
Class III: Harm
1. Anticoagulant therapy with oral direct thrombin inhibitors or anti-Xa agents should not be used in patients with mechanical valve prostheses. (Level of Evidence: B)

10.3. Bridging Therapy for Prosthetic Valves
Class I
1. Continuation of VKA anticoagulation with a therapeutic INR is recommended in patients with mechanical heart valves undergoing minor procedures (such as dental extractions or cataract removal) where bleeding is easily controlled. (Level of Evidence: C)

2. Temporary interruption of VKA anticoagulation, without bridging agents while the INR is subtherapeutic, is recommended in patients with a bileaflet mechanical AVR and no other risk factors for thrombosis who are undergoing invasive or surgical procedures. (Level of Evidence: C)

3. Bridging anticoagulation with either intravenous unfractionated heparin (UFH) or subcutaneous low-molecular-weight heparin (LMWH) is recommended during the time interval when the INR is subtherapeutic preoperatively in patients who are undergoing invasive or surgical procedures with a 1) mechanical AVR and any thromboembolic risk factor, 2) older-generation mechanical AVR, or 3) mechanical MVR. (Level of Evidence: C)

Class IIa
1. Administration of fresh frozen plasma or prothrombin complex concentrate is reasonable in patients with mechanical valves receiving VKA therapy who require emergency noncardiac surgery or invasive procedures. (Level of Evidence: C)

10.4. Excessive Anticoagulation and Serious Bleeding With Prosthetic Valves
Anticoagulation for Prosthetic Valves. Risk factors include AF, previous thromboembolism, LV dysfunction, hypercoagulable condition, and older-generation mechanical AVR. AF indicates atrial fibrillation; ASA, aspirin; AVR, aortic valve replacement; INR, international normalized ratio; LMWH, low-molecular-weight heparin; MVR, mitral valve replacement; PO, by mouth; QD, every day; SC, subcutaneous; TAVR, transcatheter aortic valve replacement; UFH, unfractionated heparin; and VKA, vitamin K antagonist.

Class IIa
1. Administration of fresh frozen plasma or prothrombin complex concentrate is reasonable in patients with mechanical valves and uncontrollable bleeding who require reversal of anticoagulation. (Level of Evidence: B)

10.5. Prosthetic Valve Thrombosis
Evaluation and Management of Suspected Prosthetic Valve Thrombosis.

10.5.1. Diagnosis and Follow-Up
Class I
1. TTE is indicated in patients with suspected prosthetic valve thrombosis to assess hemodynamic severity and follow resolution of valve dysfunction. (Level of Evidence: B)

2. TEE is indicated in patients with suspected prosthetic valve thrombosis to assess thrombus size and valve motion. (Level of Evidence: B)

Class IIa
1. Fluoroscopy or CT is reasonable in patients with suspected valve thrombosis to assess valve motion. (Level of Evidence: C)

10.5.2. Medical Therapy
Class IIa
1. Fibrinolytic therapy is reasonable for patients with a thrombosed left-sided prosthetic heart valve, recent onset (<14 days) of NYHA class I to II symptoms, and a small thrombus (<0.8 cm²). (Level of Evidence: B)

2. Fibrinolytic therapy is reasonable for thrombosed right-sided prosthetic heart valves. (Level of Evidence: B)

10.5.3. Intervention
Class I
1. Emergency surgery is recommended for patients with a thrombosed left-sided prosthetic heart valve with NYHA class III to IV symptoms. (Level of Evidence: B)

Class IIa
1. Emergency surgery is reasonable for patients with a thrombosed left-sided prosthetic heart valve with a mobile or large thrombus (>0.8 cm³). (Level of Evidence: C)

10.6. Prosthetic Valve Stenosis
Class I
1. Repeat valve replacement is indicated for severe symptomatic prosthetic valve stenosis. (Level of Evidence: C)

10.7. Prosthetic Valve Regurgitation
Class I
1. Surgery is recommended for operable patients with mechanical heart valves with intractable hemolysis or HF due to severe prosthetic or paraprosthesis regurgitation. (Level of Evidence: B)

Class IIa
1. Surgery is reasonable for operable patients with severe symptomatic or asymptomatic bioprosthetic regurgitation. (Level of Evidence C)
2. Percutaneous repair of paravalvular regurgitation is reasonable in patients with prosthetic heart valves and intractable hemolysis or NYHA class III/IV HF who are at high risk for surgery and have anatomic features suitable for catheter-based therapy when performed in centers with expertise in the procedure. (Level of Evidence B)