Guidelines for Clinical Review Determination

Preamble
Magellan is committed to the philosophy of supporting safe and effective treatment for patients. The medical necessity criteria that follow are guidelines for the provision of diagnostic imaging. These criteria are designed to guide both providers and reviewers to the most appropriate diagnostic tests based on a patient’s unique circumstances. In all cases, clinical judgment consistent with the standards of good medical practice will be used when applying the guidelines. Determinations are made based on both the guideline and clinical information provided at the time of the request. It is expected that medical necessity decisions may change as new evidence-based information is provided or based on unique aspects of the patient’s condition. The treating clinician has final authority and responsibility for treatment decisions regarding the care of the patient.

Guideline Development Process
These medical necessity criteria were developed by Magellan Healthcare for the purpose of making clinical review determinations for requests for therapies and diagnostic procedures. The developers of the criteria sets included representatives from the disciplines of radiology, internal medicine, nursing, cardiology, and other specialty groups. Magellan’s guidelines are reviewed yearly and modified when necessary following a literature search of pertinent and established clinical guidelines and accepted diagnostic imaging practices.

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All guidelines were reviewed between January 1, 2019 and September 15, 2019.

Prepared September 27, 2019
CPT Codes: 33221, 33224, 33225, 33231

INDICATIONS FOR CARDIAC RESYNCHRONIZATION THERAPY (CRT):
(Brignole 2013, Cleland 2005, Epstein 2012, Ponikowski 2016, Russo 2013, Yancy 2013)

- Left ventricular ejection fraction (LVEF) ≤ 35%, sinus rhythm, left bundle branch block (LBBB) with a QRS ≥ 150 ms, and New York Heart Association (NYHA) class II, III, or ambulatory class IV symptoms on guideline-directed medical therapy (GDMT) (Adelstein 2018, Ponikowski 2016).

- LVEF ≤ 35%, sinus rhythm, LBBB with a QRS duration 120 to 149 ms, and NYHA class II, III, or ambulatory class IV symptoms on GDMT.

- LVEF ≤ 35%, sinus rhythm, a non-LBBB pattern with a QRS duration ≥ 150 ms, and NYHA III or ambulatory class IV symptoms on GDMT (Epstein 2012, Ponikowski 2016, Yancy 2013).

- Atrial fibrillation and LVEF ≤ 35% on GDMT if:
  - Patient requires ventricular pacing or otherwise meets CRT criteria; AND
  - AV nodal ablation or pharmacologic rate control will allow nearly 100% ventricular pacing with CRT (Yancy 2013).

- LVEF ≤ 35% and undergoing new or replacement device with anticipated requirement for significant (> 40%) ventricular pacing (Adelstein 2018, Brignole 2013, Curtis 2013, Ponikowski 2016, Yancy 2013).

NOT Indicated for Cardiac Resynchronization Therapy (CRT)

- NYHA class I or II symptoms and non-LBBB pattern with QRS duration < 150 ms (Epstein 2012).

- Comorbidities and/or frailty expected to limit survival with good functional capacity to < 1 year.

INDICATIONS FOR CRT IN ADULT CONGENITAL HEART DISEASE:

- Systemic LVEF ≤ 35%, sinus rhythm, complete LBBB with a QRS complex ≥ 150 ms (spontaneous or paced) and NYHA class II to ambulatory IV.

- Systemic LVEF ≤ 35%, sinus rhythm, complete LBBB with a QRS complex 120-149 ms (spontaneous or paced), and NYHA class II to ambulatory IV.

- Systemic ventricular EF ≤ 35%, intrinsic narrow QRS complex, NYHA functional class I to ambulatory class IV and undergoing new or replacement device implantation with anticipated requirement for significant (> 40%)
ventricular pacing (single site pacing from the systemic ventricular apex or mid-lateral wall may be considered as an alternative).

- Systemic right ventricle (RV) with an EF ≤ 35%, NYHA function Class II – ambulatory class IV, complete right bundle branch block (RBBB) with a QRS complex ≥ 150 ms (spontaneous or paced).

- Single ventricle with an ejection fraction (EF) ≤ 35%, NYHA function Class II—ambulatory class IV and a QRS complex ≥ 150 ms due to intraventricular conduction delay causing either a complete right or left bundle branch block morphology (spontaneous or paced).

**NOT Indicated for CRT in Adult Congenital Heart Disease**

- Patients with a narrow QRS complex (< 120 ms).

- Patients whose co-morbidities and/or frailty limit survival with good functional capacity to less than 1 year.

**INDICATIONS FOR CRT AS THE APPROPRIATE PACING MODALITY IN SPECIAL SITUATIONS WITH < 3 MONTHS OF GDMT**

(Katsumoto 2014, Marine 2018, Russo 2013)

- Criteria are met for a non-elective implantable cardioverter defibrillator (ICD) or a non-elective pacemaker, either initial or replacement, and based upon the low likelihood of improvement in symptoms and adequate recovery of LVEF, despite less than 3 months GDMT for heart failure or < 40 days post myocardial infarction or 3 months post revascularization, criteria for CRT are otherwise met. This avoids a second implantation procedure within less than 3 months.

**BACKGROUND:**

(Brignole 2013, Epstein 2012, Ponikowski 2016, Russo 2013, Yancy 2013)

CRT, which paces the left and right ventricle in rapid sequence, also known as biventricular pacing, improves coordination of ventricular contraction in the presence of a wide QRS complex in systolic heart failure.

CRT improves cardiac function and quality of life, and it decreases cardiac events and mortality among appropriately chosen patients. The improved survival in patients with CRT is greater than that provided by ICD insertion alone.

Guiding principles in the consideration of CRT:

- NYHA class is an important qualifying factor, with candidacy ranging from New York Heart Association (NYHA) class II to ambulatory NYHA class IV.

- Bundle branch block/intraventricular conduction delay should be persistent, not rate-related (Russo 2013).

- GDMT should have been in place continuously for at least 3 months (Epstein 2012; Ponikowski 2016; Yancy 2013), unless a non-elective permanent pacemaker and/or ICD is indicated prior to completion of the 3 months, and CRT would have been likely required even after 3 months of GDMT. Otherwise, recovery of
LVEF from myocardial infarction (40 days) if no intervening revascularization or > 3 months if revascularization was performed, and reversible causes (e.g. ischemia) should be allowed (Katsumoto 2014, Marine 2018).

- The patient should have expected survival with reasonably good functional status for more than 1 year (Epstein 2012, Khairy 2014, Ponikowski 2016).

OVERVIEW:

**NYHA Class Definitions**
(Goldman 1981, Russo 2013)

- **Class I:** No limitation of functional activity or only at levels of exertion that would limit normal individuals (patient can carry 24 pounds up 8 stairs, play basketball, and shovel soil).
- **Class II:** Slight limitation of activity. Fatigue, palpitation, or dyspnea with moderate exercise (patient able to dance, garden, and walk 4 mph on level ground).
- **Class III:** Marked limitation of activity. Fatigue, palpitation, or dyspnea with minimal activity (patient able to shower, make bed, bowl or golf, dress, and walk 2.5 mph on level).
- **Class IV:** Severe limitation of activity. Symptoms even at rest, worse with activity (patient unable to comfortably perform any significant activity).
- **Ambulatory Class IV:** Class IV heart failure that is not refractory due to fluid retention, frequent hospitalization for heart failure, or dependent on continuous intravenous inotropic therapy.

**Heart Block Definitions**
(Epstein 2012)

- **First Degree:** All atrial beats are conducted to the ventricles, but with a delay of > 200 ms.
- **Second Degree:** Intermittent failure of conduction of single beats from atrium to ventricles.
  - Type I: Conducted beats have variable conduction times from atrium to ventricles.
  - Type II: Conducted beats have uniform conduction times from atrium to ventricles.
  - Advanced: Two or more consecutive non-conducted beats (premature atrial beats might not normally be conducted).
- **Third Degree:** No atrial beats are conducted from atrium to ventricle

**Guideline Directed (or Optimal) Medical Therapy in Heart Failure**
(Yancy 2013, Yancy 2017)

- Angiotensin converting enzyme inhibitor (ACE-I), angiotensin receptor blocker (ARB), or combined angiotensin receptor inhibitor and neprilysin inhibitor (ARNI)
- Beta blocker
- Addition of loop diuretic for all NYHA class II – IV patients
- Addition of hydralazine and nitrate for persistently symptomatic African Americans, NYHA class III-IV
- Addition of an aldosterone antagonist, provided eGFR is $\geq 30$ ml/min/1.73m$^2$ and K+ < 5.0, NYHA class II-IV
- Not required for consideration of CRT: Ivabradine for NYHA class II – III, when a beta blocker has failed to reduce a sinus rate to < 70 bpm. Ivabradine listed as a class IIa recommendation, while others are class I recommendations. CRT trials antedated routine use of ivabradine.
Abbreviations

- **ACE-I**: Angiotensin converting enzyme inhibitor
- **ARNI**: Combined angiotensin receptor inhibitor and neprilysin inhibitor
- **AV**: Atriocentric
- **CAD**: Coronary artery disease, same as ischemic heart disease
- **CHF**: Congestive heart failure
- **CRT**: Cardiac resynchronization therapy (also known as biventricular pacing)
- **CHD**: Congenital heart disease
- **ECG**: Electrocardiogram
- **eGFR**: Estimated glomerular filtration rate
- **EPS**: Electrophysiologic Study
- **GDMT**: Guideline-Directed Medical Therapy
- **HF**: Heart Failure
- **HRS**: Heart Rhythm Society
- **HV**: His-ventricular
- **ICD**: Implantable cardioverter-defibrillator
- **LBBB**: Left bundle-branch block
- **LV**: Left ventricular/left ventricle
- **LVEF**: Left ventricular ejection fraction
- **MI**: Myocardial infarction
- **ms**: Milliseconds
- **NYHA**: New York Heart Association
- **STEMI**: ST-Elevation Myocardial Infarction
- **SND**: Sinus node dysfunction
- **VT**: Ventricular tachycardia

**POLICY HISTORY:**

**Review Date:** August 13, 2019

**Review Summary:**

- Changed ms from 130 to 150 in indication: ‘left ventricular ejection fraction (LVEF) ≤ 35%, sinus rhythm, left bundle branch block (LBBB) with a QRS ≥ 150 ms, and NYHA class II, III or ambulatory class IV symptoms on GDMT’
- Added indication for LVEF ≤ 35%, sinus rhythm, LBBB with a QRS duration 120 to 149 ms, and NYHA class II, III, or ambulatory class IV symptoms on GDMT
- Changed ms from 130 to 150 in indication: ‘LVEF ≤ 35%, sinus rhythm, a non-LBBB pattern with a QRS duration ≥ 150 ms, and NYHA III or ambulatory class IV symptoms on GDMT’
- Revised indication to state that LVEF ≤ 35% and are undergoing new or replacement device placement with anticipated requirement for significant (> 40%) ventricular pacing
- Removed indication for LVEF ≤ 30%, ischemic etiology of HF, sinus rhythm, LBBB with a QRS duration ≥ 150 ms, and NYHA class I on GDMT
- Removed indication for LVEF ≤ 35%, sinus rhythm, a non LBBB pattern with a QRS duration ≥ 150 ms, and NYHA class II on GDMT
• Adult congenital heart disease, added indication for systemic LVEF ≤ 35%, sinus rhythm, complete LBBB with a QRS complex 120 - 149 ms (spontaneous or paced), and NYHA class II to ambulatory IV

• Adult congenital heart disease, removed the following indications:
  o Cardiac surgery with a QRS duration > 150 ms
  o Systemic RV with significant tricuspid valve regurgitation
  o Severe subpulmonic RV dysfunction
  o Severe ventricular dysfunction and NYHA class IV in attempt to delay transplant or mechanical support

• The following statement has been revised to add ‘or 3 months post-revascularization.’ Criteria are met for a non-elective implantable cardioverter defibrillator (ICD) or a non-elective pacemaker, either initial or replacement, and based upon the low likelihood of improvement in symptoms and adequate recovery of LVEF, despite less than 3 months GDMT for heart failure or < 40 days post myocardial infarction or 3 months post revascularization, criteria for CRT are otherwise met. The following statement has been added: ‘This avoids a second implantation procedure within less than 3 months.’
REFERENCES:


Motonaga KS, Dubin AM. Cardiac resynchronization therapy for pediatric patient with heart failure and congenital heart disease. Circulation. 2014;129:1879-1891. Available at: http://circ.ahajournals.org/content/129/18/1879.short

Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC), developed with the special contribution of the Heart Failure Association (HFA) of the ESC. European


INDICATIONS FOR ICD INSERTION

Ischemic Heart Disease (CAD)
(Al-Khatib 2017, Priori 2015, Russo 2013)

- Patients with documented ventricular fibrillation (VF), hemodynamically unstable ventricular tachycardia (VT), or sustained VT, after exclusion of reversible causes
- Syncope of undetermined origin, with one of the following:
  - Inducible VF or sustained VT at electrophysiological study (EPS), or
  - Left ventricular ejection fraction (LVEF) ≤ 35%
- LVEF ≤ 35% due to ischemic heart disease and NYHA class II or III, despite guideline-directed medical therapy (GDMT), and at least 40 days post myocardial infarction (MI) and 90 days post-revascularization
- LVEF ≤ 30% due to ischemic heart disease, NYHA class I, II, or III despite GDMT, and at least 40 days post-MI and 90 days post-revascularization (Al-Khatib 2017, Russo 2013)

Nonischemic cardiomyopathy (NICM)
(Al-Khatib 2017)

- Patients with documented VF, hemodynamically unstable VT, or sustained VT, after exclusion of reversible causes
- Syncope that is presumed to be due to ventricular arrhythmia
- NICM with LVEF ≤ 35% and NYHA functional Class II or III, despite at least 3 months of GDMT
- NICM due to a Lamin A/C gene mutation, who have ≥ 2 risk factors from the following (NSVT, LVEF < 45%, Male sex, nonmissense mutation)

Advanced Heart Failure & Transplantation
(Al-Khatib 2017, Priori 2015)

- In nonhospitalized patients with NYHA class IV who are candidates for cardiac transplantation or left ventricular assist device (LVAD) (Al-Khatib 2017, Priori 2015, Russo 2013)
- In a patient with an LVAD, sustained ventricular arrhythmias (Al-Khatib 2017)
- In NYHA ambulatory class IV, with appropriate indications for CRT (see Background Information section for definition of ambulatory NYHA class IV)

Myocardial Diseases

- Hypertrophic cardiomyopathy (HCM) with ≥ 1 major risk factors for SCD (Al-Khatib 2017, Epstein 2012, Gersh 2011, Shen 2017):
  - Prior sudden cardiac arrest (SCA) due to VT or VF
  - Documentation of sustained VT with syncope or hemodynamic compromise
  - Maximum LV wall thickness ≥ 30 mm
  - SCD in 1 or more first degree relatives
o > 1 episode of unexplained syncope within the preceding 6 months
o Documented NSVT with an additional SCD risk modifier (age < 30 yr, delayed hyperenhancement on cardiac MRI, LVOT obstruction, or syncope > 5 yr ago) or high-risk feature (LV aneurysm or LVEF < 50%)
o Abnormal BP response to exercise with an additional SCD risk modifier or high-risk feature (see above)
  i. BP rise < 20 mmHg or fall of > 20 mmHg during exercise

• **Cardiac Sarcoidosis** with one of the following (Al-Khatib 2017, Priori 2015, Shen 2017):
  o Cardiac arrest or documented sustained VT
  o LVEF ≤ 35%
  o LVEF > 35% with inducible sustained ventricular arrhythmia at EPS
  o Syncope and/or scar on CMR or positron emission tomography (PET)
  o Requires a permanent pacemaker

• **Neuromuscular Disorders** with one of the following (Al-Khatib 2017):
  o Primary and secondary prevention, with same indications as for NICM (Priori 2016)
  o Emery-Dreifuss or limb-girdle type I-B muscular dystrophy with progressive cardiac involvement

• **Arrhythmogenic right ventricular cardiomyopathy** and ≥ 1 of the following risk factors for SCD: (Al-Khatib 2017, Calkins 2017, Epstein 2012, Corado 2015, Shen 2017)
  o Resuscitated sudden cardiac arrest
  o Sustained VT
  o Right or left ventricular systolic dysfunction with an ejection fraction ≤ 35%
  o Syncope with documented or presumed ventricular arrhythmia

**Channelopathies**

• **Congenital long QT syndrome** with one of the following (Al-Khatib 2017, Epstein 2012, Goldenberg 2008, Priori 2015, Schwartz 2012)
  o Sudden cardiac arrest
  o Sustained VT or recurrent syncope when beta blocker is ineffective or not tolerated
  o QTc > 500 ms on a beta blocker (Al-Khatib 2017)
  o Strong family history of SCD
  o High risk genotype (type 2 and type 3)

• **Brugada syndrome and spontaneous type 1 Brugada electocardiographic pattern** with one of the following: (Al-Khatib 2017, Epstein 2012, Katsumoto 2018, Priori 2015)
  o Cardiac arrest
  o Documented sustained ventricular arrhythmia
  o Syncope due to ventricular arrhythmia

• **Catecholaminergic polymorphic VT** with one of the following (Al-Khatib 2017, Priori 2013, Epstein 2012, Russo 2013):
  o Sudden cardiac arrest
  o Syncope or sustained VT
  o Inducible VT or VF

• **Early Repolarization or Short QT Syndrome** with one of the following (Al-Khatib 2017, Priori 2015):
  o Cardiac arrest
  o Sustained ventricular arrhythmia

• **Idiopathic Polymorphic VT/VF** with one of the following (Al-Khatib 2017):
Cardiac arrest due to polymorphic VT or VF

Miscellaneous

Adult & Pediatric Congenital (Structural) Heart Disease (ACHD)

- Cardiac arrest due to VF or VT after exclusion of a reversible etiology
- Systemic LVEF ≤ 35%, biventricular physiology, and NYHA class II or III on GDMT.
- Tetralogy of Fallot with one of the following (Al-Khatib 2017, Shen 2017):
  - Spontaneous sustained VT
  - Inducible VF or sustained VT
  - ≥ 1 risk from the following list:
    - Prior palliative systemic to pulmonary shunts
    - Unexplained syncope
    - Frequent PVCs
    - Atrial tachycardia
    - Left ventricular dysfunction or diastolic dysfunction
    - NSVT
    - QRS duration ≥ 180 ms
    - Dilated right ventricle
    - Severe pulmonary regurgitation or stenosis
- Single or systemic right ventricular ejection fraction (RVEF) < 35%, in the presence of an additional risk factor such as:
  - NSVT
  - Unexplained syncope
  - NYHA class II or III, despite GDMT (Al-Khatib 2017, Priori 2015)
  - QRS duration ≥ 140 ms
  - Severe systemic AV valve regurgitation
- Syncope of unknown origin in the presence of either advanced ventricular dysfunction (EF < 35%) or marked hypertrophy or inducible sustained VT or VF (Al-Khatib 2017, Shen 2017)
- Syncope and moderate or complex congenital heart disease (CHD), with high clinical suspicion of ventricular arrhythmias
- Non-hospitalized patients with CHD awaiting heart transplantation
- Left ventricular non-compaction that meets same indications as NICM, including a familial history of SCD (Biagini 2006, Russo 2018)

EXEMPTIONS:
Indications for ICD with an Appropriate Pacing Modality in Special Situations
(Katsumoto 2014, Russo 2013)*

- ICD criteria met, and elevated troponin is deemed not due to a myocardial infarction (Al-Khatib 2017)
• ICD criteria met, except for myocardial infarction within 40 days or revascularization within 3 months, but a non-elective permanent pacemaker (new or replacement) is required, and recovery of left ventricular function to LVEF > 35% is uncertain or not expected (Russo 2013)**

• ICD criteria met, except NICM or ischemic cardiomyopathy has not had 3 months’ time for LVEF to improve on medical therapy, a non-elective permanent pacemaker is required, and recovery of LVEF is uncertain or not expected**

• Patient met primary prevention criteria for an ICD prior to coronary revascularization, and it is unlikely that LVEF will recover to > 35% despite a 90 day wait (Katsumoto 2014)

* With these ICD indications, CRT would sometimes be the appropriate pacing modality. CRT is highly likely to be the appropriate modality when > 40% rhythm requires pacing.

** These indications avoid a second implantation procedure within less than 3 months.

BACKGROUND:

The implantable cardioverter defibrillator (ICD) has become valuable in the management of patients with ventricular arrhythmias (VA) capable of causing syncope, cardiac arrest, and sudden cardiac death (SCD).

Patient eligibility for an ICD presumes all of the following:
• Anticipated reasonable quality of life for ≥ 1 year post implantation (Katsumoto 2018)
• Patient’s ability to live with a shock-delivering device that requires management
• Absence of a completely reversible cause that led to VA for which an ICD is being considered (see Background Information section on reversible causes)
• Completion of ≥ 3 months of guideline directed medical therapy (GDMT) for heart failure (HF), unless an intervening indication for pacemaker implantation arises (see Background Information section for definition of GDMT)
• ICD indications are present in the vast majority of scenarios in which cardiac resynchronization therapy (CRT) is appropriate
• Sustained VT is defined as having duration > 30 seconds or requiring termination due to hemodynamic compromise in < 30 seconds

Guidelines for the pediatric population are extrapolated from the adult population, due to a lack of relevant trials (Brugada 2013, Priori 2015)

OVERVIEW:
General

Implantable cardioverter defibrillators (ICDs) are indicated for the treatment of life-threatening ventricular tachycardia and ventricular fibrillation. An ICD system includes a pulse generator and one or more leads. ICDs are indicated both for patients who have survived life threatening rhythm disturbances (secondary prevention) and for those who are at risk for them (primary prevention)

• An ICD continually monitors heart rhythm. If a rapid rhythm is detected, the device delivers electrical therapy directly to the heart muscle in order to terminate the rapid rhythm and restore a normal heart rhythm. There are two types of therapy that can be delivered:
- Rapid pacing OR
- High-voltage shocks are necessary for ventricular fibrillation and also for instances where rapid pacing has failed to correct the abnormal rhythm

- In addition, all ICDs have pacing capability, and they deliver pacing therapy for slow heart rhythms (bradycardia)
- The parameters defining limits for pacing therapy and for tachycardia therapy are programmable using noninvasive radio signals on all available ICDs

**Waiting Period** is an important issue in ICD insertion for primary prevention. This has resulted from guidelines and payment policies which mirror the inclusion criteria of primary and secondary prevention trials (Dukkipati 2017a, Dukkipati 2017b).

**NYHA Class Definitions** (Campeau 1976, Goldman 1981, Russo 2013)

- **Class I**: No limitation of functional activity or only at levels of exertion that would limit normal individuals (patient can carry 24 pounds up 8 stairs, play basketball, and shovel soil).
- **Class II**: Slight limitation of activity. Fatigue, palpitation, or dyspnea with moderate exercise (patient able to dance, garden, and walk 4 MPH on level ground).
- **Class III**: Marked limitation of activity. Fatigue, palpitation, or dyspnea with minimal activity (patient able to shower, make bed, bowl or golf, dress, and walk 2.5 MPH on level ground).
- **Class IV**: Severe limitation of activity. Symptoms even at rest, worse with activity (patient unable to comfortably perform any significant activity).
- **Ambulatory Class IV**: Class IV heart failure with: 1) no active acute coronary syndrome; 2) no inotropes; and 3) on GDMT.

**Guideline Directed (or Optimal) Medical Therapy for Heart Failure** (Yancy 2013, Yancy 2017)

- Angiotensin converting enzyme (ACE-I), angiotensin receptor blockers (ARB), or combined angiotensin receptor inhibitor and neprilysin inhibitor (ARNI)
- Beta blocker (might be less critical in permanent atrial fibrillation, still recommended) (Kotecha 2017)
- Addition of loop diuretic for all NYHA class II – IV patients
- Addition of hydralazine and nitrate for persistently symptomatic African Americans
- Addition of an aldosterone antagonist, provided eGFR is > 30 ml/mi
- Normal serum sodium and potassium
- Not required for consideration of ICD: Ivabradine for NYHA class II – III, when a beta blocker has failed to reduce a sinus rate to < 70 bpm. Ivabradine listed as a class IIa recommendation, while others are class I recommendations. CRT trials antedated routine use of Ivabradine.
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ACE-I</td>
<td>Angiotensin converting enzyme inhibitor</td>
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<td>ACHD</td>
<td>Adult congenital heart disease</td>
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<td>ARNI</td>
<td>Combined angiotensin receptor inhibitor and neprilysin inhibitor</td>
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<td>ARVD/C</td>
<td>Arrhythmogenic right ventricular dysplasia/cardiomyopathy</td>
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<td>AV</td>
<td>Atrioventricular</td>
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<td>CAD</td>
<td>Coronary artery disease, same as ischemic heart disease</td>
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<td>Congestive heart failure</td>
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<td>CRT</td>
<td>Cardiac resynchronization therapy</td>
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<td>CRT-D</td>
<td>Cardiac resynchronization therapy ICD system</td>
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<tr>
<td>DCM</td>
<td>Dilated cardiomyopathy</td>
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<td>ECG</td>
<td>Electrocardiogram</td>
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<td>Electrophysiologic Study</td>
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<td>Guideline-Directed Medical Therapy</td>
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<td>HCM</td>
<td>Hypertrophic cardiomyopathy</td>
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<td>HF</td>
<td>Heart failure</td>
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<td>Heart Rhythm Society</td>
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<td>HV</td>
<td>His-ventricle</td>
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<td>ICD</td>
<td>Implantable cardioverter-defibrillator</td>
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<td>LBBB</td>
<td>Left bundle-branch block</td>
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<td>LV</td>
<td>Left ventricular/left ventricle</td>
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<td>LVAD</td>
<td>Left ventricular assist device, mechanical heart</td>
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<td>LVEF</td>
<td>Left ventricular ejection fraction</td>
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<td>MI</td>
<td>Myocardial infarction</td>
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<td>ms</td>
<td>Milliseconds</td>
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<td>NICM</td>
<td>Nonischemic cardiomyopathy</td>
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<td>NYHA</td>
<td>New York Heart Association</td>
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<td>RV</td>
<td>Right ventricular/right ventricle</td>
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<td>STEMI</td>
<td>ST-elevation myocardial infarction</td>
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<td>Sinus node dysfunction</td>
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<td>VT</td>
<td>Ventricular tachycardia</td>
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<td>VF</td>
<td>Ventricular fibrillation</td>
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POLICY HISTORY:
Review Date:  August 14, 2019
Review Summary:

- Removed indications under ischemic heart disease for NSVT due to prior MI, LVEF ≤ 40%, and inducible VT or VF at EPS
- Removed indications under ischemic heart disease for VT or VF < 48 hours post MI or elective coronary revascularization
- Under NICM, removed indication for peripartum cardiomyopathy with LVEF ≤ 35% that persists > 3 months
- Under advanced heart failure and transplantation, removed indication for severe allograft vasculopathy
- Revision to cardiac sarcoidosis indication to add cardiac arrest
- Under hypertrophic cardiomyopathy revised indications for documented NSVT to include an additional SCD risk modifier (age < 30 yr, delayed hyperenhancement on cardiac MRI, LVOT obstruction, or syncope > 5 yr ago) or high risk feature (LV aneurysm or LVEF < 50%)
- Removed indications for giant cell myocarditis and chronic Chagas cardiomyopathy
- Removed indication for hypertensive heart disease with LVH and LVEF ≤ 35%
- Under Tetrology of Fallot added the following indications:
  - Prior palliative systemic to pulmonary shunts
  - Unexplained syncope
  - Frequent PVCs
  - Atrial tachycardia
  - Left ventricular diastolic dysfunction
  - Dilated right ventricle
REFERENCES:


INDICATIONS FOR PACEMAKERS – ADULT (Excludes conditions that are expected to resolve)
(Epstein 2013; Hayes 2018, Kusumoto 2019)

Sinus Node Dysfunction (SND)
- Documented symptomatic sinus bradycardia, including frequent sinus pauses
- Symptomatic chronotropic incompetence (broadly defined as an inability to increase heart rate commensurate with activity or demand), documented by stress test or electrocardiography (ECG) recording data
- Symptomatic sinus bradycardia that results from required guideline-directed medical therapy (GDMT) for which there is no alternative treatment
- Heart rate less than 40 while awake, even without definite association with significant symptoms consistent with bradycardia
- Tachycardia-bradycardia syndrome and symptoms attributable to bradycardia (Kusumoto 2019)
- Syncope of unexplained origin with clinically significant SND, either seen or provoked in electrophysiologic study (EPS)

Acquired Atrioventricular (AV) Block
- Persistent third-degree (complete) AV block, regardless of symptoms
- Second-degree Mobitz Type II AV block and high-grade AV block, regardless of symptoms
- Atrial fibrillation while awake, with pauses ≥ 5 seconds, or symptomatic bradycardia
- In sinus rhythm (with AV block) while awake, pauses ≥ 3 seconds or heart rates less than 40 beats per minute or an escape rhythm below the AV node
- Following catheter ablation of the AV junction
- Second-degree AV block, third degree AV block, or an H-V interval ≥ 70 ms, associated with neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy (limb-girdle muscular dystrophy), Kearns-Sayre syndrome, and peroneal muscular atrophy, regardless of symptoms
- Symptomatic AV block that results from required medical therapy for which there is no alternative treatment
- Exercise-induced second or third-degree AV block without myocardial ischemia
- Symptomatic bradycardia associated with second-degree AV block, either Mobitz I or II
- Second-degree AV block associated with a wide QRS, or EPS-documented intra- or infra-His conduction
- First- or second-degree AV block with “pacemaker syndrome” symptoms (chronic fatigue, dyspnea on exertion, symptomatic hypotension) or hemodynamic compromise
- Marked first-degree or second-degree Mobitz Type 1 AV block with symptoms clearly attributable to the AV block

Chronic Bifascicular Block
- Type II second-degree AV block, advanced second-degree AV block (see definitions section) or intermittent third-degree AV block
- Alternating bundle-branch block
- Syncope of unexplained origin when other likely causes have been excluded, specifically ventricular tachycardia (Shen 2017)
• Syncope and bundle branch block with an HV interval ≥ 70 ms, or evidence of infranodal block at EPS (Kusomoto 2018)
• Incidental findings at EPS study of an H-V interval ≥ 100 milliseconds, or non-physiological, pacing-induced infra-His block in asymptomatic patients

**Hypersensitive Carotid Sinus Syndrome and Neurocardiogenic Syncope**
• Recurrent syncope due to spontaneously occurring carotid sinus stimulation AND carotid sinus pressure induced ventricular asystole ≥ 3 seconds, or AV block, or ≥ 50 mm Hg drop in systolic BP (Epstein 2008, Shen 2017)
• Syncope without clear, provocative events and with a hypersensitive cardioinhibitory response (asystole) ≥ 3 seconds
• Recurrent syncope and asystole ≥ 3 seconds with syncope or ≥ 6 seconds without symptoms or with presyncope, documented by implantable loop recorder (Brignole 2012, Varosy 2017)

**Pacing to Terminate or Prevent Tachycardia**
• Symptomatic recurrent supraventricular tachycardia documented to be terminated by pacing in the setting of failed catheter ablation and/or drug treatment (intolerance included)
• Sustained pause-dependent ventricular tachycardia (VT)

**INDICATIONS FOR PEDIATRIC AND CONGENITAL HEART DISEASE PACING**
(Brignole 2013, Brugada 2013, Epstein 2013, )

**Children, Adolescents (< 19 years), and Patients with Congenital Heart Disease**

**Sinus Node Dysfunction (SND)**
• SND with symptomatic age- and activity-inappropriate bradycardia
• Sinus bradycardia with complex congenital heart disease AND a resting heart rate < 40 bpm OR pauses in ventricular rate > 3 seconds
• Congenital heart disease and impaired hemodynamics due to sinus bradycardia or loss of AV synchrony
• Asymptomatic sinus bradycardia following biventricular repair of congenital heart disease with an awake resting heart rate < 40 bpm or pauses in ventricular rate > 3 seconds
• Congenital heart disease (CHD) and SND or junctional bradycardia, for the prevention of recurrent episodes of intra-atrial reentrant tachycardia (Brugada 2013, Brignole 2013, Khairy 2014).

**AV Block**
• Second- or third-degree AV block with symptomatic bradycardia, ventricular dysfunction, or low cardiac output
• Congenital third-degree AV block with a wide QRS escape rhythm, complex ventricular ectopy, or ventricular dysfunction
• Congenital third-degree AV block in the infant with a ventricular rate < 55 bpm or with congenital heart disease and a ventricular rate < 70 bpm
• Congenital third-degree AV block after age 1 year with an average heart rate < 50 bpm, abrupt pauses in ventricular rate that are 2 or 3 times the basic cycle length, or associated with symptoms due to chronotropic incompetence
• Adults with congenital complete AV block with symptomatic bradycardia, wide QRS escape rhythm, mean daytime heart rate < 50 bpm, complex ventricular ectopy, or ventricular dysfunction (Kusomoto 2018)
• Adults with congenital complete AV block, regardless of symptoms (Kusomoto 2018)
• Unexplained syncope after prior congenital heart surgery complicated by transient complete heart block, with residual fascicular block after excluding other causes of syncope
• Congenital third-degree AV block in asymptomatic children or adolescents with an acceptable rate, a narrow QRS, and normal ventricular function
Scenarios in which Pacemakers are Not Indicated

- SND in patients that are asymptomatic or symptoms occur without documented bradycardia
- Asymptomatic first-degree AV block or Mobitz I second-degree AV block with a narrow QRS
- Asymptomatic fascicular block (left anterior or posterior fascicular block)
- Hypersensitive cardioinhibitory response to carotid sinus stimulation without symptoms or with vague symptoms
- Asymptomatic bifascicular block +/- first-degree AV block after surgery for congenital heart disease without prior transient complete AV block

BACKGROUND

( Epstein 2013, Hayes 2018)

Pacemaker implantation generally serves to address bradycardias, with the intention of ameliorating related symptoms, preventing complications of syncope, and/or reducing mortality risk.

Guidelines for the pediatric and congenital heart disease population are provided in the latter portion of this guideline.

This guideline is not intended to cover the type of bradycardia pacing device. CRT (cardiac resynchronization therapy or biventricular pacing) and ICD (implantable cardioverter defibrillator) implantation are covered in separate guidelines.

OVERVIEW

General

A pacemaker system is composed of a pulse generator and one or more leads. The pulse generator is implanted under the skin, usually below one of the collarbones (clavicles). It contains a battery, a microprocessor that governs timing and function, and a radio antenna to allow for noninvasive interrogation and reprogramming. The leads are insulated cables that conduct electricity from the pulse generator to the heart. Leads are most commonly inserted into a vein and then advanced under fluoroscopy (X-ray guidance) to within one or more heart chambers. The leads are fastened within the chambers to the heart muscle using either hooks or retractable/extendable screws, which are built into their tips. Timed electrical impulses are delivered from the pulse generator via the leads to the heart, where stimulation results in heart muscle contraction.

Heart Block Definitions

( Epstein 2013)

- First Degree: All sinus or atrial beats are conducted to the ventricles, but with a delay (PR interval of > 200 ms)
- Second Degree: Intermittent failure of conduction of single beats from atrium to ventricles
  - ( Mobitz) Type I: Conducted beats have variable conduction times from atrium to ventricles
  - ( Mobitz) Type II: Conducted beats have uniform conduction times from atrium to ventricles
  - Advanced or high degree: Two or more consecutive non-conducted sinus or (non-premature) atrial beats with some conducted beats
- Third Degree: No atrial beats are conducted from atrium to ventricle

Abbreviations
AV Atrioventricular
CHF Congestive heart failure
CRT Cardiac resynchronization therapy (same as biventricular pacing)
ECG Electrocardiogram
EPS Electrophysiologic Study
GDMT Guideline-Directed Medical Therapy
HRS Heart Rhythm Society
HV His-ventricular
ICD Implantable cardioverter-defibrillator
LBBB Left bundle-branch block
LV Left ventricular/left ventricle
LVEF Left ventricular ejection fraction
MI Myocardial infarction
ms Milliseconds
s Seconds
STEMI ST-elevation Myocardial Infarction
SND Sinus node dysfunction
VT Ventricular tachycardia

POLICY HISTORY:
Review Date: July 2019
Review Summary:
- Added broad definition of chronotropic incompetence
- For sinus node dysfunction added indication for tachycardia-bradycardia syndrome “and symptoms attributable to bradycardia”
- Indications after the acute phase of myocardial infarction were removed
- For hypersensitive carotid sinus syndrome and neurocardiogenic syncope:
  - Added indication for recurrent syncope and asystole ≥ 3 seconds with syncope or ≥ 6 seconds without symptoms or with presyncope, documented by implantable loop recorder
  - Removed indication for neurocardiogenic syncope associated with bradycardia occurring spontaneously or at the time of tilt table testing
- For hypertrophic cardiomyopathy, removed symptomatic hypertrophic cardiomyopathy and hemodynamically significant resting (peak > 30 mmHg) or provoked (peak > 50 mmHg) LV outflow tract gradient, refractory to medical therapy, and suboptimal candidates for septal reduction therapy (including high risk for developing heart block post procedure)
- For pediatric and congenital heart disease pacing, AV block, the following indications were added:
  - Adults with congenital complete AV block with symptomatic bradycardia, wide QRS escape rhythm, mean daytime heart rate < 50 bpm, complex ventricular ectopy, or ventricular dysfunction
  - Adults with congenital complete AV block, regardless of symptoms
- For pediatric and congenital heart disease pacing, AV block, removed postoperative advanced second or third degree AV block that is expected to be permanent or that persists ≥ 7 days after cardiac surgery; and transient postoperative third degree AV block that reverts to sinus rhythm with residual bifascicular block
- For pediatric and congenital heart disease pacing, scenarios in which pacemakers are not indicated, the following were added:
  - Asymptomatic first-degree AV block or Mobitz I second-degree AV block with a narrow QRS
  - Asymptomatic fascicular block (left anterior or posterior fascicular block)
  - Hypersensitive cardioinhibitory response to carotid sinus stimulation without symptoms or with vague symptoms
REFERENCES


ADULT PATIENTS – INDICATIONS FOR TRANSTHORACIC ECHOCARDIOGRAPHY (TTE)
(Indications for pediatric patients follow this section)
(Douglas 2011)

Evaluation of Cardiac Structure and Function

- Symptoms with a suspected cardiac etiology including, but not limited to, chest pain, shortness of breath (not clearly pulmonary in origin), or recent embolic event
- Palpitations with symptoms or signs of cardiovascular disease (i.e. abnormal physical exam or ECG)
- Hypotension of suspected cardiac etiology

Murmur or Click

- Initial evaluation when there is a reasonable suspicion for valvular or structural heart disease such as high grade, holosystolic, continuous or diastolic murmur

Arrhythmias

- Frequent ventricular premature contractions (PVCs) (greater than 30 per hour)
- Sustained or nonsustained ventricular tachycardia (VT) or ventricular fibrillation (VF), or ventricular bigeminy
- Atrial fibrillation without a prior transthoracic echocardiogram (TTE) to evaluate
- Unevaluated left bundle branch block

Syncope (Doherty 2017, Shen 2017)

- When initial evaluation including history, physical examination or electrocardiogram (ECG) suggests a cardiac etiology
- Exercise induced syncope


- Preoperative left ventricular function assessment in patients who are candidates for solid organ transplantation (can be done yearly prior to transplant)

Pulmonary Hypertension

- Evaluation of suspected pulmonary hypertension including evaluation of right ventricular function and estimated pulmonary artery pressure
- Re-evaluation of known pulmonary hypertension if there is a change in clinical status or cardiac exam, or to guide therapy (can be performed every 6 - 12 months, or more frequently to guide therapy (Nazzareno 2016)
- Evaluation of patients with pulmonary embolism to risk stratify and initiate appropriate therapy (Saric 2016)
Screening test for pulmonary hypertension in patients with scleroderma

**Evaluation of Valvular Function**  
(Doherty 2017, Doherty 2018, Nishimura 2014)

**Native Valvular Stenosis**

- Routine surveillance (≥ 3 yrs) of bicuspid aortic valve, aortic sclerosis, or mild valvular stenosis, without a change in clinical status or cardiac exam  
- Re-evaluation (≥ 1 yr) of moderate stenosis without a change in clinical status or cardiac exam  
- Re-evaluation of an asymptomatic patient with severe aortic stenosis (AS) every 6 - 12 months without a change in clinical status or cardiac exam  
- Re-evaluation after medical therapy in patients with low-flow/low gradient severe AS

**Native Valvular Regurgitation with TTE** (Doherty 2017, Lancellotti 2013)

- Re-evaluation (≥ 3 yrs) of mild valvular regurgitation without change in clinical status or cardiac exam  
- Re-evaluation (≥ 1 yr) of moderate valvular regurgitation without change in clinical status or cardiac exam  
- Re-evaluation of asymptomatic patient every 6 - 12 months with severe aortic regurgitation  
- Re-evaluation of asymptomatic patient every 6 - 12 months with severe mitral regurgitation

**Prosthetic Valves with TTE**

- Initial evaluation of prosthetic valve or native valve repair, for establishment of baseline, typically 6 weeks to 3 months postoperative  
- Re-evaluation (≥ 3 yrs after valve implantation) of prosthetic valve or native valve repair if no known or suspected valve dysfunction  
- Evaluation of prosthetic valve or native valve repair with suspected dysfunction  
- Re-evaluation of known prosthetic valve dysfunction when it would change management  
- Annual evaluation of prosthetic heart valves older than 10 years  
- Evaluation prior to pregnancy in patients with a prosthetic valve and no echocardiography within the past year

**Transcatheter Heart Interventions**

**Transcatheter Aortic Valve Replacement (TAVR)** (Doherty 2017, Otto 2017)

- Pre TAVR evaluation  
- Post TAVR at 30 days (6 weeks to 3 months also acceptable) and annually  
- Assessment post TAVR when there is suspicion of valvular dysfunction  
- Assessment of stroke post TAVR with suspicion of valve dysfunction or thrombus

**Percutaneous Mitral Valve Repair** (Doherty 2017)

- Determination of patient eligibility  
- Reassessment for degree of MR and left ventricular function (1, 6, and 12 months, and then annually to 5 yrs)

**Closure of PFO or ASD** (Doherty 2019)

- Pre-procedure evaluation  
- Routine follow-up at 6 months for device position and integrity  
- Evaluation for clinical concern for infection, malposition, embolization, or persistent shunt
Left Atrial Appendage (LAA) Occlusion (Doherty 2019)

- Pre-procedure evaluation

Pericardial Disease and Cardiac Source of Emboli (Doherty 2017, Klein 2013, Saric 2016)

- Suspected pericardial effusion or re-evaluation when findings would alter therapy
- Suspected pericardial constriction or re-evaluation of status when findings would alter therapy
- Re-evaluation of cardiac mass or tumor when findings would alter therapy
- Suspected cardiovascular source of embolus

Infective Endocarditis (Native or Prosthetic Valves) (Doherty 2017, Habib 2010, Nishimura 2014)

- Initial evaluation of suspected infective endocarditis with positive blood cultures or a new murmur
- Re-evaluation of infective endocarditis with a change in clinical status or cardiac exam, or when findings would change management
- Re-evaluation of patient with infective endocarditis at high risk of progression or complication (extensive infective tissue/large vegetation, or staphylococcal, enterococcal, or fungal infections)
- At completion of antimicrobial therapy and serial examinations at 1,3,6, and 12 months during the subsequent year (Habib 2010)


In the absence of recent computed tomography (CT) or cardiovascular magnetic resonance (CMR), which are preferred for imaging beyond the proximal ascending aorta

- Screening of first degree relatives of individuals with a thoracic aortic aneurysm (defined as ≥ 50% above normal) or dissection, or if an associated high-risk mutation is present
- If one or more first degree relatives of a patient with a known thoracic aortic aneurysm or dissection, have thoracic aortic dilatation, aneurysm or dissection, then imaging of 2nd degree relatives is reasonable
- Six-month follow up after initial finding of a dilated thoracic aorta, for assessment of rate of change
- Annual follow up of enlarged thoracic aorta that is above top normal for age, gender, and body surface area
- Biannual (twice/year) follow up of enlarged aortic root > 4.5 cm or showing growth rate ≥ 0.5 cm/year
- Evaluation of the ascending aorta in known or suspected connective tissue disease or genetic conditions that predispose to aortic aneurysm or dissection (e.g., Marfan syndrome, Ehlers Danlos or Loeys-Dietz syndromes) at time of diagnosis and 6 months thereafter for growth rate assessment, followed by annual imaging, or biannual (twice yearly) if diameter ≥ 4.5 or expanding ≥ 0.5 cm/yr
- Patients with Turner’s syndrome should undergo imaging to assess for bicuspid aortic valve, coarctation of the aorta or dilation of the ascending or thoracic aorta. If the initial imaging is normal and there are no additional risk factors for dissection, imaging can be done every 5 - 10 years. If an abnormality exists, annual imaging is recommended
- Screening of first-degree relatives of patients with a bicuspid aortic valve
- Re-evaluation of known ascending aortic dilation or history of aortic dissection with a change in clinical status or cardiac exam or when findings may alter management
- Re-evaluation (< 1 y, generally twice a year) of the size and morphology of the aortic sinuses and ascending aorta in patients with a bicuspid AV with 1 of the following:
  - Aortic diameter ≥ 4.5 cm
  - Rapid rate of change in aortic diameter when an annual growth rate of ≥ 0.5 cm is suspected.
  - Family history (first-degree relative) of aortic dissection
• Follow up post medical treatment of aortic disease:
  o Acute dissection: 1 month, 6 months, then annually
  o Chronic dissection: annually
• Follow up post either root repair or AVR plus ascending aortic root/arch repair:
  baseline post-op, then annually (Svensson 2013)
• Evaluation of sinus of Valsalva aneurysms and associated shunting secondary to rupture (Terdjman 1984). Echo imaging every 4-12 weeks is recommended during pregnancy and 6 months post-partum in patients with ascending aortic dilation (Regitz-Zagrosek 2018)

**Hypertension, Heart Failure, or Cardiomyopathy**

**Hypertension (Doherty 2018)**

- Initial evaluation of suspected hypertensive heart disease

**Heart Failure & LV Function (Doherty 2018, Nagueh 2016, Patel 2013, Yancy 2013)**

- Initial evaluation of suspected heart failure (HF) (systolic or diastolic) based on symptoms, signs, or abnormal test results
- Re-evaluation of known HF (systolic or diastolic) with a change in clinical status or cardiac exam without a clear precipitating change in medication or diet
- Re-evaluation of known HF (systolic or diastolic) when essential to guide therapy
- Evaluation of LV function prior to cardiotoxic chemotherapy, and subsequently for monitoring
- Re-evaluation for CRT device optimization in a patient with worsening HF

**Cardiomyopathy (Doherty 2018, Gersh 2011, Patel 2013, Regitz-Zagrosek 2018, Yancy 2013)**

- Initial evaluation of suspected inherited or acquired cardiomyopathy
- Re-evaluation of known cardiomyopathy with a change in clinical status or cardiac exam or to guide therapy
- Screening evaluation in first-degree relatives of a patient with an inherited cardiomyopathy
- Suspected cardiac sarcoidosis (see Overview)
- Hypertrophic Cardiomyopathy (HCM) (Gersh 2011)
  o Initial evaluation of suspected HCM
  o Re-evaluation of patients with HCM with a change in clinical status or new cardiovascular event
  o Evaluation of the result of surgical myomectomy or alcohol septal ablation
  o Re-evaluation every 1 - 2 years for symptomatically stable patients to assess degree of myocardial hypertrophy, dynamic obstruction, and myocardial function
  o Re-evaluation of clinically unaffected patients with a first-degree relative with HCM every 5 years
- Assessment of peripartum cardiomyopathy at onset and 3 months, then at 6 month intervals for minimum two years, or longer if required for surveillance during weaning medication, with additional follow up annually to 5 yrs. Re-evaluation for intended or actual recurrent pregnancy (Hilfiker-Kleiner 2015).

**Device Candidacy (Pacemaker, ICD, or CRT)**

- Initial evaluation or re-evaluation after revascularization (≥ 90 days) and/or myocardial infarction (≥ 40 days) and/or 3 months of guideline-directed medical therapy to determine candidacy for device therapy and/or to determine optimal choice of device (Al-Khatib 2017)
- Initial evaluation for CRT device optimization after implantation
• Known implanted pacing device with symptoms possibly due to device complication or suboptimal pacing device settings

Ventricular Assist Devices (VADs) and Cardiac Transplantation
(Doherty 2018, Stainback 2015)

• To determine candidacy for VAD
• Optimization of VAD settings and assessment of response post device
• Re-evaluation for signs/symptoms suggestive of VAD-related complications
• Monitoring for rejection in a cardiac transplant recipient

Adult Congenital Heart Disease
(Baumgartner 2010, Stout 2019, Warnes 2008)

• Initial evaluation of suspected adult congenital heart disease
• Known adult congenital heart disease with a change in clinical status or cardiac exam, or to guide therapy
• Screening of first-degree relatives of patients with bicuspid or unicuspid aortic valve
• Evaluation of patients following repair of Atrial Septal Defect (ASD), Patent Foramen Ovale (PFO), Ventricular Septal Defect (VSD) or Patent Ductus Arteriosus (PDA), within the first year following correction
• Adults with Williams syndrome or patients suspected of having supravalvular stenosis should have aortic imaging with TTE, TEE, CMR, or CTA
• Asymptomatic small coronary arteriovenous fistula every 3 years
• Annual evaluation in adults after Fontan palliation
• Annual evaluation for pulmonary hypertension and Eisenmenger syndrome
• Serial follow-up based on the defect and physiological stage is summarized below (See Overview for Definitions of Physiological Stage)

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PEDIATRIC PATIENTS - INDICATIONS FOR TRANSTHORACIC ECHOCARDIOGRAPHY (TTE (PATIENTS UNDER THE AGE OF 18))
(Campbell 2014)

- Hypertension
- Renal failure
- Palpitations, if one:
  - Family history at age < 50 of either:
    - Sudden cardiac death/arrest OR
    - Pacemaker or ICD
  - History or family history of cardiomyopathy
- Chest pain, if one or more of the following:
  - Exertional chest pain
  - Abnormal ECG
  - Family history with unexplained sudden death or cardiomyopathy
- Syncope, if any one of:
  - Abnormal ECG
  - Exertional syncope
  - Family history at age < 50 of either one:
    - Sudden cardiac death/arrest OR
    - Pacemaker or ICD
  - Family history of cardiomyopathy
- Signs and/or symptoms of heart failure, including, but not limited to:
  - Respiratory distress
  - Poor peripheral pulses
  - Feeding difficulty
  - Decreased urine output
  - Edema
  - Hepatomegaly
- Abnormal physical findings, including any one of:
  - Clicks, snaps, or gallops
  - Fixed and/or abnormally split S2
  - Decreased pulses.
  - Central cyanosis
- Arrhythmia, if one of:
  - Supraventricular tachycardia
  - Ventricular tachycardia
- Murmur
  - Pathologic sounding or harsh murmur, diastolic murmur, holosystolic or continuous murmur, late systolic murmur, grade 3/6 systolic murmur or louder, or murmurs that are provoked are become louder with changes in position
  - Presumptively innocent murmur, but in the presence of signs, symptoms, or findings of cardiovascular disease
- Abnormal basic data, including any one of:
  - Abnormal electrocardiogram (ECG)
Abnormal cardiac biomarkers
- Desaturation on pulse oximetry
- Abnormal chest x-ray
- Suspected pulmonary hypertension
- Signs and symptoms of endocarditis
- Thromboembolic events:
  - Patients on anticoagulants, when required to evaluate for thrombus
  - Thromboembolic events or stroke (Saric 2016)
- Systemic hematologic diseases that are associated with cardiac findings:
  - Sickle cell disease and other hemoglobinopathies
  - HIV infection
- Oncologic Therapy, any one:
  - Cardiotoxic chemotherapy, before and following exposure
  - Radiation therapy to chest, before and long term follow up (Lancellotti 2013)
- Inflammatory & Autoimmune, any one:
  - Suspected Rheumatic Fever
  - Systemic lupus erythematosus
  - Takayasu Arteritis
  - Kawasaki Disease (Newburger 2004)
- Suspicion of Structural Disease, any one:
  - Premature birth where there is suspicion of a Patent Ductus Arteriosus.
  - Vascular Ring, based upon either one:
    ▪ Difficulty breathing with stridor and eating solid foods that might suggest a vascular ring
    ▪ Abnormal barium swallow or bronchoscopy suggesting a vascular ring
- Genetic & Syndrome Related, any one:
  - Genotype positive for cardiomyopathy, family history of hypertrophic cardiomyopathy, other heritable cardiomyopathy, genetic disorder at high risk for cardiovascular involvement, heritable pulmonary arterial hypertension
  - Patient with a known syndrome associated with congenital or acquired heart disease (Down’s syndrome, Noonan’s syndrome, DiGeorge syndrome, William’s syndrome, Trisomy Thirteen, Trisomy Eighteen, Allagille syndrome, chromosomal abnormality associated with cardiovascular disease)
  - Abnormalities of visceral or cardiac situs
  - Known or suspected connective tissue diseases that are associated with congenital or acquired heart disease. (e.g. Marfan’s, Loeys-Dietz)
  - Known or suspected muscular dystrophies associated with congenital heart disease.
  - Mitochondrial or metabolic storage disease (e.g. Fabry’s disease)
  - Patients with a first degree relative with a genetic abnormality, such as cardiomyopathies (hypertrophic, dilated, arrhythmogenic right ventricular dysplasia, restrictive, left ventricular noncompaction).
- Maternal-Fetal Related, any one:
  - Maternal infection during pregnancy or delivery with potential fetal/neonatal cardiac sequelae
  - Maternal phenylketonuria
  - Suspected cardiovascular abnormality on fetal echocardiogram

INDICATIONS FOR FOLLOW-UP ECHOCARDIOGRAPHY IN PEDIATRIC PATIENTS
(Davey 2004)

Specific Indications for Follow-Up Echocardiograms in Pediatric Patients:
Infancy is defined as between birth and 1 year of age; childhood from 1-11 years of age; and adolescence from 11 to 21 years of age; Hagin 2017) The guidelines for adult congenital heart disease (Stout 2018) are not intended to be used for patients under 18 years of age.

- **Congenital Heart Disease (CHD) with a change in clinical status**
- **Kawasaki Disease**, upon diagnosis, two weeks later and 4 to 6 weeks later. If any coronary abnormalities are present, echocardiograms may need to be more frequent as clinically indicated. (Newburger 2004)
- Periodic screening of children of patients with hypertrophic cardiomyopathy every 12-18 months starting by age 12 or earlier if a growth spurt or signs of puberty are evident and/or when there are plans for engaging in intensive competitive sports or there is a family history of sudden cardiac death (Gersh 2011)
- Re-evaluation annually of valvular regurgitation that is more than mild in asymptomatic child
- **Pulmonic Stenosis (PS):** (Mahle 2008)
  - (Peak Doppler [mm Hg]: Mild < 40, Moderate 40-60, Severe > 60)
  - Mild to moderate PS in an infant: repeat at 2 weeks and 6 weeks to assess for increasing gradient as PVR drops
  - Mild stenosis that persists after 6 weeks of age: every 6 months until age 2 years
    - If the gradient regresses to < 25 mm Hg, reduce follow up to every 5 years.
    - If the gradient remains 25 - 40 after one year, follow up in one year and then every 3 years, if stable
  - Moderate stenosis post infancy (6 weeks): every 1-2 years
  - Post intervention for severe: every year for two years, then every 3 - 5 years, if stable
- **Aortic Stenosis (AS):** (Van Hare 2015): (Mean Gradients [mm Hg] mild < 25, moderate 25 - 40 or maximum instantaneous gradient 40 - 70, severe > 40 or maximum instantaneous gradient > 70)
  - Mild AS in an infant: every 6 months, or more depending on the patient’s clinical status and rate of progression.
  - Moderate AS in an infant: every 1 - 3 months to assess for progression and indication for valvuloplasty.
  - Mild in an asymptomatic child: every 1 - 2 years to assess for progression of stenosis
  - Moderate AS in an asymptomatic child: at least every 6 - 12 months to assess for progressive stenosis, left ventricular hypertrophy, or post-stenotic dilation.
  - In asymptomatic adolescents, annual TTE for aortic stenosis with mean Doppler gradient > 30 mm Hg or peak instantaneous gradient > 50 mm Hg, and every 2 years for patients with lesser gradients (Warnes 2008)
- **Aortic valve prosthesis** (Van Hare 2015)
  - Mechanical: every 6 - 12 months
  - Bioprosthetic: every 3 - 6 months
- **Mitral Stenosis (MS):**
  - Annual echocardiogram for MS from rheumatic heart disease in asymptomatic patient
  - Echocardiogram every 3-6 months for MS with treated CHF
- **Tricuspid Stenosis (TS):**
  - Frequency based on the patient’s clinical course and treatment
- **Shunt lesions:**
  - **Ventricular Septal Defect (VSD):** (Rudolph 2001):
    - (Pulmonary to systemic shunt ratio: small < 1.5, moderate 1.5 - 2.3, large > 2.3) (Oakley 2008)
      - Infants with VSD: repeat echocardiogram at 2 weeks and 6 weeks to assess for increasing shunt as the PVR drops
      - Small VSD: annual echocardiogram
      - Moderate to large VSD, asymptomatic: follow up in response to patient’s clinical status, if after one year, there is no pulmonary hypertension or left ventricular dilation, echo can be performed every 2 years
    - **Atrial Septal Defect (ASD)**
- Moderate to large secundum ASD (≥ 6 mm in diameter or shunt ≥ 1.5:1) and all primum, sinus venosus, and coronary sinus ASD: every 6 months
  Small secundum ASD (< 6mm in diameter and shunt < 1.5: 1): every 1 - 3 years

**BACKGROUND:**
Transthoracic echocardiography (TTE) uses ultrasound to image the structures of the heart in a real time format, providing 2-dimensional, cross sectional images. The addition of Doppler ultrasound derives hemodynamic data from flow velocity versus time measurements, as well as from color coded two dimensional representations of flow velocities.

TTE’s safety and versatility in examining cardiac structure, function, and hemodynamics lends to its utility for numerous indications in children and adults.

TEE (transesophageal echocardiography) widens the scope of utility for echocardiographic imaging, and its indications are covered in a separate guideline.

**OVERVIEW:**

**Imaging Surveillance for Cardiotoxic Chemotherapy**
(Herrmann 2014, Maleszewski 2018, Plana 2014, Zamorano 2016)

**TTE is the method of choice** for the evaluation of patients before, during, and after cancer therapy.

**CMR** is recommended when TTE has been unreliable and/or candidacy for cardiotoxic chemotherapy based upon LVEF is questionable (Plana 2014) (MUGA can also be considered when TTE is inadequate and CMR is not available).

**MUGA** is accurate and reproducible, but lacks information about pericardium and valves, incurs repeated radiation exposure, and is inaccurate during an irregular cardiac rhythm (Plana 2014).

**Cardiac Sarcoidosis** (Birnie 2014)
The most recent consensus recommendations on the criteria for diagnosis of cardiac sarcoidosis proposed by the Heart Rhythm Society is provided below.
There are 2 pathways to a diagnosis of Cardiac Sarcoidosis:

1. **Histological Diagnosis from Myocardial Tissue**
   CS is diagnosed in the presence of non-caseating granuloma on histological examination of myocardial tissue with no alternative cause identified (including negative organismal stains if applicable).

2. **Clinical Diagnosis from Invasive and Non-Invasive Studies**:
   It is probable* that there is CS if:
   a) There is a histological diagnosis of extra-cardiac sarcoidosis
   *and*
   b) One or more of following is present
   - Steroid +/- immunosuppressant responsive cardiomyopathy or heart block
   - Unexplained reduced LVEF (<40%)
   - Unexplained sustained (spontaneous or induced) VT
   - Mobitz type II 2nd degree heart block or 3rd degree heart block
   - Patchy uptake on dedicated cardiac PET (in a pattern consistent with CS)
   - Late Gadolinium Enhancement on CMR (in a pattern consistent with CS)
   - Positive gallium uptake (in a pattern consistent with CS)
   *and*
   c) Other causes for the cardiac manifestation(s) have been reasonably excluded

*In general, ‘probable involvement’ is considered adequate to establish a clinical diagnosis of CS.*

---

**Adult Congenital Heart Disease (Stout 2018)**

**Physiologic Stages in CHD**

<table>
<thead>
<tr>
<th>Physiological Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
</tr>
<tr>
<td>- NYHA FC I symptoms</td>
</tr>
<tr>
<td>- No hemodynamic or anatomic sequelae</td>
</tr>
<tr>
<td>- No arrhythmias</td>
</tr>
<tr>
<td>- Normal exercise capacity</td>
</tr>
<tr>
<td>- Normal renal/hepatic/pulmonary function</td>
</tr>
</tbody>
</table>

| B                   |
| - NYHA FC II symptoms|
| - Mild hemodynamic sequelae (mild aortic enlargement, mild ventricular enlargement, mild ventricular dysfunction) |
| - Mild valvular disease|
| - Trivial or small shunt (not hemodynamically significant) |
| - Arrhythmia not requiring treatment |
| - Abnormal objective cardiac limitation to exercise |
General Information on TTE
(Campbell 2014, Doherty 2017, Douglas 2011, Nishimura 2014)

Pediatric Post-Operative Patients
Congenital heart disease, which requires surgical palliation, is, by its very nature, quite varied. No written consensus criteria currently exist for monitoring post-operative patients, but rather is based upon the clinical experience and training of the pediatric cardiologists caring for the patient. Criteria for performing an echocardiogram in the outpatient setting will vary greatly based upon whether the patient has a complex lesion, which must be repaired in stages, had post-operative complications, or is on medications which will be weaned over the ensuing weeks.

TTE versus TEE
Specific situations where transesophageal echocardiography (TEE) is preferred over TTE and may be an appropriate initial study include the evaluation of a prosthetic device, suspected peri-annular complications, children with complex congenital cardiac lesions, selected patients with Staphylococcus aureus bacteremia, etc. Visualization of left atrial thrombus is far superior with TEE, which is the recommended strategy.
Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
<td>Atrial septal defect</td>
</tr>
<tr>
<td>CABG</td>
<td>Coronary artery bypass grafting surgery</td>
</tr>
<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>CMR</td>
<td>Cardiovascular magnetic resonance</td>
</tr>
<tr>
<td>CRT</td>
<td>Cardiac resynchronization therapy</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>HCM</td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>HF</td>
<td>Heart failure</td>
</tr>
<tr>
<td>ICD</td>
<td>Implantable cardioverter-defibrillator</td>
</tr>
<tr>
<td>LV</td>
<td>Left ventricular</td>
</tr>
<tr>
<td>LVEF</td>
<td>Left ventricular ejection fraction</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>PDA</td>
<td>Patent ductus arteriosus</td>
</tr>
<tr>
<td>PFO</td>
<td>Patent foramen ovale</td>
</tr>
<tr>
<td>SVT</td>
<td>Supraventricular tachycardia</td>
</tr>
<tr>
<td>TAVR</td>
<td>Transcatheter aortic valve replacement</td>
</tr>
<tr>
<td>TEE</td>
<td>Transesophageal echocardiogram</td>
</tr>
<tr>
<td>TIA</td>
<td>Transient ischemic attack</td>
</tr>
<tr>
<td>Tn</td>
<td>Troponin</td>
</tr>
<tr>
<td>TTE</td>
<td>Transthoracic echocardiogram</td>
</tr>
<tr>
<td>PVC</td>
<td>Ventricular premature contraction</td>
</tr>
<tr>
<td>VSD</td>
<td>Ventricular septal defect</td>
</tr>
<tr>
<td>VT</td>
<td>Ventricular tachycardia</td>
</tr>
</tbody>
</table>

POLICY HISTORY:

Review Date: August 14, 2019

Review Summary:

- Added indication for hypotension of suspected cardiac etiology
- Removed indication for respiratory failure or hypoxemia of uncertain etiology
- Clarified palpitations indication with “symptoms or signs of cardiovascular disease (i.e. abnormal physical exam or ECG)”
- Clarification of murmur indication with “when there is a reasonable suspicion of valvular heart disease such as high grade, holosystolic, continuous, or diastolic murmur”
- Clarified frequent PVCs as greater than 30 per hour
- Added indication for unevaluated left bundle branch block
- Added indication for exercise induced syncope
- For perioperative evaluation for solid organ transplantation, added annual study prior to transplantation
- Removed indication for re-evaluation (<1 yr) in patients with moderate or severe aortic stenosis, who will be subjected to increased hemodynamic demands (e.g. noncardiac surgery, pregnancy
- Removed tertiary syphilis or Takayasu’s Arteritis indication
- Pulmonary hypertension:
  - Clarified re-evaluation for a change in clinical status or cardiac exam, or to guide therapy (every 6 - 12 months, or more frequently to guide therapy). Annual indication removed.
Screening for scleroderma added
- Removed indications for history of rheumatic heart disease and exposure to medications that could result in valvular heart disease
- Added mild valvular regurgitation as an indication for testing every 3 years
- Added indication for annual evaluation of prosthetic heart valves older than 10 years
- In depth indications for HOCM
- LVAD and transplant indications added
- Removed chart on specific chemotherapeutic agents
- Added detailed indications for adult congenital heart disease and serial follow up
- Removed indications for presyncope for pediatric patients
- Revised murmur indication in pediatric patients with more criteria for pathologic murmur
- Added definitions of age groups for pediatric patients (infancy, childhood, and adolescence)
REFERENCES


Hiratzka LF. 2010 ACC Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease. *JACC.* 2010;55(14):e27-129. Available at:


INDICATIONS FOR TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE)

**General Criteria** (Doherty 2019, Flachskampf 2014, Hahn 2013, Lancelotti 2013, Ogbara 2011)

- TEE may be performed after a nondiagnostic TTE or a high likelihood of a nondiagnostic TTE due to patient characteristics or inadequate visualization of relevant structures

**Aortic Pathology**
- Suspected acute aortic pathology such as aortic dissection (Bhave 2018, Doherty 2019)
- Dilated aortic sinuses or ascending aorta on transthoracic echocardiogram (TTE)
- Evaluation of aortic sinuses, sinotubular junction, or ascending aorta in patients with bicuspid aortic valve when morphology cannot be assessed by TTE, and other imaging including CT or MRI have not been done

**Valvular Disease** (Doherty 2017, Nishimura 2014)
- Discordance between clinical assessment and TTE assessment of the severity of mitral regurgitation (MR)
- Evaluation of mitral stenosis, when there is a discrepancy between clinical signs or symptoms, and TTE is inadequate
- Discordance between clinical assessment and TTE assessment of the severity of aortic regurgitation (AR)
- Evaluation of native or prosthetic valves with clinical signs or symptoms suggesting valve dysfunction, when TTE is inadequate
- Re-evaluation of known prosthetic valve dysfunction when it would change management or guide therapy, and TTE is inadequate

**Infective Endocarditis** (Doherty 2017, Douglas 2011, Saric 2016)
- Suspected infective endocarditis (IE) of native valve, prosthetic valve, or endocardial lead with positive blood culture or new murmur
- Moderate to high pretest probability of IE (i.e. staph bacteremia, fungemia, prosthetic heart valve, or intracardiac device) when TTE is negative
- Re-evaluation of IE in a patient with a change in clinical status or cardiac examination (e.g. new murmur, embolism, persistent fever, heart failure (HF), abscess, or atrioventricular block)
- Re-evaluation of IE if the patient is at high risk for progression/complications or when the findings would alter therapy, when TTE is inadequate

**Cardiac Mass or Source of Emboli**
- Evaluation of cardiac mass, suspected tumor or thrombus, or potential cardiac source of emboli (Doherty 2019, Saric 2016)
- Re-evaluation of prior TEE finding for interval change (e.g. resolution of thrombus after anticoagulation) when the findings would change therapy

**Atrial Fibrillation/Flutter** (January 2019)
- Evaluation for clinical decision making regarding anticoagulation, cardioversion, and/or radiofrequency ablation
TAVR (Transcatheter Aortic Valve Replacement/Repair) (Doherty 2017, Otto 2017)
- Pre-procedural assessment of annular size and shape, number of cusps, and degree of calcification, when computed tomography (CT) cannot be performed
- Post procedural assessment of degree of aortic regurgitation (including valvular and paravalvular) with suspicion of valve dysfunction, if TTE is inadequate

Patent Foramen Ovale or Atrial Septal Defect (Doherty 2019)
- Evaluation for anatomy, potential cardiac source of emboli, and suitability for percutaneous device closure
- Evaluation post device closure with clinical concern for infection, malposition, embolization or persistent shunt

Left Atrial Appendage Occlusion (Doherty 2019)
- Evaluation for anatomy, potential cardiac source of emboli, and suitability for percutaneous occlusion device placement
- Surveillance at 45 days or FDA guidance/guidelines for follow-up to assess device stability and device leak, and exclude migration, displacement, or erosion

Percutaneous Mitral Valve Repair (Doherty 2017)
- Determination of patient eligibility for percutaneous mitral valve procedures
- Pre-procedural evaluation for percutaneous mitral valve procedures may be performed in addition to CT imaging (Wunderlich 2018)
- Exclude the presence of intracardiac mass, thrombus, or vegetation prior to (within 3 days of) the procedure

Adult Congenital Heart Disease (Stout 2018)
- Imaging with provocative maneuvers (Valsalva, cough) to assess for the presence of right-to-left cardiac shunt
- Evaluation when TTE, CMR, or CTA are not adequate in the setting of:
  - Pulmonary venous connections with ASD
  - Aortic imaging in Williams syndrome or patient suspected of having supravalvular stenosis
  - Surgical planning for Ebstein anomaly
  - Evaluation of baffle leak after atrial switch repair for d-Transposition of the Great Arteries

Ventricular Assist Devices (Doherty 2019, Stainback 2015)
- Preoperative evaluation of suitability for ventricular assist device (VAD)
- Re-evaluation for VAD-related complication or suspected infection

BACKGROUND:
Transesophageal echocardiography (TEE) enables cardiac ultrasound imaging from within the esophagus, which provides a window for enhanced quality images as well as additional views, beyond that acquired by standard transthoracic echocardiography (TTE).
Abbreviations

AR        aortic regurgitation
CMR       cardiac magnetic resonance
CT(A)     computed tomography (angiography)
IE         infective endocarditis
MR         mitral regurgitation
MRI       magnetic resonance imaging
TEE        transesophageal echocardiography
TTE        transthoracic echocardiography
VAD        ventricular assist device

POLICY HISTORY:
Review Date: July 26, 2019

Review Summary:

- For ventricular assist devices added indication for re-evaluation for VAD-related complication or suspected infection
- Aortic Pathology section rewritten as follows:
  - Suspected acute aortic pathology such as aortic dissection (Bhave 2018, Doherty 2019)
  - Dilated aortic sinuses or ascending aorta on transthoracic echocardiogram (TTE)
  - Evaluation of aortic sinuses, sinotubular junction, or ascending aorta in patients with bicuspid aortic valve when morphology cannot be assessed by TTE, and other imaging including CT or MRI have not been done
- Added infective endocarditis indication for moderate to high pretest probability of IE (i.e. staph bacteremia, fungemia, prosthetic heart valve, or intracardiac device) when TTE is negative
- For cardiac mass or source of emboli added indication for re-evaluation of prior TEE finding for interval change (e.g., resolution of thrombus after anticoagulation) when the findings would change therapy
- Added indications for Patent Foramen Ovale or Atrial Septal Defect as follows:
  - Evaluation for anatomy, potential cardiac source of emboli, and suitability for percutaneous device closure
  - Evaluation post device closure with clinical concern for infection, malposition, embolization or persistent shunt
- Added indications for Left Atrial Appendage Occlusion as follows:
  - Evaluation for anatomy, potential cardiac source of emboli, and suitability for percutaneous occlusion device placement
  - Surveillance at 45 days or FDA guidance/guidelines for follow-up to assess device stability and device leak, and exclude migration, displacement, or erosion
- Added indications for Adult Congenital Heart Disease as follows:
  - Imaging with provocative maneuvers (Valsalva, cough) to assess for the presence of right-to-left cardiac shunt
  - Evaluation when TTE, CMR, or CTA are not adequate in the setting of:
    - Pulmonary venous connections with ASD
    - Aortic imaging in Williams syndrome or patient suspected of having supravalvular stenosis
- Surgical planning for Ebstein anomaly
- Evaluation of baffle leak after atrial switch repair for d-Transposition of the Great Arteries
- Removed section on “Frequency of Echo Studies”
REFERENCES


CPT Codes: 93350, 93351, +93320, +93321, +93325, +93352

INDICATIONS for STRESS ECHO

SUSPECTED CORONARY ARTERY DISEASE (CAD)

Symptomatic patients without known CAD (use Diamond Forrester table)
- Low pretest probability, if electrocardiogram (ECG) is uninterpretable and patient can exercise
- Intermediate pretest probability, if ECG is uninterpretable (Wolk 2014)
- High pretest probability
  Repeat testing in patient with new or worse symptoms and negative result at least one year ago

Asymptomatic patients without known CAD
- Previously unevaluated ECG evidence of possible myocardial ischemia such as substantial ischemic ST segment or T wave abnormalities
- Previously unevaluated pathologic Q waves
- Unevaluated complete left bundle branch block

INCONCLUSIVE CAD EVALUATION WITH IN THE PAST 2 YEARS AND OBSTRUCTIVE CAD REMAINS A CONCERN

- Exercise stress ECG with low risk Duke treadmill score ≥5), but patient’s current symptoms indicate an intermediate or high pretest probability
- Exercise stress ECG with an intermediate Duke treadmill score
- Intermediate coronary computed tomography angiography (CCTA) (e.g. 30 - 70% lesions
- An indeterminate (equivocal, borderline, or discordant) evaluation by prior stress imaging (SE or CMR) within the past 2 years

FOLLOW-UP OF PATENTS POST CORONARY REVASCULARIZATION (PCI or CABG)
(Doherty 2019)

- Asymptomatic follow-up stress imaging (MPI or SE), at a minimum of 2 years post coronary artery bypass grafting (CABG), or percutaneous coronary intervention (PCI), whichever is later, is appropriate only for patients with a history of silent ischemia or a history of a prior left main stent
  OR
- For patients with high occupational risk (e.g. associated with public safety, airline and boat pilots, bus and train drivers, bridge and tunnel workers/toll collectors, police officers and firefighters)

- New, recurrent or worsening symptoms post coronary revascularization, is an indication for stress imaging (MPI or SE), if it will alter management

FOLLOW-UP OF KNOWN CAD

- Routine follow-up of asymptomatic or stable symptoms when last invasive or non-invasive assessment of coronary disease showed hemodynamically significant CAD (ischemia on stress test or FFR less than or equal to
0.80 or stenosis greater than or equal to 70% of a major vessel) over two years ago without intervening coronary revascularization is an appropriate indication for stress imaging (MPI or SE) in patients if it will alter management.

**SPECIAL DIAGNOSTIC CONDITIONS REQUIRING CORONARY EVALUATION**

- Prior acute coronary syndrome (as documented in MD notes), without invasive or non-invasive coronary evaluation
- Newly diagnosed systolic heart failure (EF > 50%), especially when symptoms or signs of ischemia are present or suspected, unless invasive coronary angiography is immediately planned (Fihn 2012, Patel 2013, Yancy, 2013).
- New wall motion abnormality
- Ventricular arrhythmias:
  - Sustained ventricular tachycardia (VT) > 100 bpm, ventricular fibrillation (VF), or exercise induced VT, when invasive coronary arteriography is not the initially planned test (Al-Khatib 2018)
  - Nonsustained VT, multiple episodes, each ≥ 3 beats at ≥ 100 bpm, frequent VPC’s (defined as greater than or equal to 30/hour), without known cause or associated cardiac pathology when an exercise ECG could not be performed (Zimetbaum 2018)
- Prior to Class IC antiarrhythmic drug initiation (Propafenone or Flecainide), in intermediate and high global risk patients (Reiffel 2015)
- Assessment of hemodynamic significance of known
  - Anomalous coronary arteries (Grani 2017);
  - Myocardial bridging of a coronary artery (perform with exercise stress) (Tang 2011);
  - Coronary aneurysms in Kawasaki’s disease (McCrindle 2017) or due to atherosclerosis
  - Following radiation therapy to the anterior or left chest, at 5 years post initiation and every 5 years thereafter (Lancellotti 2013)

**CHRONIC VALVULAR DISEASE**

Evaluation with Inclusion of Doppler
(Baumgartner 2017, Nishimura 2014, Steiner 2017)

- Low dose dobutamine SE for the evaluation of aortic stenosis and flow (contractile) reserve in symptomatic patients with severe aortic stenosis by calculated valve area, low flow / low gradient, and ejection fraction < 50%
- Exercise echo Doppler evaluation for mitral stenosis when there is a discrepancy between resting Doppler and clinical signs or symptoms.
- Exercise echo Doppler evaluation for mitral regurgitation (MR) if there is:
  - Discrepancy between exertional symptoms and severity of MR at rest; **OR**
  - Need to distinguish moderate from severe MR in the asymptomatic patient

**PRIOR TO ELECTIVE NONCARDIAC SURGERY**
(Fleischer 2014, Patel 2015)

- Patients who have no other indication for a non-invasive coronary evaluation, but are referred for preoperative cardiac evaluation, are eligible for SE, based upon cardiac risk ≥ 1%, if **ALL 4** criteria are met:
  - Surgery is supra-inguinal vascular, intrathoracic, or intra-abdominal; **AND**
  - The patient has **at least** one of these additional cardiac complication risk factors:
    - Ischemic Heart Disease
    - History of stroke or trans-ischemic attack (TIA)
    - History of congestive heart failure (CHF) or ejection fraction ≤ 35%
▪ Insulin-requiring diabetes mellitus
▪ Creatinine ≥ 2.0 mg/dl

AND

 o The patient has limited functional capacity (< 4 metabolic equivalents) such as one of the following: (would likely be requested as MPI)
  ▪ Cannot take care of their ADLs or ambulate
  ▪ Cannot walk 2 blocks on level ground
  ▪ Cannot climb 1 flight of stairs

AND

 o There has been no non-invasive coronary testing within one year, and the result of such a test would be likely to substantially alter therapy and/or preclude proceeding with the intended surgery

• Planning for solid organ transplantation (liver or kidney), is an indication for preoperative dobutamine SE, if there has not been a conclusive stress evaluation within the past year (Lentine, 2012):
  o In a patient with poor or unknown functional capacity (4 metabolic equivalents, as characterized under preoperative evaluation for noncardiac surgery section above) (Wolk 2013); OR
  o In a patient with ≥ 3 of the following (Lentine, 2012):
    ▪ Age > 60
    ▪ Smoking
    ▪ Hypertension
    ▪ Dyslipidemia
    ▪ Left ventricular hypertrophy
    ▪ > 1 year on dialysis (for renal transplant patients)
    ▪ Diabetes mellitus
    ▪ Prior ischemic heart disease

POST CARDIAC TRANSPANTATION

Annually, for the first five years post cardiac transplantation, in patient who otherwise should not undergo annual invasive coronary arteriography

• After the first five years post cardiac transplantation:
  o Patients with transplant coronary vasculopathy, can be screened annually if the risk of annual invasive coronary arteriography is not acceptable (e.g. high risk of contrast nephropathy) or desired.

BACKGROUND:

Stress echocardiography (SE) refers to ultrasound imaging of the heart during exercise electrocardiography (ECG) testing, during which visualized wall motion abnormalities can provide evidence of significant coronary artery disease (CAD).

While drug-induced stress with dobutamine can be an alternative to exercise stress testing in patients who are unable to exercise, this guideline does not require use of this modality Hence, reference in this document to SE almost always refers to exercise stress echocardiography.

Although SE provides comparable accuracy, without radiation risk, relative to myocardial perfusion imaging (MPI), scenarios which do not permit effective use of SE might be better suited for stress imaging with MPI, cardiovascular
magnetic resonance imaging (CMR) or positron emission tomography (PET), or coronary computed tomography angiography (CCTA)

**Stable patients without known CAD** fall into 2 categories: (Fihn 2012, Montalescot 2013, Wolk 2013)
- **Asymptomatic patients**, for whom Global Risk of CAD events can be determined from coronary risk factors using calculators available online section
- **Symptomatic patients**, for whom we estimate the Pretest Probability that their chest-related symptoms are due to clinically significant CAD (see below):

**The 3 Types of Chest Pain or Discomfort:**
- **Typical Angina (Definite)** is defined as including all 3 of these characteristics:
  - Substernal chest pain or discomfort with characteristic quality and duration
  - Provoked by exertion or emotional stress
  - Relieved by rest and/or nitroglycerine
- **Atypical Angina (Probable)** has only 2 of the above characteristics
- **Nonanginal Chest Pain/Discomfort** has only 0-1 of the above characteristics

Once the type of chest pain has been established from the medical record, the Pretest Probability of obstructive CAD is estimated from the **Diamond Forrester Table** below, recognizing that in some cases multiple additional coronary risk factors could increase pretest probability (Fihn 2012, Wolk 2013):

**Diamond Forrester Table**

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Gender</th>
<th>Typical/Definite Angina Pectoris</th>
<th>Atypical/Probable Angina Pectoris</th>
<th>Nonanginal Chest Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 39</td>
<td>Men</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td>40 – 49</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Low</td>
<td>Very low</td>
</tr>
<tr>
<td>50 – 59</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
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<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td>≥ 60</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>

- **Very low:** < 5% pretest probability of CAD, usually not requiring stress evaluation (Fihn, 2012)
- **Low:** 5 - 10% pretest probability of CAD
- **Intermediate:** 10% - 90% pretest probability of CAD
- **High:** > 90% pretest probability of CAD

**OVERVIEW**

MPI may be performed without diversion to SE in any of the following (Henzlova 2016, Wolk 2013):
- Inability to exercise
  - Physical limitations precluding ability to exercise for at least 3 full minutes of Bruce protocol
  - The patient has limited functional capacity (< 4 metabolic equivalents) **such as one** of the following:
    - Cannot take care of their activities of daily living (ADLs) or ambulate
- Cannot walk 2 blocks on level ground
- Cannot climb 1 flight of stairs
- Cannot vacuum, dust, do dishes, sweep, or carry a small grocery bag

- Other comorbidities
  - Severe chronic obstructive pulmonary disease with pulmonary function test (PFT) documentation, severe shortness of breath on minimal exertion, or requirement of home oxygen during the day
  - Poorly controlled hypertension, with systolic BP > 180 or Diastolic BP > 120 (and clinical urgency not to delay MPI)

- Risk related scenarios
  - High pretest probability in suspected CAD
  - Intermediate or high global risk in patients requiring type IC antiarrhythmic drugs (prior to initiation of therapy)
  - Arrhythmia risk with exercise

- ECG and Echo Related Uninterpretable Wall Motion
  - Prior cardiac surgery
  - Obesity with body mass index (BMI) over 40 or poor acoustic imaging window
  - Left ventricular ejection fraction ≤ 40%
  - Pacemaker or ICD
  - Atrial fibrillation
  - Resting wall motion abnormalities that would make SE interpretation difficult
  - Complete LBBB

**ECG Stress Test Alone versus Stress Testing with Imaging**

Prominent scenarios suitable for an ECG stress test WITHOUT imaging (i.e. exercise treadmill ECG test) are inferred from the guidelines presented above, often (but not always) requiring that the patient can exercise for at least 3 minutes of Bruce protocol with achievement of near maximal heart rate AND has an interpretable ECG for ischemia during exercise (Wolk 2013):

- The (symptomatic) low or intermediate pretest probability patient who is able to exercise and has an interpretable ECG
- The (asymptomatic) high global risk patient who is able to exercise and has an interpretable ECG
- The patient who is under evaluation for exercise induced arrhythmia (Al-Khatib 2017)
- The patient who requires an entrance stress test ECG for a cardiac rehab program or for an exercise prescription.

**Duke Exercise ECG Treadmill Score** calculates risk from ECG treadmill alone:

- The equation for calculating the Duke treadmill score (DTS) is: \[ \text{DTS} = \text{exercise time in minutes} - (5 \times \text{ST deviation in mm or 0.1 mV increments}) - (4 \times \text{exercise angina score}), \] with angina score being 0 = none, 1 = non-limiting, and 2 = exercise-limiting.
- The score typically ranges from -25 to +15. These values correspond to low-risk (with a score of ≥ +5), intermediate risk (with scores ranging from -10 to +4), and high-risk (with a score of ≤ -11) categories.

An uninterpretable baseline ECG includes (Fihn 2012):

- ST segment depression 1 mm or more; (Not for non-specific ST- T wave changes)
- Ischemic looking T wave -- at least 2.5 mm inversions (excluding V1 and V2)
- LVH, pre excitation pattern such as WPW, a ventricular paced rhythm, or left bundle branch block
- Digitalis use with associated ST segment
- Resting HR under 50 bpm on a medication that is required for patient’s treatment and cannot be stopped with an anticipated suboptimal workload.
Global Risk of Cardiovascular Disease

Global risk of CAD is defined as the probability of manifesting cardiovascular disease over the next 10 years and refers to asymptomatic patients without known cardiovascular disease. It should be determined using one of the risk calculators below. A high risk is considered greater than a 20% risk of a cardiovascular event over the ensuing 10 years. High global risk by itself generally lacks scientific support as an indication for stress imaging. (There are rare exemptions, such as patients requiring an I-C antiarrhythmic drug, who might require coronary risk stratification prior to initiation of the drug, when global risk is moderate or high.

- **CAD Risk—Low**
  10-year absolute coronary or cardiovascular risk less than 10%.

- **CAD Risk—Moderate**
  10-year absolute coronary or cardiovascular risk between 10% and 20%.

- **CAD Risk—High**
  10-year absolute coronary or cardiovascular risk of greater than 20%.

**Websites for Global Cardiovascular Risk Calculators***

*Patients who have already manifested cardiovascular disease are already at high global risk and are not applicable to the calculators (D’Agostino 2008, Goff 2014, McClelland 2015, Ridker 2007).

<table>
<thead>
<tr>
<th>Risk Calculator</th>
<th>Link to Online Calculator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds Risk Score</td>
<td><a href="http://www.reynoldsriskscore.org/">http://www.reynoldsriskscore.org/</a></td>
</tr>
<tr>
<td>Can use if no diabetes</td>
<td></td>
</tr>
<tr>
<td>Unique for use of family history</td>
<td></td>
</tr>
<tr>
<td>Pooled Cohort Equation</td>
<td><a href="http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx?example">http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx?example</a></td>
</tr>
<tr>
<td>MESA Risk Calculator</td>
<td><a href="https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx">https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx</a></td>
</tr>
<tr>
<td>With addition of Coronary Artery</td>
<td></td>
</tr>
<tr>
<td>Calcium Score, for CAD-only risk</td>
<td></td>
</tr>
</tbody>
</table>

**Definitions of Coronary Artery Disease**


- Percentage stenosis refers to the reduction in diameter stenosis when angiography is the method and refers to cross sectional narrowing when IVUS (intravascular ultrasound) is the method of determination.
- Coronary artery calcification is a marker of risk, as measured by Agatston score on coronary artery calcium imaging. It is not a diagnostic tool so much as it is a risk stratification tool. Its incorporation into Global Risk can be achieved by using the MESA risk calculator.
- Ischemia-producing disease (also called hemodynamically or functionally significant disease, for which revascularization might be appropriate) generally implies at least one of the following:
  - Suggested by percentage diameter stenosis ≥ 70% by angiography; borderline lesions are 40 - 70% (Fihn 2012, Tobis 2007)
  - For a left main artery, suggested by a percentage stenosis ≥ 50% or minimum lumen cross sectional area on IVUS ≤ 6 square mm (Fihn 2012, Mintz 2016)
- FFR (fractional flow reserve) ≤ 0.80 for a major vessel (Mintz 2016)
- iFR (instantaneous wave-free ratio) ≤ 0.89 for a major vessel (Davies 2017, Gotberg 2017)

- A major vessel is a coronary vessel that would typically be substantial enough for revascularization, if indicated. A major vessel is a coronary vessel that would typically be substantial enough for revascularization, if indicated. This assessment is made based on the diameter of the vessel and/or the extent of myocardial territory served by the vessel.
- FFR (fractional flow reserve) is the distal to proximal pressure ratio across a coronary lesion during maximal hyperemia induced by either intravenous or intracoronary adenosine. Less than or equal to 0.80 is considered a significant reduction in coronary flow.
- iFR (instantaneous wave-free ratio) ≤ 0.89 for a major vessel (Davies 2017, Gotberg 2017)
- New technology is evolving that estimates FFR from CCTA images. This is covered under the separate NIA Guideline for FFR-CT.

**Anginal Equivalent**
(Fihn 2012, Moya 2009, Shen 2017)

Development of an anginal equivalent (e.g. shortness of breath, fatigue, or weakness) either with or without prior coronary revascularization should be based upon the documentation of reasons to suspect that symptoms other than chest discomfort are not due to other organ systems (e.g. dyspnea due to lung disease, fatigue due to anemia. This may include respiratory rate, oximetry, lung exam, etc. (as well as d-dimer, chest CT(A), and/or PFTs, when appropriate), and then incorporated into the evaluation of coronary artery disease as would chest discomfort. Syncope per se is not an anginal equivalent.

**Abbreviations**

- AAD: Antiarrhythmic drug
- ADLs: Activities of daily living
- BSA: Body surface area in square meters
- CAD: Coronary artery disease
- ECG: Electrocardiogram
- FFR: Fractional flow reserve
- LBBB: Left bundle-branch block
- LVEF: Left ventricular ejection fraction
- LVH: Left ventricular hypertrophy
- MI: Myocardial infarction
- MET: Estimated metabolic equivalent of exercise
- MPI: Myocardial perfusion imaging
- PFT: Pulmonary function test
- PVCs: Premature ventricular contractions
- SE: Stress echocardiography
- VT: Ventricular tachycardia
- VF: Ventricular fibrillation
- WPW: Wolf Parkinson White
POLICY HISTORY:
Review Date: July 23, 2019
Review Summary:
- Stress echo for suspected CAD deleted the following indication: Repeat testing in patient with recurrent symptomatic presentation and negative result over 2 years ago
- Added indications: ‘For assessment of hemodynamic significance due to atherosclerosis or following radiation therapy to the anterior or left chest, at 5 years post initiation inception of radiation and every 5 years thereafter’; and ‘Following radiation therapy to the anterior or left chest, at 5 years post initiation inception of radiation and every 5 years thereafter’
- Removed secondary mitral regurgitation indication under doppler evaluation section
- Clarified indication as follows: Routine follow-up of asymptomatic or stable symptoms when last invasive or non-invasive assessment of coronary disease showed hemodynamically significant CAD (ischemia on stress test or FFR less than or equal to 0.80 or stenosis greater than or equal to 70% of a major vessel) over two years ago without intervening coronary revascularization is an appropriate indication for stress imaging (MPI or SE) in patients if it will alter management
REFERENCES


Einstein, A. Effects of radiation exposure from cardiac imaging: how good are the data? *Journal of the American College of Cardiology.* 2012; 59(6): 553-565. Available at: http://content.onlinejacc.org/cgi/content/short/59/6/553


Lentine KL, Costa SP, Weir MR. Cardiac disease evaluation and management among kidney and liver transplantation candidates. JACC. 2012; 60(5); 434-480.

Marwick, TH. Stress echocardiography. Heart. 2003; 89(1): 113-118. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1767520/


INDICATIONS FOR INVASIVE CORONARY ARTERIOGRAPHY

Stable Ischemic Heart Disease

- Exercise electrocardiogram (ECG) stress test with high-risk findings such as Duke Score ≤ - 11, ST segment elevation, hypotension, exercise induced ventricular tachycardia (VT), or several minutes of ST segment depression post exercise (Patel 2012).
- Stress imaging with high risk findings (see Overview section)
- Stress imaging with intermediate risk findings (see Overview section) in a patient with one of the following:
  - Symptoms consistent with ischemia (Patel 2012)
  - Unsatisfactory quality of life due to angina (Fihn 2012)
  - Ejection fraction (EF) < 50% (Fihn 2012)
- Non-invasive test with low risk findings with new, worsening, or limiting symptoms with reasonable suspicion of cardiac origin despite optimal medical therapy (OMT) or inability to tolerate OMT (Fihn 2012, Fihn 2014, Patel 2012)
- New, worsening, or limiting symptoms, with known unvascularized obstructive coronary artery disease (CAD), in a patient eligible for revascularization (Fihn 2012, Fihn 2014)
- Discordant, equivocal, or inconclusive non-invasive evaluation in patients with suspected symptomatic stable ischemic heart disease, including the following (Montalescot 2013, Patel 2012, Wolk 2013):
  - Low risk stress imaging with high risk stress ECG response or stress induced typical angina (Patel 2012)
  - Equivocal, uninterpretable, or inconclusive stress imaging due to issues of attenuation or other problems with interpretability (Fihn 2012, Patel 2012)

CCTA Abnormalities

- Symptomatic patient with one of the following (Fihn 2012; Patel 2012; Patel 2017):
  - One vessel CAD with ≥ 70% stenosis
  - Two or three vessel CAD with moderate stenosis (50% to 69% stenosis)
  - A stenosis ≥ 30% with FFR-CT ≤ 0.8 (Douglas 2016)
  - Any patient with evidence of ≥ 50% left main stenosis

Heart Failure with Left Ventricular Dysfunction

- New heart failure, cardiomyopathy, or wall motion abnormality in patients who are candidates for coronary revascularization; including one of the following (Fihn 2012, Patel 2012, Patel 2013, Wolk 2013, Yancy 2013):
  - Newly recognized reduction in EF to ≤ 50%, with intermediate risk findings on noninvasive testing and symptoms or signs of ischemia
  - Newly recognized reduction in EF to ≤ 40% with evidence of viability on stress imaging
  - Symptomatic from HF or ischemia with new, unexplained wall motion abnormality (Fihn 2012, Patel 2012)
- Structural abnormality (severe mitral regurgitation or ventricular septal defect) with reason to suspect ischemic origin
- Deterioration in clinical status of heart failure or cardiomyopathy requiring invasive evaluation for guidance or alteration in therapy
- Clarification of the diagnosis of myocarditis versus acute coronary syndrome (Sarda 2010)

**Ventricular Arrhythmias**

- Ventricular Arrhythmias, without identified non-cardiac cause:
  - Following recovery from unexplained sudden cardiac arrest (Al-Khatib 2017)
  - Sustained VT or VF (Patel 2012)
  - Exercise-induced non-sustained VT in a patient with signs or symptoms of ischemia (Patel 2012)

**Prior to Non-Coronary Intervention and Cardiac Surgery**

- Evaluation of coronary anatomy, with consideration of coronary revascularization, prior to cardiac surgery in patients with any of the following (Doherty 2017, Nishimura 2014, Ramee 2016, Svensson 2013):
  - Symptoms of angina
  - Stress imaging with evidence of ischemia
  - Decreased LV systolic function (EF < 50%)
  - History of CAD
  - Coronary risk factors, including men > 40 and postmenopausal women
  - Non-invasive data that is inconclusive
  - Chronic severe secondary mitral regurgitation
  - Requirement for detailed assessment of coronary artery anatomy prior to aortic valve homograft surgery, pulmonary autograft (Ross procedure), or aortic root procedure
  - Patients undergoing transcatheter aortic valve replacement (TAVR) (Nishimura 2017)

**Post Cardiac Transplantation** (Costanzo 2010)

- Assessment for allograft vasculopathy annually for the first 5 years, followed by annual assessment in those with documented allograft vasculopathy, if stress imaging has not been performed
- Assessment of change in clinical status, including any of the following, if stress imaging has not been performed:
  - New left ventricular dysfunction
  - Symptoms of ischemia
  - Non-invasive findings of ischemia

**Hemodynamic Assessment**

- Indications for angiographic and/or hemodynamic assessment of valvular function or shunt physiology (Doherty 2017, Patel 2012, Stout 2018)
  - Assessment of bioprosthetic valve when transthoracic echocardiography (TTE) and transesophageal electrocardiography (TEE) were inadequate, and cardiac magnetic resonance (CMR) or cardiac computed tomography (CCT) are not available
  - Assessment of mechanical valve prostheses when TTE and TEE are inadequate and CCT is not available
  - Discordance between non-invasive data and clinical impression of severity of valvular disease
  - Evaluation of indeterminate shunt anatomy or shunt flows/ratio
• Indications for Hemodynamic Assessment only (Patel 2012, Stout 2018)
  o Assessment of constrictive and restrictive physiology
  o Assessment of pulmonary hypertension when non-invasive data provides inadequate information for management, or to evaluate response to intravenous drug therapy
  o Assessment of hemodynamics in heart failure, cardiomyopathy, or adult congenital heart disease, when
    ▪ Non-invasive data is discordant or conflicts with the clinical presentation
    ▪ Non-invasive data is inadequate for clinical management

**These guidelines only cover procedures that include left heart catheterization. NIA does not manage right heart catheterization as a stand-alone procedure.**

**BACKGROUND:**
Heart catheterization is an invasive angiographic procedure used to evaluate the presence and extent of coronary artery disease (CAD).

In addition to angiography, it can also include ventriculography, aortography, acquisition of hemodynamic data, measurement of cardiac output, detection and quantification of shunts and flows, intravascular ultrasound (IVUS), and fractional flow reserve (FFR)/instantaneous wave free ratio (iFR) for determination of a lesion’s hemodynamic severity. CAD stenosis ≥ 70% (≥ 50% in the left main coronary artery) is considered clinically significant or obstructive CAD (Fihn 2012, Montalescot 2013, Wolk 2013).

This guideline applies to patients with a stable clinical presentation, not to those with acute coronary syndromes or acute valvular abnormalities.

In stable patients, prior to a recommendation for cardiac catheterization, preliminary evaluation with non-invasive cardiac testing is usually indicated.

**Stable Patients without Known CAD** fall into 2 categories (Fihn 2012, Montalescot 2013, Wolk 2013):

• **Asymptomatic**, for whom global risk of CAD events can be determined from coronary risk factors, using calculators available online (see Websites for Global Cardiovascular Risk Calculators section).
• **Symptomatic**, for whom the pretest probability that their chest-related symptoms are due to clinically significant CAD is estimated.

**The Three Types of Chest Pain or Discomfort and Pretest Probability of CAD**

• **Typical Angina (Definite)** is defined as including all 3 characteristics:
  o Substernal chest pain or discomfort with characteristic quality and duration
  o Provoked by exertion or emotional stress
  o Relieved by rest and/or nitroglycerine

• **Atypical Angina (Probable)** has only 2 of the above characteristics

• **Non-anginal Chest Pain/Discomfort** has only 0 - 1 of the above characteristics
Once the type of chest pain has been established from the medical record, the pretest probability of obstructive CAD is estimated from the **Diamond Forrester Table** below, recognizing that in some cases multiple additional coronary risk factors could increase pretest probability (Wolk 2013, Fihn 2012).

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Gender</th>
<th>Typical/Definite Angina Pectoris</th>
<th>Atypical/Probable Angina Pectoris</th>
<th>Non-anginal Chest Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 39</td>
<td>Men</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Very low</td>
<td>Very low</td>
</tr>
<tr>
<td>40 – 49</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Low</td>
<td>Very low</td>
</tr>
<tr>
<td>50 – 59</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>Low</td>
</tr>
<tr>
<td>≥ 60</td>
<td>Men</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>High</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>

- **Low**: 5 - 10% pretest probability of CAD
- **Intermediate**: 10% - 90% pretest probability of CAD
- **High**: > 90% pretest probability of CAD

**Coronary Risk Categories Derived from Non-invasive Testing**  
(Fihn 2012; Patel 2017)

**High risk (> 3% annual death or MI)**
- Severe resting left ventricular (LV) dysfunction (LVEF < 35%) not readily explained by non-coronary causes
- Resting perfusion abnormalities ≥ 10% of the myocardium in patients without prior history or evidence of myocardial infarction (MI)
- Stress ECG findings including ≥ 2 mm of ST-segment depression at low workload or persisting into recovery, exercise-induced ST-segment elevation, or exercise-induced ventricular tachycardia (VT)/ventricular fibrillation (VF)
- Severe stress-induced left ventricular (LV) dysfunction (peak exercise EF < 45% or drop in EF with stress ≥ 10%)
- Stress-induced perfusion abnormalities involving ≥ 10% myocardium or stress segmental scores indicating multiple abnormal vascular territories
- Stress-induced LV dilation. Transient ischemic dilation (TID) is the ratio of left ventricular area immediately post-exercise divided by the area of the 4-hour redistribution image, with an abnormal ratio defined as > 1.12 (Weiss 1987)
- Inducible wall motion abnormality (involving > 2 segments or 2 vascular territories)
- Wall motion abnormality developing at low dose of dobutamine (≤ 10 mg/kg/min) or at a low heart rate (< 120 beats/min)
- Multivessel obstructive CAD (≥ 70% stenosis) or left main stenosis (≥ 50% stenosis) on CCTA

**Intermediate risk (1% to 3% annual death or MI)**
- Mild or moderate resting LV dysfunction (EF 35% to 49%) not readily explained by non-coronary causes
- Resting perfusion abnormalities in 5% to 9.9% of the myocardium in patients without a history or prior evidence of MI
• ≥1 mm of ST-segment depression occurring with exertional symptoms
• Stress-induced perfusion abnormalities involving 5% to 9.9% of the myocardium or stress segmental scores (in multiple segments) indicating 1 vascular territory with abnormalities but without LV dilation
• Small wall motion abnormality involving 1 to 2 segments and only 1 vascular territory
• CAC score 100 to 399 Agatston units (only for use in primary prevention, not for heart catheterization decision making) (Fihn 2012, Goff 2014, Montalescot 2013, Patel 2012)
• One vessel CAD with ≥ 70% stenosis or moderate CAD stenosis (50% to 69% stenosis) in ≥ 2 arteries on CCTA

Low risk (< 1% annual death or MI)
• Low-risk treadmill score (score ≥ 5) or no new ST segment changes or exercise-induced chest pain symptoms; when achieving maximal levels of exercise
• Normal or small myocardial perfusion defect at rest or with stress involving < 5% of the myocardium
• Normal stress or no change of baseline wall motion abnormalities during stress
• CAC score < 100 Agatston units (only for use in primary prevention, not for heart catheterization decision making) (Fihn 2012, Goff 2014, Montalescot 2013, Patel 2012)
• No coronary stenosis > 50% on CCTA

Global Risk of Cardiovascular Disease

Global risk of CAD is defined as the probability of manifesting cardiovascular disease over the next 10 years and refers to asymptomatic patients without known cardiovascular disease. It should be determined using one of the risk calculators below. A high risk is considered greater than a 20% risk of a cardiovascular event over the ensuing 10 years. High global risk by itself generally lacks scientific support as an indication for stress imaging (Douglas 2018). There are rare exemptions, such as patients requiring I-C antiarrhythmic drugs, who might require coronary risk stratification prior to initiation of the drug, when global risk is moderate or high.

• CAD Risk—Low
  10-year absolute coronary or cardiovascular risk less than 10%
• CAD Risk—Moderate
  10-year absolute coronary or cardiovascular risk between 10% and 20%
• CAD Risk—High
  10-year absolute coronary or cardiovascular risk of greater than 20%

Websites for Global Cardiovascular Risk Calculators*
*Patients who have already manifested cardiovascular disease are already at high global risk and are not applicable to the calculators.

<table>
<thead>
<tr>
<th>Risk Calculator</th>
<th>Websites for Online Calculator</th>
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<tbody>
<tr>
<td>Reynolds Risk Score</td>
<td><a href="http://www.reynoldsriskscore.org/">http://www.reynoldsriskscore.org/</a></td>
</tr>
<tr>
<td>Can use if no diabetes Unique for use of family history</td>
<td></td>
</tr>
<tr>
<td>Pooled Cohort Equation</td>
<td><a href="http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx?example">http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx?example</a></td>
</tr>
</tbody>
</table>
MESA Risk Calculator
With addition of Coronary Artery Calcium Score, for CAD-only risk

https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx

Definitions of Coronary Artery Disease
(Fihn 2012, Mintz 2016, Montalescot 2013, Patel 2017)

- Percentage stenosis refers to the reduction in diameter stenosis when angiography is the method and can be estimated or measured using angiography or more accurately measured with intravascular ultrasound (IVUS).
- Coronary artery calcification is a marker of risk, as measured by Agatston score on coronary artery calcium imaging. It is not a diagnostic tool so much as it is a risk stratification tool. Its incorporation into global risk can be achieved by using the MESA risk calculator.
- Ischemia-producing disease (also called hemodynamically or functionally significant disease, for which revascularization might be appropriate) generally implies at least one of the following:
  - Suggested by percentage diameter stenosis ≥ 70% by angiography; borderline lesions are 40 - 70% (Fihn 2012)
  - For a left main artery, suggested by a percentage stenosis ≥ 50% or minimum luminal cross sectional area on IVUS ≤ 6 square mm (Fihn 2012, Mintz 2016)
  - FFR (fractional flow reserve) ≤ 0.80 for a major vessel (Mintz 2016)
  - iFR (instantaneous wave-free ratio) ≤ 0.89 for a major vessel (Davies 2017, Gotberg 2017)
- A major vessel would be a coronary vessel that would be amenable to revascularization, if indicated. This assessment is made based on the diameter of the vessel and/or the extent of myocardial territory served by the vessel.
- FFR is the distal to proximal pressure ratio across a coronary lesion during maximal hyperemia induced by either intravenous or intracoronary adenosine. Less than or equal to 0.80 is considered a significant reduction in coronary flow.
- Instantaneous wave-free ratio (iFR) measures the ratio of distal coronary to aortic pressure during the wave free period of diastole, with a value ≤ 0.89 considered hemodynamically significant. (Gotberg 2017, Davies 2017)

Anginal Equivalent
(Fihn 2012, Moya 2009, Shen 2017)

Development of an anginal equivalent (e.g. shortness of breath, fatigue, or weakness) either with or without prior coronary revascularization should be based upon the documentation of reasons that symptoms other than chest discomfort are not due to other organ systems (e.g. dyspnea due to lung disease, fatigue due to anemia), by presentation of clinical data such as respiratory rate, oximetry, lung exam, etc. (as well as d-dimer, chest CT(A), and/or PFTs, when appropriate), and then incorporated into the evaluation of coronary artery disease as would chest discomfort. Syncope per se is not an anginal equivalent.

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>CAC</td>
<td>Coronary artery calcium</td>
</tr>
<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>CCT</td>
<td>Cardiac computed tomography</td>
</tr>
<tr>
<td>CCTA</td>
<td>Coronary computed tomographic angiography</td>
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</tbody>
</table>
POLICY HISTORY:
Review Date: August 14, 2019
Review Summary:
- Added indications for new heart failure/cardiac myopathy/wall motion abnormality, in patients who are candidates and would be eligible for coronary revascularization including one of the following:
  - Newly recognized reduction in ejection fraction to ≤ 50%, with intermediate risk findings on noninvasive testing and symptoms or signs of ischemia
  - Newly recognized reduction in ejection fraction to ≤ 40% with evidence of viability on stress imaging
- Removed indication for diastolic heart failure, when symptoms, signs or stress imaging provides evidence of contributory ischemia
- Clarified indication for evaluation of coronary anatomy prior to TAVR
- Clarified indication for assessment of allograft vasculopathy if stress imaging has not been performed
- Clarified indications for assessment of hemodynamics in heart failure, cardiomyopathy or adult congenital heart disease.
REFERENCES:


