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 unrevascularized 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:
  o New left ventricular dysfunction
  o Symptoms of ischemia
  o 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)
  o 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
  o Assessment of mechanical valve prostheses when TTE and TEE are inadequate and CCT is not available
  o Discordance between non-invasive data and clinical impression of severity of valvular disease
  o 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:
  - 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
- **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. (D’Agostino 2008, Goff 2014, McClelland 2015, Ridker 2007)*

<table>
<thead>
<tr>
<th>Risk Calculator</th>
<th>Websites for 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 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>
</tbody>
</table>
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

CAC  Coronary artery calcium
CAD  Coronary artery disease
CCT  Cardiac computed tomography
CCTA  Coronary computed tomographic angiography
CMR  Cardiac magnetic resonance
LV  Left ventricular
LVEF  Left ventricular ejection fraction
MI  Myocardial infarction
MR  Mitral regurgitation
TAVR  Transcatheter aortic valve replacement
TTE  Transthoracic echocardiography
TEE  Transesophageal echocardiography
VT  Ventricular tachycardia
VF  Ventricular fibrillation

POLICY HISTORY:
Review Date: August 14, 2019
Review Summary:
- Added indications for new heart failure/ cardiomyopathy/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:


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