

National Imaging Associates, Inc.	
Clinical guidelines HEART (Cardiac) PET with CT for Attenuation	Original Date: July 1999
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Guideline Number: NIA_CG_079	Implementation Date: January 2024 3

GENERAL INFORMATION

- It is an expectation that all patients receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.*
- Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines and state/national recommendations.*

GENERAL INFORMATION

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This guideline is for stress imaging, specifically Heart (Cardiac) PET imaging, with appropriate preference for suitable alternatives, such as stress echocardiography (SE) or myocardial perfusion imaging (MPI), when more suitable, unless otherwise stated (refer to [Background section](#)).

INDICATIONS FOR HEART PET WITH CT FOR ATTENUATION¹⁻⁴

SUSPECTED CAD (When neither SE nor MPI have provided or are expected to provide optimal imaging)

- Symptomatic patients without known CAD (use [Diamond Forrester Table](#))

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- Low or intermediate pretest probability and unable to exercise (SE diversion not required)
- High pretest probability (SE diversion not required)
- Repeat testing in a patient with new or worsening symptoms and negative result at least one year ago **AND** meets one of the criteria above
- **Asymptomatic patients without known CAD (SE diversion not required)**
 - Previously unevaluated ECG evidence of possible myocardial ischemia including substantial ischemic ST segment or T wave abnormalities (~~see section in Overview~~)(see section in Overview)
 - Previously unevaluated pathologic Q waves (~~see section in Overview~~)(see section in Overview)
 - Unevaluated complete left bundle branch block

ABNORMAL CALCIUM SCORES (CAC)⁴⁻⁸ (When neither SE nor MPI have provided, or are expected to provide, optimal imaging)

- ASYMPTOMATIC patient with a calcium score >400, not previously evaluated
- SYMPTOMATIC patient with prior CAC ≥100

INCONCLUSIVE CAD EVALUATION ~~WITHIN THE PAST 2 YEARS~~ AND OBSTRUCTIVE CAD REMAINS A CONCERN (When neither SE nor MPI have provided, or are expected to provide, optimal imaging)

- Exercise stress ECG with low-risk Duke treadmill score (≥5), (~~see section in Overview~~)(see section in Overview) but patient's current symptoms indicate an intermediate or high pretest probability (SE diversion not required for high pretest probability)
- Exercise stress ECG with an intermediate Duke treadmill score (SE diversion not required for symptoms consistent with high pretest probability)
- Inconclusive/borderline coronary computed tomography angiography (CCTA) (e.g., 40 - 70% lesions)
- Non-diagnostic exercise stress test with physical inability to achieve target heart rate (THR) (SE diversion not required)
- An intermediate evaluation by prior stress imaging (~~within the past 2 years~~) (SE diversion not required)
- Coronary stenosis of unclear significance on previous coronary angiography⁴

FOLLOW-UP OF PATIENT'S POST CORONARY REVASCULARIZATION (PCI or CABG) (When neither SE nor MPI have provided, or are expected to provide, optimal imaging)⁴

- **Asymptomatic, follow-up stress imaging** 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, if it will alter management (SE diversion not required for typical anginal symptoms or symptoms documented to be similar to those prior to revascularization)

FOLLOW-UP OF KNOWN CAD (When neither SE nor MPI have provided or are expected to provide optimal imaging)

- **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 $\text{FFR} \leq 0.80$ or significant stenosis- in a major vessel ($\geq 50\%$ left main coronary artery or $\geq 70\%$ LAD, LCX, RCA) 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 in patients if it will alter management
- ~~Ischemia-guided approach for the evaluation of non-culprit (and possibly hemodynamically significant) CAD noted at the time of recent myocardial infarction~~

SPECIAL DIAGNOSTIC CONDITIONS REQUIRING CORONARY EVALUATION (When neither SE nor MPI have provided, or are expected to provide, optimal imaging)

- Prior acute coronary syndrome (as documented in MD notes), without subsequent invasive or non-invasive coronary evaluation
- Newly diagnosed systolic heart failure or diastolic heart failure, *with reasonable suspicion of cardiac ischemia (prior events, risk factors)*, unless invasive coronary angiography is immediately planned^{2, 9, 10}
- Reduced LVEF $\leq 50\%$ requiring myocardial viability assessment to assist with decisions regarding coronary revascularization. (Diversion from PET not required when LVEF less than or equal to 40%)⁹⁻¹¹
- Ventricular arrhythmias
 - Sustained ventricular tachycardia (VT) > 100 bpm, ventricular fibrillation (VF), or exercise-induced VT, when invasive coronary arteriography is not the immediately planned test¹²
 - Nonsustained VT, multiple episodes, each ≥ 3 beats at ≥ 100 bpm, frequent PVC's (defined as greater than or equal to 30/hour on remote monitoring) without

known cause or associated cardiac pathology, when an exercise ECG cannot be performed

- Prior to Class IC antiarrhythmic drug initiation (Propafenone or ~~Flecainide~~Flecainide), as well as annually in intermediate and high global risk patients (SE diversion not required)¹³
- Assessment of hemodynamic significance of one of the following documented conditions¹⁴:
 - Anomalous coronary arteries¹⁵
 - Muscle bridging of coronary artery^{4, 16}
- Coronary aneurysms in Kawasaki's disease¹⁷ or due to atherosclerosis
- Following radiation therapy to the anterior or left chest, at 5 years post initiation and every 5 years thereafter¹⁸
- To diagnose microvascular dysfunction in patients with persistent stable anginal chest pain with suspected ischemia and nonobstructive coronary artery disease (INOCA), as documented in provider notes (no MPI diversion required).¹⁹
- **Cardiac Sarcoidosis²⁰⁻²²** (may be approved as a combination study with MPI for the evaluation and treatment of sarcoidosis)²³
 - Evaluation and therapy monitoring in patients with sarcoidosis, after documentation of suspected cardiac involvement by echo or ECG, when CMR has not been performed
 - Evaluation of suspected cardiac sarcoid, after CMR has shown equivocal or negative findings in the setting of a high clinical suspicion²²
 - Evaluation of CMR findings showing highly probable cardiac sarcoidosis, when PET could serve to identify inflammation and the consequent potential role for immunosuppressive therapy²²
 - Initial and follow-up PET in monitoring therapy for cardiac sarcoid with immunosuppressive therapy, typically about 4 times over 2 years
- **Infective Endocarditis**
 - In suspected infective endocarditis with moderate to high probability (i.e., staph bacteremia, fungemia, prosthetic heart valve, or intracardiac device), when TTE and TEE have been inconclusive with respect to diagnosis of infective endocarditis or characterization of paravalvular invasive complications²⁴⁻²⁶
- **Aortitis**
 - For diagnosis and surveillance of Aortitis, PET/CT or PET/MRI* hybrid imaging²⁷
*NOTE: If PET/MR study is requested, there is no specific CPT Code for this imaging study and a Health Plan review will be required.

PRIOR TO ELECTIVE NON-CARDIAC SURGERY (When neither SE nor MPI have provided or are expected to provide optimal imaging)

- An intermediate or high risk surgery with of one or more risk factors (see below), AND documentation of an inability to walk (or <4 METs) AND there has not been an imaging stress test within 1 year^{28-30*}
 - **Risk factors:** history of ischemic heart disease, history of congestive heart failure, history of cerebrovascular disease, preoperative treatment with insulin, and preoperative serum creatinine >2.0 mg/dL.
 - **Surgical Risk:**
 - **High risk surgery:** Aortic and other major vascular surgery, peripheral vascular surgery, anticipated prolonged surgical procedures associated with large fluid shifts and/or blood loss
 - **Intermediate risk surgery:** Carotid endarterectomy, head and neck surgery, intraperitoneal and intrathoracic surgery, orthopedic surgery, prostate surgery
 - **Low risk surgery:** Endoscopic procedures, superficial procedure, cataract surgery, breast surgery
- Planning for any organ or stem cell transplantation is an indication for preoperative stress imaging, if there has not been a conclusive stress evaluation, CTA, or heart catheterization within the past year, at the discretion of the transplant service³¹

POST CARDIAC TRANSPLANT (SE diversion not required)³²

- Annually, for the first five years post cardiac transplantation, in a patient not undergoing invasive coronary arteriography
- After the first five years post cardiac transplantation, patients with documented transplant coronary vasculopathy can be screened annually if invasive coronary arteriography is not planned

~~Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines, and state/national recommendations.~~

BACKGROUND^{33, 34}

Cardiac PET scanning, when used in conjunction with CT attenuation, includes evaluation of perfusion, function, viability, inflammation, anatomy, and risk stratification for cardiac-related events such as myocardial infarction and death. Maximum diagnostic accuracy of cardiac PET/CT is achieved when images are interpreted in conjunction with other relevant imaging, clinical information, and laboratory data.

PET Scan

- Indicated when all the criteria for MPI are met **AND** there is likely to be equivocal imaging results because of BMI, ~~or~~ large breasts or implants, mastectomy, chest wall deformity, pleural or pericardial effusion or prior thoracic surgery or results of a prior MPI
- Can identify regions of myocardial viability with hibernating myocardium (viable, with poor flow and contractility) by imaging with fluorine-18 (F-18) fluorodeoxyglucose (FDG or 18-FDG) for this purpose
- Useful in the evaluation of inflammation: e.g., evaluation and therapy monitoring in patients with sarcoidosis, after documentation of cardiac involvement by echo or electrocardiography (ECG), in place of, or subsequent to CMR if needed to help with an uncertain diagnosis

Coronary application of PET includes evaluation of **stable patients without known CAD**, who fall into two categories²⁻⁴

- **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 we estimate the pretest probability that their chest-related symptoms are due to clinically significant ($\geq 50\%$) CAD (below):

The 3 Types of Chest Pain or Discomfort

- **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
- **Nonanginal Chest Pain/Discomfort** has only **0 - 1** of the above characteristics

The medical record should provide enough detail to establish the type of chest pain. From those details, 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^{2, 4}:

Diamond Forrester Table

Age (Years)	Gender	Typical/Definite Angina Pectoris	Atypical/Probable Angina Pectoris	Nonanginal Chest Pain
≤ 39	Men	Intermediate	Intermediate	Low
	Women	Intermediate	Very low	Very low
40 – 49	Men	High	Intermediate	Intermediate
	Women	Intermediate	Low	Very low
50 – 59	Men	High	Intermediate	Intermediate
	Women	Intermediate	Intermediate	Low
≥ 60	Men	High	Intermediate	Intermediate
	Women	High	Intermediate	Intermediate

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

OVERVIEW

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) require 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 exercise⁴:

- The (symptomatic) low or intermediate pretest probability patient who can exercise and has an interpretable ECG⁴
- The patient who is under evaluation for exercise-induced arrhythmia
- The patient who requires an entrance stress test ECG for a cardiac rehab program or for an exercise prescription
- For the evaluation of syncope or presyncope during exertion³⁵

Duke Exercise ECG Treadmill Score

Calculates risk from ECG treadmill alone³⁶:

- The equation for calculating the Duke treadmill score (DTS) is: DTS = exercise time in minutes - (5 x ST deviation in mm or 0.1 mV increments) - (4 x 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 includes²:

- ST segment depression 1 mm or more (not for non-specific ST- T wave changes)
- Ischemic looking T waves; at least 2.5 mm inversions (excluding V1 and V2)
- LVH with repolarization abnormalities, pre-excitation pattern such as WPW, ventricular paced rhythm, or left bundle branch block
- Digitalis use with associated ST segment abnormalities
-

Previously unevaluated pathologic Q waves (in two contiguous leads) defined as the following:

- > 40 ms (1 mm) wide
- > 2 mm deep
- > 25% of depth of QRS complex
-

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 I-C antiarrhythmic drugs who might require coronary risk stratification prior to initiation of the drug.

- **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.³⁷⁻⁴⁰~~

Risk Calculator	Websites for Online Calculator
Framingham Cardiovascular Risk	https://reference.medscape.com/calculator/framingham-cardiovascular-disease-risk
Reynolds Risk Score Can use if no diabetes Unique for use of family history	http://www.reynoldsriskscore.org/
Pooled Cohort Equation	http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx?example
ACC/AHA Risk Calculator	http://tools.acc.org/ASCVD-Risk-Estimator/
MESA Risk Calculator With addition of Coronary Artery Calcium Score, for CAD-only risk	https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx

~~*Patients who have already manifested cardiovascular disease are already at high global risk and are not applicable to the calculators.³⁷⁻⁴⁰~~

Definitions of Coronary Artery Disease^{2, 3, 6}

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. 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 $\geq 70\%$ by angiography; intermediate lesions are 50 – 69%⁴¹

- For a left main artery, suggested by a percentage stenosis $\geq 50\%$ or minimum lumen cross-sectional area on IVUS ≤ 6 square mm^{2, 42}
- FFR (fractional flow reserve) ≤ 0.80 for a major vessel⁴²
- Demonstrable ischemic findings on stress testing (ECG or stress imaging), that are at least mild in degree
- 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 (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.
- Newer technology that estimates FFR from CCTA image is covered under the separate NIA Guideline for FFR-CT.

Anginal Equivalent^{2, 35}

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), 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. Most syncope per se is not an anginal equivalent.

Abbreviations

ADLs	Activities of daily living
BMI	Body mass index
CABG	Coronary artery bypass grafting
CAC	Coronary artery calcium
CAD	Coronary artery disease
CCTA	Coronary computed tomography angiography
CMR	Cardiac magnetic resonance imaging
CT(A)	Computed tomography (angiography)
DTS	Duke Treadmill Score
ECG	Electrocardiogram
FFR	Fractional flow reserve
IVUS	Intravascular ultrasound
LBBB	Left bundle-branch block
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
MESA	Multi-Ethnic Study of Atherosclerosis
MET	Estimated metabolic equivalent of exercise
MI	Myocardial infarction
MPI	Myocardial perfusion imaging
MR(I)	Magnetic resonance (imaging)
PCI	Percutaneous coronary intervention
PET	Positron emission tomography
PFT	Pulmonary function test
PVCs	Premature ventricular contractions
SE	Stress echocardiography
TEE	Transesophageal echocardiography
THR	Target heart rate
TTE	Transthoracic echocardiography
VF	Ventricular fibrillation
VT	Ventricular tachycardia
WPW	Wolff-Parkinson-White

Policy History

Date	Summary
<u>February 2023</u>	— Removed time limitation “within past two years” for further evaluation inconclusive prior CAD evaluation

	<ul style="list-style-type: none"> — <u>Added ischemia guided approach for evaluation of possibly hemodynamically significant non-culprit CAD noted at the time myocardial infarction.</u> — <u>Added indication for evaluation of ischemia and nonobstructive coronary artery disease (INOCA)</u> — <u>Clarified indication for PET/MPI combination study for evaluation of cardiac sarcoidosis</u> — <u>Added statement on clinical indications not addressed in this guideline</u>
February 2022	<ul style="list-style-type: none"> • Moved the sentence regarding utilization of suitable alternatives to the General Information section • Clarified evaluation of possible ischemia in newly diagnosed heart failure by stating “with reasonable suspicion of cardiac ischemia (prior events, risk factors, or symptoms and signs)” • Clarified “intermediate lesions are 50-69%” for ischemia-producing disease • Placed Link to Overview Section in General Information • Added stress imaging approval for calcium score > 100 with low to intermediate probability symptoms • Deleted the requirement for diabetes when calcium score > 400 for stress imaging • Added Calcium score section: <ul style="list-style-type: none"> ○ Added stress imaging approval for calcium score > 100 with symptoms consistent with low to intermediate pretest probability • Added reminder (SE diversion not required for CABG) • Changed preoperative guideline to include intermediate risk surgery with one or more risk factors AND documentation of an inability to walk (or <4 METs) AND there has not been an imaging stress test within 1 year • Changed solid organ transplant guideline to include stem cell transplant and “any” organ transplant • Added definition of surgical risk to preop guidelines • In Background section clarified the requirement for description of chest pain by adding sentence “The medical record should provide enough detail to establish the type of chest pain.” • Added definition of Q waves • Deleted sentence regarding calcium scoring within the Global Risk Section • Deleted sentence regarding using calcium score solely for risk stratification

	<ul style="list-style-type: none"> Deleted redundant statement on viability Deleted IFR references
March 2021	<ul style="list-style-type: none"> Added annual indication for IC antiarrhythmics Added History of diabetes mellitus, > 40 years old, with calcium score >400
March 2020	<ul style="list-style-type: none"> The following statement was added to reflect an additional CPT code: Cardiac PET scanning, when used in conjunction with CT attenuation, includes evaluation of perfusion, function, viability, inflammation, anatomy, and risk stratification for cardiac related events such as myocardial infarction and death. Maximum diagnostic accuracy of cardiac PET/CT is achieved when images are interpreted in conjunction with other relevant imaging, clinical information, and laboratory data. Added general information section as Introduction which outlines requirements for documentation of pertinent office notes by a licensed clinician, and inclusion of laboratory testing and relevant imaging results for case review Added clarification of repeat testing in a patient with new or worsening symptoms and negative result at least one year prior to include the statement "AND meets one of the criteria above" Added clarification of frequent PVCs under ventricular arrhythmias which states defined as greater than or equal to 30/hour to include "on remote monitoring" Edited indication of planning for solid organ transplantation to remove the requirement of limited functional capacity but maintaining requirement of ≥ 3 listed risk factors Edits to the Background section include the following: <ul style="list-style-type: none"> Indication changed to read as follows: PET is indicated when all the criteria for MPI are met AND There is likely to be equivocal imaging results because of BMI or large breasts or implants or prior thoracic surgery or results of a prior MPI Removed the statement regarding radiation burden Added edits to the Coronary Artery disease definition section Updated and added new references

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Policy History

Date	Summary
<u>May 2023</u>	<ul style="list-style-type: none"> Removed time limitation “within past two years” for further evaluation inconclusive prior CAD evaluation Added ischemia guided approach for evaluation of possibly hemodynamically significant non-culprit CAD noted at the time myocardial infarction. Added coronary stenosis of unclear significance on previous coronary angiography Added indication for evaluation of ischemia and nonobstructive coronary artery disease (INOCA) Clarified indication for PET/MPI combination study for evaluation of cardiac sarcoidosis Added statement on clinical indications not addressed in this guideline
<u>February 2022</u>	<ul style="list-style-type: none"> Moved the sentence regarding utilization of suitable alternatives to the General Information section Clarified evaluation of possible ischemia in newly diagnosed heart failure by stating “with reasonable suspicion of cardiac ischemia (prior events, risk factors, or symptoms and signs)” Clarified “intermediate lesions are 50-69%” for ischemia-producing disease Placed Link to Overview Section in General Information Added stress imaging approval for calcium score > 100 with low to intermediate probability symptoms Deleted the requirement for diabetes when calcium score > 400 for stress imaging Added Calcium score section: <ul style="list-style-type: none"> Added stress imaging approval for calcium score > 100 with symptoms consistent with low to intermediate pretest probability Added reminder (SE diversion not required for CABG)

	<ul style="list-style-type: none"> • <u>Changed preoperative guideline to include intermediate risk surgery with one or more risk factors AND documentation of an inability to walk (or <4 METs) AND there has not been an imaging stress test within 1 year</u> • <u>Changed solid organ transplant guideline to include stem cell transplant and “any” organ transplant</u> • <u>Added definition of surgical risk to preop guidelines</u> • <u>In Background section clarified the requirement for description of chest pain by adding sentence “The medical record should provide enough detail to establish the type of chest pain.”</u> • <u>Added definition of Q waves</u> • <u>Deleted sentence regarding calcium scoring within the Global Risk Section</u> • <u>Deleted sentence regarding using calcium score solely for risk stratification</u> • <u>Deleted redundant statement on viability</u> • <u>Deleted IFR references</u>
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