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Title: Positron Emission Tomography (PET) Scanning: Cardiac Applications

Related Policies:
- *PET Scanning: In Oncology to Detect Early Response during Treatment*
- *PET Scanning: Miscellaneous (Non-cardiac, Non-oncologic) Applications of Fluorine 18 Fluorodeoxyglucose*
- *PET-Scanning: Oncologic Applications*

Professional
Original Effective Date: October 1, 1997
Revision Date(s): October 30, 2013; October 22, 2015; October 1, 2017; November 26, 2018; January 1, 2020; May 18, 2020; December 2, 2021
Current Effective Date: November 26, 2018

Institutional
Original Effective Date: September 11, 2004
Revision Date(s): October 30, 2013; October 22, 2015; October 1, 2017; November 26, 2018; January 1, 2020; May 18, 2020; December 2, 2021
Current Effective Date: November 26, 2018

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Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected coronary artery disease with an indeterminate single-photon emission computed tomography scan	Interventions of interest are: • Cardiac positron emission tomography perfusion imaging	Comparators of interest are: • Coronary angiography • Other noninvasive tests for coronary artery disease (eg, stress echocardiography, exercise electrocardiography)	Relevant outcomes include: • Test accuracy • Disease-specific survival •Morbid events •Resource utilization
Individuals:	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include: • Test accuracy

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Populations	Interventions	Comparators	Outcomes
• With severe left ventricular dysfunction and are potential candidates for revascularization	• Cardiac positron emission tomography scanning to assess myocardial viability	• Cardiac magnetic resonance imaging • Cardiac single-photon emission computed tomography scanning	• Disease-specific survival • Morbid events
Individuals: • With coronary artery disease and require quantification myocardial blood flow quantification	Interventions of interest are: • Quantitative cardiac positron emission tomography perfusion imaging	Comparators of interest are: • Coronary angiography with fractional flow reserve • Clinical risk models	Relevant outcomes include: • Disease-specific survival • Morbid events
Individuals: • With suspected or diagnosed cardiac sarcoidosis who require evaluation	Interventions of interest are: • Cardiac positron emission tomography scanning	Comparators of interest are: • Clinical evaluation • Myocardial biopsy	Relevant outcomes include: • Disease-specific survival • Test accuracy • Morbid events

DESCRIPTION

Positron emission tomography (PET) scans use positron-emitting radionuclide tracers, which simultaneously emit 2 high-energy photons in opposite directions. These photons can be simultaneously detected (referred to as coincidence detection) by a PET scanner, comprising multiple stationary detectors that encircle the thorax. Compared with single photon emission computed tomography (SPECT) scans, coincidence detection offers a greater spatial resolution. PET has been investigated as an option to diagnose and evaluate patients with cardiac conditions such as coronary artery disease, left ventricular dysfunction, and cardiac sarcoidosis.

OBJECTIVE

The objective of this evidence review is to determine whether positron emission tomography scanning improves the net health outcome in individuals with suspected or diagnosed coronary artery disease, severe left ventricular dysfunction, and cardiac sarcoidosis.

BACKGROUND

Positron Emission Tomography

Positron emission tomography (PET) scans use positron-emitting radionuclide tracers, which simultaneously emit 2 high-energy photons in opposite directions. These photons can be simultaneously detected (referred to as coincidence detection) by a PET scanner, comprising multiple stationary detectors that encircle the thorax. Compared with single-photon emission computed tomography (SPECT) scans, coincidence detection offers a greater spatial resolution.

Myocardial Perfusion Imaging

For myocardial perfusion studies, patient selection criteria for PET includes an individual assessment of the pretest probability of coronary artery disease (CAD), based both on patient symptoms and risk factors. Patients at low-risk for CAD may be adequately evaluated with exercise electrocardiography. Patients at high-risk for CAD typically will not benefit from noninvasive assessment of myocardial perfusion; a negative test will not alter disease probability sufficiently to avoid invasive angiography. Accordingly, myocardial perfusion imaging is potentially beneficial for patients at intermediate risk of CAD (variably defined as 25% to 75% or

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10% to 90% disease probability).[1,a] Risk can be estimated using the patient's age, sex, and chest pain quality. Table 1 summarizes patient populations at intermediate risk for CAD.[2,]

[a] Intermediate-risk ranges used in different studies may differ from the range used here. These pretest probability risk groups are based on a TEC Assessment (1995) and take into account spectrum effect. American College of Cardiology guidelines have defined low risk as less than 10%, intermediate risk as 10% to 90%, and high risk as greater than 90%.

Table 1. Individuals at Intermediate Risk for Coronary Artery Disease According to Chest Pain Quality

Populations	Typical Angina[a]	Atypical Angina[b]	Nonanginal Chest Pain[c]
Men	30-39	30-70	≥50
Women	30-60	≥50	≥60

Values are age or age range in years.
[a] Chest pain with all of the following characteristics: (1) substernal chest discomfort with characteristic quality and duration, (2) provoked by exertion or emotional stress, and (3) relieved by rest or nitroglycerin.
[b] Chest pain that lacks one of the characteristics of typical angina.
[c] Chest pain that has one or none of the typical angina characteristics.

Body habitus can limit SPECT; particularly moderate-to-severe obesity, which can attenuate tissue tracer leading to inaccurate images. In patients for whom body habitus is expected to lead to suboptimal SPECT scans, PET scanning is preferred.

Among patients with CAD, myocardial perfusion imaging can be used to quantify myocardial blood flow and myocardial flow reserve (MFR).[3,] Quantitative assessment of myocardial perfusion is sensitive for detection of ischemic tissue within the myocardium, and can allow for accurate determination of risk for cardiovascular events. These quantitative measurements can also be predictive of adverse cardiovascular outcomes. For example, the presence of an abnormally low MFR can identify patients at higher risk of cardiovascular death.

Myocardial perfusion studies with PET are also useful in the diagnosis of cardiac sarcoidosis.[4,] Perfusion studies performed in patients with sarcoidosis and suspected cardiac involvement can detect presence of inflammation, fibrosis of the myocardial tissue, and function and involvement of the left and right ventricles.

Myocardial Viability

Patients selected to undergo PET scanning for myocardial viability are typically those with severe left ventricular dysfunction who are being considered for revascularization. A PET scan may determine whether the left ventricular dysfunction is related to the viable or nonviable myocardium. Patients with viable myocardium may benefit from revascularization but those with nonviable myocardium will not. As an example, PET scanning is commonly performed in potential heart transplant candidates to rule out the presence of viable myocardium.

Radionuclide Tracers

A variety of radionuclide tracers are used for PET scanning, including fluorine 18, rubidium 82, oxygen 15, nitrogen 13, and carbon 11. Most tracers have a short half-life and must be manufactured with an on-site cyclotron. Rubidium 82 is produced by a strontium 82/rubidium 82

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generator. The half-life of fluorine-18 is long enough that it can be manufactured commercially offsite and shipped to imaging centers. Radionuclides may be coupled with a variety of physiologically active molecules, such as oxygen, water, or ammonia. Fluorine 18 is often coupled with fluorodeoxyglucose to detect glucose metabolism, which in turn reflects metabolic activity, and thus viability, of the target tissue. Tracers that target the mitochondrial complex also are being developed.

REGULATORY STATUS

A number of PET platforms have been cleared by the U.S. Food and Drug Administration (FDA) through the 510(k) process since the Penn-PET scanner was approved in 1989. These systems are intended to aid in detecting, localizing, diagnosing, staging, and restaging of lesions, tumors, disease, and organ function for the evaluation of diseases and disorders such as, but not limited to, cardiovascular disease, neurologic disorders, and cancer. The images produced by the system can aid in radiotherapy treatment planning and interventional radiology procedures.

PET radiopharmaceuticals have been evaluated and approved by the FDA for use as diagnostic imaging agents. These radiopharmaceuticals are approved for specific conditions.

In December 2009, the FDA issued guidance for Current Good Manufacturing Practice for PET drug manufacturers,[5,] and in August 2011, the FDA issued similar Current Good Manufacturing Practice guidance for small businesses[6,]. An additional final guidance document issued in December 2012 required all PET drug manufacturers and compounders to operate under an approved new drug application (NDA) or abbreviated NDA, or investigational new drug application, by December 2015.[7,]

To avoid interruption of the use of PET radiotracers already in use in clinical practice, before the issuance of specific guidance documents, the FDA made determinations of safety and effectiveness for certain uses of PET radiotracers. The following radiopharmaceuticals used with PET for cardiac-related indications were reviewed in this manner and subsequently had approved NDAs as summarized in Table 2.

Table 2. Radiopharmaceuticals Approved for Use With Positron Emission Tomography for Cardiac Indications

Radiopharmaceutical	Manufacturer	NDA	Approved	Cardiac-Related Indication With PET
Fluorine 18 fluorodeoxyglucose (F-18-FDG)	Various	20306	2000	CAD and left ventricular dysfunction, when used with myocardial perfusion imaging, to identify left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function
Ammonia N 13	Zevacor Pharma	22119	2000	Imaging of the myocardium under rest

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Radiopharmaceutical	Manufacturer	NDA	Approved	Cardiac-Related Indication With PET
				or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing CAD
Rubidium 82 chloride	Bracco Diagnostics	19414	1989	Assessing regional myocardial perfusion in the diagnosis and localization of myocardial infarction

CAD: coronary artery disease; NDA: new drug application; PET: positron emission tomography.

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POLICY

A. Cardiac positron emission tomography (PET) scanning may be considered **medically necessary** to assess myocardial perfusion and thus diagnose coronary artery disease in patients with indeterminate single-photon emission computed tomography (SPECT) scan; or in patients for whom SPECT could be reasonably expected to be suboptimal in quality on the basis of body habitus.

B. Cardiac positron emission tomography (PET) scanning may be considered **medically necessary** to assess myocardial viability in patients with severe left ventricular dysfunction as a technique to determine candidacy for a revascularization procedure. (See the Background section regarding the relative effectiveness of PET and SPECT scanning.)

C. Cardiac positron emission tomography (PET) scanning may be considered **medically necessary** for diagnosing cardiac sarcoidosis in patients who are unable to undergo magnetic resonance imaging. Examples of patients who are unable to undergo magnetic resonance imaging include, but are not limited to, patients with pacemakers, automatic implanted cardioverter defibrillators, or other metal implants.

D. Cardiac positron emission tomography (PET) scanning is **experimental / investigational** for quantification of myocardial blood flow in patients diagnosed with coronary artery disease.

E. All other indications for Cardiac positron emission tomography (PET) scanning are considered **not medically necessary**

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RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through July 20, 2021.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful.

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Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

SUSPECTED CORONARY ARTERY DISEASE

Clinical Context and Test Purpose

The purpose of positron emission tomography (PET) scanning in patients who have suspected coronary artery disease (CAD) is to evaluate perfusion to the heart. Positron emission tomography can assess relative perfusion, coronary flow reserve, absolute myocardial blood flow (MBF) at stress and rest, left ventricular ejection fraction (LVEF), possible ischemic dilatation, and coronary artery calcium levels. These parameters can be used to diagnose CAD.

The question addressed in this evidence review is : Does testing with PET improve the net health outcome in individuals with suspected CAD?

The following PICO was used to select literature to inform this review.

Populations

The population of interest is patients with suspected CAD who have indeterminate single photon emission computed tomography (SPECT) scans.

Interventions

The intervention of interest is cardiac PET perfusion imaging.

Comparators

The following tests are currently being used to make decisions about managing suspected CAD: coronary angiography or noninvasive tests for CAD (eg, stress echocardiography, exercise electrocardiography).

Outcomes

For patients with suspected CAD, the outcomes of interest are the avoidance of unnecessary invasive procedures, cardiac events, and mortality. Additional outcomes of interest, including PET sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and test accuracy are measured from time to diagnosis.

Study Selection Criteria

For the evaluation of the clinical validity of cardiac PET perfusion imaging, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard (describe the reference standard)
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

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The sensitivity and specificity of PET may be slightly better than for those for SPECT. Performance characteristics for PET and SPECT based on a 2007 Canadian joint position statement are shown in Table 3.[8,]

Table 3. Performance Characteristics of Positron Emission Tomography and Single Photon Emission Computed Tomography

Outcome Measures	PET	SPECT
Sensitivity, %	91	88
Specificity, %	89	77
Estimated positive likelihood ratio[a]	8.27	3.83
Estimated negative likelihood ratio[b]	0.10	0.16

Adapted from Beanlands et al (2007).[8,]
PET: positron emission tomography; SPECT: single photon emission computed tomography.
[a] Estimated positive likelihood ratio = sensitivity/(1 - specificity).
[b] Estimated negative likelihood ratio = (1 - sensitivity)/specificity.

REVIEW OF EVIDENCE

DIAGNOSTIC PERFORMANCE

Systematic Reviews

Xu et al (2021) conducted a meta-analysis that compared cardiac magnetic resonance imaging (MRI), SPECT, and PET for the diagnosis of CAD.[9,] Diagnostic studies were eligible for inclusion if either coronary angiography or fractional flow reserve (FFR) was used as the reference standard. The literature search, conducted through July 2020, identified 203 articles (N=23,942) that assessed the diagnostic performance of cardiac MRI (56 articles), SPECT (134 articles), and PET (25 articles). There were no statistically significant differences in sensitivities between cardiac MRI, SPECT, and PET (86% [95% CI, 84% to 88%], 83% [95% CI, 81% to 85%], 85% [95% CI, 80% to 89%], respectively; p=.109). For specificity, cardiac MRI (83% [95% CI, 81% to 86%]) and PET (86% [95% CI, 81% to 89%]) performed significantly better than SPECT (77% [95% CI, 74% to 80%]; p<.01 for both comparisons); there was no statistically significant difference between cardiac MRI and PET. Similarly, the area under the curve values of cardiac MRI (0.92 [95% CI, 0.89 to 0.94]), SPECT (0.87 [95% CI, 0.84 to 0.90]), and PET (0.92 [95% CI, 0.89 to 0.94) indicated that cardiac MRI and PET had better diagnostic performance for the detection of CAD as compared with SPECT (p<.01 for both comparisons).

Knuuti et al (2018) reported on the results of a meta-analysis of the performance of noninvasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina including publications through April 2017 that included at least 100 patients with stable CAD and either invasive coronary angiography or invasive coronary angiography with FFR measurement as reference standard.[10,] A total of 132 studies (28,664 patients) using invasive coronary angiography as the reference standard and 23 studies (4131 patients) using FFR as the reference standard were included. The pooled analysis for the outcome of anatomically significant CAD included 418 patients for PET and the sensitivity, specificity, positive likelihood ratio, and

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negative likelihood ratio were as follows: 90% (95% CI, 78% to 96%); 85% (95% CI, 78% to 90%); 5.87 (95% CI, 3.40 to 10.15); and 0.12 (95% CI, 0.05 to 0.29), respectively. The pooled analysis for outcome of functionally significant CAD included 709 patients for PET and the sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio were as follows: 89% (95% CI, 82% to 93%); 85% (95% CI, 81% to 88%); 6.04 (95% CI, 4.29 to 8.51); and 0.13 (95% CI, 0.08 to 0.22).

Dai et al (2016) conducted a meta-analysis comparing the abilities of the following cardiac imaging modalities to diagnose CAD: SPECT, PET, dobutamine stress echocardiography, cardiac MRI, and computed tomography (CT) perfusion imaging.[11,] The reference standard was FFR derived from CT. The literature search, conducted through June 2015, identified 74 studies for inclusion, 5 of which used PET. Study quality was assessed using Standards for Reporting Diagnostic Accuracy and Quality Assessment of Diagnostic Accuracy Studies tools. Pooled sensitivity and specificity for PET were 90% (95% CI, 80% to 95%) and 84% (95% CI, 81% to 90%), respectively. These rates were similar to FFR, the reference standard (sensitivity, 90% [95% CI, 85% to 93%]; specificity, 75% [95% CI, 62% to 85%]).

Takx et al (2015) reported a meta-analysis of studies that compared noninvasive myocardial perfusion imaging modalities (MRI, CT, PET, SPECT, echocardiography) with coronary angiography plus FFR.[12,] Literature was searched to May 2014, and 37 studies met inclusion criteria (N=4698 vessels). Three PET studies of moderate-to-high quality were included (870 vessels); pretest probability of CAD was intermediate to intermediate-high in these studies. Negative likelihood ratio was chosen as the primary outcome of interest because ruling out hemodynamically significant CAD is a primary purpose of noninvasive imaging. At the vessel level, pooled negative likelihood ratios for PET, MRI, and CT were similar and were lower (better) than the pooled negative likelihood ratio for SPECT (PET pooled negative likelihood ratio =0.15 [95% CI, 0.05 to 0.44]; SPECT pooled negative likelihood ratio =0.47 [95% CI, 0.37 to 0.59]). Similarly, at the patient-level, pooled negative likelihood ratios for PET, MRI, and CT were better than the pooled negative likelihood ratios for SPECT and echocardiography (PET pooled negative likelihood ratio =0.14 [95% CI, 0.02 to 0.87]; SPECT pooled negative likelihood ratio =0.39 [95% CI, 0.27 to 0.55]). The area under the receiver operating characteristic analyses was similar at both the vessel level (PET, 0.95 vs SPECT, 0.83) and the patient-level (PET, 0.93 vs SPECT, 0.82).

Retrospective Studies

Another consideration is that there are fewer indeterminate results with PET than SPECT. Bateman et al (2006) retrospectively matched 112 SPECT and 112 PET studies by sex, body mass index, and presence and extent of CAD, and compared diagnostic accuracy and degree of interpretative certainty (age, 65 years; 52% male; mean body mass index, 32 kg/m^2; 76% with CAD diagnosed on angiography).[13,] Eighteen (16%) of 112 SPECT studies were classified as indeterminate compared with 4 (4%) of 112 PET studies. Liver and bowel uptake were believed to affect 46 (41%) of 112 SPECT studies, compared with 6 (5%) of 112 PET studies. In obese patients (body mass index, >30 kg/m^2), the accuracy of SPECT was 67% and 85% for PET; accuracy in non-obese patients was 70% for SPECT and 87% for PET.

PROGNOSTIC PERFORMANCE

Systematic Reviews

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Chen et al (2017) published a meta-analysis assessing the prognostic value of PET myocardial perfusion imaging in patients with known or suspected CAD.[14,] For inclusion, studies had to have at least 1 of the following outcomes: mortality, cardiac infarction, or major adverse cardiac event (MACE). The literature search, conducted through June 2016, identified 11 studies for inclusion. Quality assessment was based on: (1) cohort follow-up of 90% or more; (2) blinded outcome assessors; and (3) corroboration of outcomes with hospital records or death certificates. Nine of the studies were of good quality, and 2 were fair. All 11 studies included cardiac death as the primary or secondary outcome, with a pooled negative predictive value (NPV) of 99% (95% CI, 98% to 99%). Seven studies included all-cause death as an outcome, with a pooled NPV of 95% (95% CI, 93% to 96%). Four studies included MACE as an outcome, with a pooled NPV of 90% (95% CI, 78% to 96%).

Smulders et al (2017) published a meta-analysis comparing the prognostic value of the following negative noninvasive cardiac tests: coronary CT angiography, cardiovascular MRI, exercise electrocardiographic testing, PET, stress echocardiography, and SPECT.[15,] Outcomes of interest were annual event rates of myocardial infarction and cardiac death. The literature search, conducted through April 2015, identified 165 studies for inclusion, 4 of which involved PET. Study quality was assessed using the Newcastle-Ottawa Scale for observational studies. Pooled annual event rates for cardiac death and myocardial infarction for PET were low (0.41; 95% CI, 0.15 to 0.80), indicating that a patient with a negative PET test has a good prognosis.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

No RCTs comparing outcomes for patients undergoing PET perfusion imaging to patients who did not undergo PET perfusion imaging were identified.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Meta-analyses have shown that PET is a useful prognostic tool that can be performed successfully in some patients in whom SPECT may be indeterminate due to body habitus or other anatomic factors. Therefore, PET results can be useful in informing clinical decisions in these intermediate-risk patients.

Section Summary: Suspected Coronary Artery Disease
Evidence on the diagnostic accuracy of PET for CAD consists of several systematic reviews and meta-analyses. Meta-analyses comparing PET with reference standards such as invasive coronary angiography and FFR have shown that PET is comparable in diagnostic accuracy. Additionally, some of these meta-analyses found PET to have significantly greater sensitivity or specificity

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compared to SPECT, which further validates its use among patients with indeterminate SPECT results. Meta-analyses evaluating the clinical utility of PET have looked at outcomes such as mortality and adverse cardiac events. These meta-analyses have shown that PET is a useful prognostic tool.

SEVERE LEFT VENTRICULAR DYSFUNCTION CONSIDERING REVASCULARIZATION

Clinical Context and Test Purpose

The purpose of PET scanning in patients with severe left ventricular (LV) dysfunction is to determine myocardial viability to assist with revascularization.

The question addressed in this evidence review is: Does testing with PET improve the net health outcome in individuals with severe LV dysfunction considering revascularization?

The following PICO was used to select literature to inform this review.

Populations

The population of interest is patients with severe LV dysfunction who are potential candidates for revascularization.

Interventions

The intervention of interest is PET scanning.

Comparators

The following tests are currently being used to make decisions about managing severe LV dysfunction: cardiac MRI or cardiac SPECT scanning

Outcomes

For patients with severe LV dysfunction who are potential candidates for revascularization, the intermediate outcome is a viability assessment. If there is sufficient viable myocardium detected, the patient would be a candidate for revascularization. For severe LV dysfunction, the outcome of interest would be the time to cardiac events.

Study Selection Criteria

For the evaluation of the clinical validity of cardiac PET perfusion imaging, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard (describe the reference standard)
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

PET has perhaps been most thoroughly researched as a technique to assess myocardial viability to determine candidacy for a coronary revascularization procedure. A fixed perfusion defect, as imaged on SPECT scanning or stress thallium echocardiography, may suggest nonviable

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myocardium. However, a PET scan may reveal metabolically active myocardium, suggesting areas of "hibernating" myocardium that would benefit from revascularization. The most common PET technique for this application consists of N 13 ammonia as a perfusion tracer and fluorine 18-labeled fluorodeoxyglucose (18F-FDG) as a metabolic marker of glucose utilization. FDG uptake in areas of hypoperfusion (referred to as FDG/blood flow mismatch) suggests viable but hibernating myocardium. The ultimate clinical validation of this diagnostic test is the proportion of patients who experience improvement in LV dysfunction after revascularization of hibernating myocardium, as identified by PET scanning.

SPECT scanning also may be used to assess myocardial viability. Initial myocardial uptake of thallium 201 reflects myocardial perfusion, and redistribution after prolonged periods can be a marker of myocardial viability. Initial protocols required redistribution imaging after 24 to 72 hours. Although this technique was associated with a strong positive predictive value, there was a low NPV; ie, 40% of patients without redistribution nevertheless showed clinical improvement after revascularization. NPVs have improved with the practice of thallium reinjection. Twenty-four to 72 hours after initial imaging, patients receive a reinjection of thallium and undergo redistribution imaging.

Review of Evidence
Studies identified in literature have shown the equivalence of SPECT and PET in their ability to assess myocardium viability.

Using a thorax-cardiac phantom with different sized inserts that simulated infarcts, Knesaurek and Machac (2006) tested SPECT and PET images.[16,] The investigators concluded that PET was better at detecting smaller defects than SPECT. In this study, a 1-cm insert, not detected by SPECT, was detected by PET.

Slart et al (2005) compared dual-isotope simultaneous acquisition SPECT and PET in the detection of myocardial viability in 58 patients with CAD and dysfunctional LV myocardium.[17,] Tracer uptake for PET and SPECT was compared by linear regression and correlation analysis, which showed there was an overall good agreement between SPECT and PET for the assessment of myocardial viability in patients with severe LV dysfunction.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

Randomized Controlled Trials
The Positron Emission Tomography and Recovery Following Revascularization study evaluated the impact of FDG-PET viability imaging on patients with severe LV dysfunction. Patients from 9 sites were randomized to FDG-PET-assisted physician management (n=218) or standard care management by a physician without PET imaging available (n=212). Physicians in the standard

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care management group could order a different test to determine viability; however, the study did not indicate what specific tests were ordered or in what frequency. Management decision options were: revascularization, revascularization workup, or neither. The primary outcome was a composite of cardiac death, myocardial infarction, or recurrent hospital stay for a cardiac cause. Beanlands et al (2007) reported on results after 1 year of follow-up.[18,] The intention-to-treat hazard ratio (HR) of a composite event occurring at 1 year was not significant (0.78; 95% CI, 0.58 to 1.1; p=.15) for PET-assisted management of care compared with standard care. However, among patients in the PET-assisted management of care group who had high or medium myocardium viability and who therefore were recommended to receive revascularization or a revascularization workup, 26% did not ultimately receive the recommended care. Reasons given included symptoms stabilizing, renal failure, multiple comorbidities, and patient refusal. When subgroup analysis included only those patients who received the treatment as recommended based on PET images, the HR for a composite event was significant (0.62; 95% CI, 0.42 to 0.93).

Mc Ardle et al (2016) published long-term follow-up results for the Positron Emission Tomography and Recovery Following Revascularization trial.[19,] Six of the 9 original sites participated in the long-term follow-up study (197 patients in the PET-assisted arm, 195 patients in the standard care arm). Long-term results were similar to the 1 year results. The HR for time to composite event for the whole study population did not differ significantly between the PET-assisted group and the standard care group (0.82; 95% CI, 0.62 to 1.1); however, when analysis was conducted using only the subgroup of patients who adhered to the PET imaging-based recommendations, the HR was statistically significant (0.73; 95% CI, 0.54 to 0.99).

Siebelink et al (2001) performed a prospective randomized study comparing management decisions with outcomes based on PET imaging (n=49) or SPECT imaging (n=54) in patients who had chronic CAD and LV dysfunction and were being evaluated for myocardial viability.[20,] Management decisions based on readings of the PET or SPECT images included either drug therapy for patients without viable myocardium or revascularization with either angioplasty or coronary artery bypass grafting (CABG) for patients with viable myocardium. This study is unique in that the diagnostic performance of PET and SPECT was tied to actual patient outcomes. No difference in patient management or cardiac event-free survival was demonstrated between management based on the 2 imaging techniques. The authors concluded that either technique could be used to manage patients considered for revascularization. However, the sample size for the study was determined based on the assumption that patients randomized to SPECT would have a 20% higher cardiac event rate. Therefore, the study may have been underpowered to detect a difference in cardiac outcomes between groups.

Nonrandomized Studies

Srivatsava et al (2016) published a study of 120 patients with LV dysfunction who underwent both SPECT-CT and FDG-PET/CT to determine myocardial viability.[21,] If both tests showed defects (ie, matched defects), the tissue was considered nonviable. If a defect was seen in the SPECT-CT test but uptake of 18F-FDG was seen with the FDG-PET test (ie, mismatched defects), the tissue was considered hibernating but viable. If more than 7% of the myocardium was considered viable, patients underwent revascularization by either stenting or CABG (78 patients). Patients assessed as having less than 7% viable myocardium were medically managed (42 patients). Among 786 segments of myocardium with evidence of reduced perfusion, 432 segments (55%) were matched defects and 354 segments (45%) were mismatched defects. The primary outcome

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was global LVEF. Change in LVEF after 3 months was significantly larger in the surgically managed group (3.5; 95% CI, 2.5 to 4.5) than in the medically managed group (0.7; 95% CI, -0.8 to 2.2). All patients with observed viability of the myocardium on PET were managed surgically. A decline in LVEF was seen in 5 patients (6.4%) who received surgical management compared with 9 patients (21.4%) who were managed medically.

Section Summary: Severe Left Ventricular Dysfunction Considering Revascularization
Evidence for the use of PET to assess myocardial viability consists of a large, controlled trial that randomized patients with LV dysfunction into 2 groups: one was managed by physicians receiving PET images to inform care decisions, and the other was managed by physicians who did not receive PET images. Follow-up at 1 year and 5 years showed that when patients received care as indicated by the PET images, they were at a decreased risk for cardiac death, myocardial infarction, or recurrent hospital stay compared with patients who did not. Although the study did not define what standard care consisted of, physicians were permitted to order non-PET viability tests for patients in the standard care group. However, it is unclear how many patients received other tests for viability, and what tests were administered. A small prospective study has suggested that the accuracy of PET and SPECT are roughly similar for this purpose; however, this study may have been underpowered to detect a difference between groups. A small, nonrandomized study also showed that PET may be useful for detecting viable myocardium when SPECT shows nonviable tissue.

MYOCARDIAL BLOOD FLOW QUANTIFICATION

Clinical Context and Test Purpose
The purpose of PET scanning in patients who have CAD is to quantify MBF for cardiac event risk stratification.

The question addressed in this evidence review is: Does testing with PET improve the net health outcome in individuals with diagnosed CAD who require cardiac event risk stratification?

The following PICO was used to select literature to inform this review.

Populations
The population of interest is patients with CAD in need of quantifying MBF for cardiac event risk stratification.

Interventions
The intervention of interest is quantitative cardiac PET perfusion imaging. Both MBF and myocardial flow reserve (MFR; defined as stress MBF/rest MBF) can be quantified. Generally, a MFR ≥ 2 is indicative of normal perfusion and is associated with a good prognosis.[22,] Lower values of MFR may require further invasive testing to rule out epicardial CAD. As MFR decreases, the likelihood of multivessel obstructive CAD increases with a corresponding worsening prognosis.

Comparators
The following tests are currently being used to make decisions about quantifying MBF in patients with CAD: coronary angiography with FFR and clinical risk models

Outcomes

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For patients with CAD who require MBF quantification, the intermediate outcome is accurate quantification. The relevant follow-up would be the time to cardiac events.

Study Selection Criteria
For the evaluation of the clinical validity of cardiac PET perfusion imaging, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard (describe the reference standard)
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

REVIEW OF EVIDENCE

DIAGNOSTIC PERFORMANCE

Cohort Studies
Several publications have described the use of PET imaging to quantify both MBF and MFR.[23,24,] However, as noted in an accompanying editorial[25,] and by subsequent reviewers,[26,] larger prospective clinical trials are needed to understand the clinical utility of these approaches. Diagnostic accuracy of PET myocardial perfusion imaging, as compared to FFR as a reference standard, is limited to 15-oxygen (O)-water PET imaging, which is not available in the US.[12,] Most PET examinations are performed with 82-Rubidium (Rb) chloride instead, which has less favorable flow-extraction characteristics. Therefore, it is not possible to extrapolate the findings from 15O-water PET studies to clinical settings in which 82Rb-chloride is used.

PROGNOSTIC PERFORMANCE

Systematic Reviews
Green et al (2021) conducted a meta-analysis on the prognostic value of MFR (called coronary flow reserve [CFR] in this analysis), as assessed by PET, for predicting adverse cardiovascular events in patients with suspected or known CAD.[27,] The prognostic value of MFR was analyzed as a dichotomous variable (ie, impaired vs. preserved MFR); cut-off values used were as reported by the individual study. Thirteen studies (N=12,334) were identified. Four of the studies included patients with suspected CAD only; the remainder of the studies included a mixed population (suspected or known CAD). Eleven studies reported MACE outcomes, and the pooled HR for patients with impaired versus preserved MFR was 1.93 (95% CI, 1.65 to 2.27; I^2=11%). Only 5 studies reported on hard events (ie, cardiac death, myocardial infarction) and there was significant heterogeneity (I^2=72.8%); the pooled HR was 3.11 (95% CI, 1.88 to 5.14). Six studies included data useful to calculate separately the incidence rate of MACE events. The pooled incidence rate ratio for patients with impaired versus preserved MFR was 2.26 (95% CI, 1.79 to 2.85; I^2=20.3%). Funnel plots for the MACE, but not hard events, indicated significant bias towards positive results. Publication bias may result in overstating the benefits of MFR

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prognostic value. Heterogeneity between studies and small sample sizes of some of the included studies further complicate interpretation. For instance, the cut-off value for designating an impaired MFR was not consistent across trials, stemming from differences in tracers, imaging protocols, and stress agents used in the studies. The authors note that due to the large heterogeneity in the study population, there is a need for further investigations to maximize the prognostic role of MFR.

Juarez-Orozco et al (2017) reported on the results of a systematic review of prognostic studies of quantitative myocardial perfusion evaluation with PET in patients with suspected or known CAD.[28,] Eight studies (N=6804 patients) were included. Risk of bias was assessed using the Quality in Prognostic Studies tool. The risk of bias was rated as low overall with the exception of 1 domain (prognostic factor measurement) with the uncertain risk of bias due to the differences in population characteristics and tracer used. The mean follow-up range was 12 to 117 months for the MACE outcome, 66 to 88 months for the cardiac death outcome, and 43 to 117 months for the all-cause mortality outcome. MFR was independently associated with MACE in all 8 studies with the range of adjusted HRs from 1.19 to 2.93. Pooled analyses for MACE included only 2 studies due to the differences in populations and cutoff values for MFR; the pooled HR was 1.92 (95% CI,1.29 to 2.84) for the 2 studies, which included patients with a previous myocardial infarction and a MFR cut-off of 2.0. There was not enough evidence to pool reported HRs to establish the prognostic value of MFR for cardiac death or all-cause mortality.

Cohort Studies

As available meta-analyses have identified the need for larger, and preferably prospective, cohort investigations to more precisely identify the prognostic value of MFR measurements, cohort studies not included in the previously summarized meta-analyses that included at least 1000 participants are included below. Meta-analyses by Green et al (2021) and Juarez-Orozco et al (2017) incorporated 16 studies, which evaluated diverse populations that included both patients with suspected and confirmed CAD.[23,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,]

Gould et al (2021) prospectively examined the relationship between regional, artery-specific MFR (called CFR in this analysis) and coronary flow capacity (CFC) and mortality in patients with suspected or known CAD who received and did not receive revascularization.[44,] Patients were recruited from a single center institution that routinely performs quantitative PET myocardial perfusion imaging in all patients with or at risk of CAD. CFC color maps are created using 5 color ranges for combined CFR and stress perfusion values of each pixel, which is mapped back to its location in the left ventricle. For the CFC maps, any with pixels that had both MFR ≤1.27 and stress perfusion ≤0.83 were defined as severely reduced CFC (CFCsevere). A total of 5274 patients were included in the cohort, who were followed for 4.2 years on average. Thirty-eight percent of patients had established CAD. Within 90 days of the PET scan, 245 patients (7.4%) received a coronary angiogram; of those patients, 76% underwent a revascularization procedure and 24% were deemed to not be appropriate candidates due to diffuse or complex CAD. Among the patients undergoing revascularization procedures (n=187), 152 (81%) were classified as CFCsevere and 35 (19%) were classified as moderately reduced CFC (no CFCsevere). Severely reduced regional MFR of 1.0 to 1.5 was associated with an increasing risk of all-cause death, myocardial infarction, stroke, or revascularization. Cox regression modeling showed that mortality risk was 54% lower (HR, 0.46; 95% CI, 0.26 to 0.79) after revascularization in patients classified as CFCsevere. For global assessments, patients with a global MFR <2.0 and global stress perfusion <1.8 had a significantly lower mortality risk with revascularization compared to no

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revascularization (p<.003). For other combinations with less severe global MFR or global stress perfusion, revascularization had no statistically significant impact on mortality risk. The authors note that generalizability may be a limitation as protocols, methodologies, and thresholds for intervention vary among institutions.

Patel et al (2020) retrospectively evaluated the association between MFR and mortality, and whether the association was modified by early revascularization in a cohort of 12,549 patients referred for rest/stress 82Rb PET myocardial perfusion imaging.[45,] Patients with a history of CABG or LVEF <40% were excluded. The primary outcome was all-cause mortality; cardiac mortality was a secondary outcome. Early revascularization was defined as receipt of percutaneous coronary intervention or CABG within 90 days of the myocardial perfusion imaging test. All patients had at least 1 year of follow-up and the median duration was 3.2 years. The majority of patients (77.4%) did not have a documented history of CAD. Chest pain was the predominant presenting symptom in approximately 60% of all patients. Mean MFR values were classified as low (<1.8), intermediate (1.8 to 2), and normal (≥2); 38.5%, 15%, and 46.4% of the cohort fell into these categories, respectively. Early revascularization was performed in 897 patients; of those, 66.8%, 10.8%, and 22.4% had MFR values of low, intermediate, or normal, respectively. The all-cause mortality rate through the study follow-up period was 13.5% for the entire cohort. The mortality rate in the low, intermediate, and normal MFR was 21.9%, 12.4%, and 6.9%, respectively (p<.001). Adjusted HR estimates found that every 0.1-unit decrease in MFR was associated with 9% greater hazard of all-cause death [HR, 1.09; 95% CI, 1.08 to 1.10). In the fully adjusted Cox proportional hazards model, there was a significant interaction between MFR and early revascularization; such that patients with MFR ≤1.8 had a survival benefit with early revascularization (HR, 0.76; 95% CI, 0.62 to 0.94), and those with MBFR >1.8 had similar or worse outcomes with early revascularization (HR, 1.39; 95% CI, 1.01 to 1.94).

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No RCTs comparing clinical outcomes for patients undergoing PET to calculate MFR with patients who did not undergo PET were identified.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity and explication of evidence-based decisions informed by the test. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Specificity on how the test would fit into current management guidelines for making treatment decisions is needed to evaluate a chain of evidence.

Section Summary: Myocardial Blood Flow Quantification

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Evidence is accumulating on the association between quantitative MBF and MFR and cardiovascular outcomes, including if quantifying MFR can assist in identifying patients who may gain a survival benefit from early revascularization. Meta-analyses of cohort studies and individual cohorts have found that impaired MFR is significantly associated with an increase in all-cause mortality. Interpretation of the available literature is complicated due to differences in populations studied, procedures and radiotracers used, cut points used for classification, covariates used in models, lack of reclassification analyses, and potential for publication bias. Recent prospective and retrospective cohorts have reported that identification of MFR can assist in identifying patients who may receive a survival benefit with early revascularization compared to medical therapy. The benefits observed in these single-center studies may be difficult to generalize due to differences in protocols, methodologies, and thresholds for intervention among institutions. These methods are considered to be in a developmental stage for clinical use. Large, prospective clinical trials are needed to better define the potential utility of MBF quantification.

CARDIAC SARCOIDOSIS

Clinical Context and Test Purpose

The purpose of PET scanning in patients with suspected cardiac sarcoidosis is to diagnose sarcoidosis via detection of inflammatory lesions.

There are no universally accepted diagnostic criteria for cardiac sarcoidosis. The American Thoracic Society guideline (2020) notes that diagnosis is based on 3 major criteria: compatible clinical presentation, finding nonnecrotizing granulomatous inflammation in ≥1 tissue samples, and the exclusion of alternative causes of granulomatous disease.[46,] Imaging techniques are commonly used for cardiac sarcoidosis detection, along with the collection of additional clinical data. Transthoracic echocardiogram, cardiac MRI, and FDG PET have all been evaluated for making a sarcoidosis diagnosis.

The question addressed in this evidence review is: Does testing with PET improve the net health outcome in individuals with suspected cardiac sarcoidosis?

The following PICO was used to select literature to inform this review.

Populations

The population of interest is patients with suspected cardiac sarcoidosis who cannot undergo MRI.

Interventions

The intervention of interest is PET scanning.

Comparators

The following tests and practices are currently being used to make decisions about managing cardiac sarcoidosis: clinical evaluation and myocardial biopsy.

Outcomes

For patients with suspected cardiac sarcoidosis, the outcome of interest is a diagnosis confirmation.

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Study Selection Criteria

For the evaluation of the clinical validity of cardiac PET perfusion imaging, studies that met the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard (describe the reference standard)
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Studies evaluating the diagnostic performance of PET for cardiac sarcoidosis are limited by the absence of a gold standard reference.[47,] The Japanese Ministry of Health and Welfare (JMHW), the modified JMHW, or the Heart Rhythm Society diagnostic criteria are often used as the reference standard, but all have imperfect diagnostic accuracy.

REVIEW OF EVIDENCE

Systematic Review

Kim et al (2020) conducted a systematic review on the diagnostic performance of 18F-FDG PET or PET/CT for cardiac sarcoidosis. [48,] A total of 17 studies (N=891) were identified for inclusion. Thirteen studies were retrospectively designed, with the other 4 studies enrolling patients prospectively. The reference standards used in the included studies was the JMHW guideline or the modified JMHW. Across all studies, the pooled sensitivity was 84% (95% CI, 71% to 91%; I^2=77.5) and the pooled specificity was 83% (95% CI, 74% to 89%; I^2=80.0). The pooled sensitivity and specificity for the 6 studies that evaluated 18F-FDG PET alone was 92% (95% CI, 79% to 97%) and 66% (47% to 81%), respectively. The pooled sensitivity and specificity for the 11 studies that evaluated combination 18F-FDG PET/CT was 72% (95% CI, 66% to 78%) and 89% (86% to 92%), respectively. The overall positive likelihood ratio was 4.9 (95% CI, 3.3 to 7.3) and the negative likelihood ratio was 0.2 (95% CI, 0.11 to 0.35). The pooled diagnostic odds ratio was 27 (95% CI, 14 to 55). Pooled accuracy was assessed using a summary receiver operator characteristic curve; the area under the curve was 0.90 (95% CI, 0.87 to 0.92). The authors concluded that further large multicenter studies are necessary to substantiate the diagnostic accuracy of 18F-FDG PET for cardiac sarcoidosis.

Nonrandomized Studies

Wicks et al (2018) reported on results of simultaneous PET/MRI to diagnose cardiac sarcoidosis including 51 consecutive patients in the U.K. with known or suspected cardiac sarcoidosis.[49,] The PET and MRI images were analyzed qualitatively in consensus by 2 experienced blinded readers. Using the JMHW guidelines as the reference standard, the prevalence of cardiac sarcoidosis was 65%. Twenty-eight (55%) patients had abnormal cardiac PET findings. The sensitivity of PET and cardiac MRI alone for diagnosing cardiac sarcoidosis was 85% (95% CI, 68% to 95%) and 82% (95% CI, 65% to 93%), respectively. The sensitivity, specificity, positive predictive value, and NPV for hybrid PET/MRI were 94% (95% CI, 80% to 99%), 44% (95% CI, 22% to 69%), 76% (95% CI, 60% to 88%), and 80% (95% CI, 44% to 97%), respectively.

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Lapa et al (2016) published a study to determine whether PET/CT using radiolabeled somatostatin receptor ligands for visualization of inflammation would accurately diagnose cardiac sarcoidosis.[50,] Fifteen patients with sarcoidosis and suspicion of cardiac involvement underwent both somatostatin receptor-PET/CT and cardiac MRI. Concordant results between PET/CT and MRI occurred in 12 of the 15 patients.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No studies evaluating the clinical utility of using PET or PET/CT in diagnosing cardiac sarcoidosis were identified.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Cardiac sarcoidosis can lead to arrhythmia, heart failure, pericarditis, and myocardial infarction. There is no criterion standard for diagnosing cardiac sarcoidosis but a clinical diagnosis is made through a combination of clinical evaluations and imaging. Results from nonrandomized studies have shown that PET can be a useful tool in the clinical diagnostic process.

Section Summary: Cardiac Sarcoidosis
Left untreated, cardiac sarcoidosis can lead to serious developments such as arrhythmia, heart failure, pericarditis, and myocardial infarction. However, there is no criterion standard for diagnosing cardiac sarcoidosis. A combination of clinical evaluations and results from imaging techniques are used in the clinician's assessment. Magnetic resonance imaging is generally recommended first-line for imaging of patients with suspected cardiac sarcoidosis; however, PET may be utilized in patients who are unable to undergo MRI. A meta-analysis found moderate sensitivity and specificity of 18F-FDG PET or PET/CT for diagnosis of cardiac sarcoidosis. Two nonrandomized studies have been published comparing MRI and PET for diagnosis of cardiac sarcoidosis. Both studies found concordance between the 2 tests in their ability to detect cardiac sarcoidosis, thus supporting the use of PET scanning in patients with sarcoidosis unable to undergo MRI.

Summary of Evidence
For individuals with suspected CAD and an indeterminate SPECT scan who receive cardiac PET perfusion imaging, the evidence includes several systematic reviews and meta-analyses. Relevant outcomes are test accuracy, disease-specific survival, morbid events, and resource utilization. Meta-analyses of studies in which PET results were compared with results from coronary angiography and FFR have shown that PET is comparable in diagnostic accuracy to these referent standards. In meta-analyses of studies that included clinical outcomes such as mortality and

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adverse cardiac events, results have shown that PET is a useful prognostic tool. Meta-analyses have also found PET to have greater sensitivity or specificity compared to SPECT, which provides further evidence to support the use of PET when SPECT is indeterminate. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with LV dysfunction who are potential candidates for revascularization who receive cardiac PET scanning to assess myocardial viability, the evidence includes a large randomized controlled trial with long-term follow-up and several small trials comparing SPECT with PET. Relevant outcomes are test accuracy, disease-specific survival, and morbid events. In the large, controlled trial, patients with LV dysfunction were randomized to care from physicians who would make management decisions based on PET images or to care from physicians who would make management decisions without PET images. Physicians who would make management decisions without PET images were permitted to administer other tests for myocardial viability, although details were not available as to which tests were performed, if any. At 1- and 5-year follow-ups, patients who received care indicated by the PET images were at a decreased risk for cardiac death, myocardial infarction, and recurrent hospital stays compared with patients who did not. One trial comparing SPECT with PET showed that both modalities were useful in managing patients considering revascularization; however, this trial was small and may have been underpowered to detect a difference in outcomes. Evidence-based recommendations from specialty societies have concluded that PET scanning is at least as good as, and likely superior, to SPECT scanning for this purpose. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with CAD who require MBF quantification for cardiac event risk stratification who receive quantitative cardiac PET perfusion imaging, the evidence includes observational studies and meta-analyses of those observational studies. Relevant outcomes are disease-specific survival and morbid events. Studies evaluating PET-derived quantitative MBF and MFR have found that impaired MFR is significantly associated with an increase in all-cause mortality and can assist in identifying patients who may receive a survival benefit with early revascularization compared to medical therapy. The benefits observed in these single-center studies may be difficult to generalize due to differences in protocols, methodologies, and thresholds for intervention among institutions. These methods are considered to be in a developmental stage for clinical use. Large, prospective clinical trials are needed to better define the potential utility of MBF quantification. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with suspected cardiac sarcoidosis who cannot undergo MRI, the evidence includes nonrandomized studies and a meta-analysis of observational studies. Relevant outcomes are disease-specific survival, test accuracy, and morbid events. Currently, there is no criterion standard for diagnosing cardiac sarcoidosis. A combination of clinical evaluations and results from imaging techniques, usually MRI, are used during the clinician's assessment. A meta-analysis found moderate sensitivity and specificity of 18F-FDG PET or PET/CT for diagnosis of cardiac sarcoidosis. Two small studies have evaluated variations in PET techniques such as using a radiolabeled somatostatin receptor ligand and adding a simultaneous cardiac MRI. Reported results were positive in these small studies, showing concordance between MRI and PET, but larger samples are needed to confirm the usefulness of these changes. While MRI is the technique most often used to evaluate cardiac sarcoidosis, for patients who are unable to undergo MRI (eg, patients with a metal implant), evidence supports PET scanning as the

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preferred test. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers
In response to requests, input was received while this policy was under review in 2011. The input was in general agreement with the medical necessity of positron emission tomography (PET) for myocardial viability or for patients with an indeterminate single photon emission computed tomography (SPECT) scan. However, reviewers disagreed on using a strict body mass index cutoff to define patients in whom a SPECT scan would be expected to be suboptimal. Therefore, the language of the policy statement was changed to "Cardiac PET scanning may be considered medically necessary to assess myocardial perfusion and thus diagnose coronary artery disease in patients with indeterminate SPECT scan; or in patients for whom SPECT could be reasonably expected to be suboptimal in quality on the basis of body habitus."

Three reviewers responded to the question of whether PET scanning was medically necessary for the workup of patients with suspected cardiac sarcoidosis. All 3 agreed that PET scanning was medically necessary for this patient group. Two of these reviewers indicated that magnetic resonance imaging (MRI) scanning was the preferred test in the workup of cardiac sarcoidosis but that PET scanning was medically necessary for patients who were unable to undergo MRI. As a result, an additional indication was added to the policy statement for workup of cardiac sarcoidosis: "Cardiac PET scanning may be considered medically necessary for the diagnosis of cardiac sarcoidosis in patients who are unable to undergo MRI scanning. Examples of patients who are unable to undergo MRI include, but are not limited to, patients with pacemakers, automatic implanted cardioverter defibrillators, or other metal implants."

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Society for Nuclear Cardiology/Society of Nuclear Medicine and Molecular Imaging
The American Society of Nuclear Cardiology (ASNC) and the Society of Nuclear Medicine and Molecular Imaging (SNMMI) (2016) updated their joint guideline on procedure standards for cardiac PET procedures.[51,] PET myocardial perfusion imaging is used "to detect physiologically significant coronary artery narrowing to guide clinical management of patients with known or suspected CAD [coronary artery disease] and those without overt CAD but with cardiovascular risk factors in order to: evaluate the progression of atherosclerosis, determine cause of ischemic symptoms and recommend medical or revascularization therapy, estimate the potential for future adverse events, and improve patient survival." Perfusion defects can be reported through qualitative scoring, semiquantitative scoring systems, or absolute quantification of myocardial blood flow (MBF). The guideline is limited by not providing direct recommendations with

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associated levels of evidence and strength of recommendations. However, the authors note that "quantitative absolute MBF measurements with PET appear most helpful in:

- patients without known prior history of cardiac disease who present with symptoms suspicious for myocardial ischemia,
- patients with known CAD, in whom more specific physiological assessment is desired,
- identifying an increased suspicion for multivessel CAD,
- situations with a disparity between visual perfusion abnormalities and apparently normal coronary angiography, in order to assess possible microvascular dysfunction, and
- heart transplant when there is a question of vasculopathy.

In contrast, there are particular patients for whom reporting hyperemic blood flow or flow reserve may not add diagnostic value or can be ambiguous or misleading, including:

- patients post-CABG [coronary artery bypass graft] who can have diffuse reduction on MBF despite patent grafts,
- patients with large transmural infarcts where resting flow may be severely reduced such that small increases in flow lead to normal or near-normal flow reserve,
- patients with advanced severe chronic renal dysfunction who likewise often have diffuse coronary disease, and
- patients with severe LV [left ventricular] dysfunction."

A joint position paper from SNMMI/ASNC (2018) further discussed clinical quantification of MBF.[52,] Stress MBF and myocardial reserve flow (MFR) are associated with improved diagnostic sensitivity, but specificity has varied in studies. Treatment guidance noted that "[a]t present there are no randomized data supporting the use of any stress imaging modality for selection of patients for revascularization or for guidance of medical therapy. Observational data have established a paradigm that patients with greater degrees of ischemia on relative MPI [myocardial perfusion imaging] are more likely to benefit from revascularization. This paradigm has been conceptually extended to include MFR and stress MBF but has not yet been evaluated prospectively." The following key points were highlighted:

- "Use of stress MBF and MFR for diagnosis is complex, as diabetes, hypertension, age, smoking, and other risk factors may decrease stress MBF and MFR without focal epicardial stenosis.
- Patients with preserved stress MBF and MFR are unlikely to have high-risk epicardial CAD.
- Preserved stress MBF of more than 2 mL/min/g and MFR of more than 2 reliably exclude the presence of high-risk angiographic disease (negative predictive value > 95%) and are reasonable to report when used in clinical interpretation.
- A severely decreased global MFR (<1.5 mL/min/g) should be reported as a high-risk feature for adverse cardiac events but is not always due to multivessel obstructive disease. The likelihood of multivessel obstructive disease may be refined by examination of the electrocardiogram, regional perfusion, coronary calcification, and cardiac volumes and function.
- Regional decreases in stress MBF (<1.5 mL/min/g) and MFR (<1.5) in a vascular territory may indicate regional flow-limiting disease."

The position paper additionally calls for further data on quantifying MBF and MFR in suspected or established CAD: "[t]hese methods are at the cusp of translation to clinical practice. However, further efforts are necessary to standardize measures across laboratories, radiotracers,

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equipment, and software. Most critically, data are needed supporting improved clinical outcomes when treatment selection is based on these measures."

A joint expert consensus document from SNMMI/ASNC (2017) covered the role of F-18 FDG PET for cardiac sarcoidosis detection and therapy monitoring.[47,] The document discusses the need to integrate multiple sources of data, including F-18 FDG PET in some cases, to diagnose cardiac sarcoidosis. The following outlines clinical scenarios where cardiac PET may be useful in patients with suspected or known disease. Associated levels of evidence and strength of recommendations were not provided with these scenarios.

- "Patients with histologic evidence of extraCS [extracardiac sarcoidosis], and abnormal screening for CS [cardiac sarcoidosis], defined as one or more of following:
    - Abnormal electrocardiographic findings of complete left or right bundle branch block or presence of unexplained pathologic Q waves in two or more leads
    - Echocardiographic findings of regional wall motion abnormality, wall aneurysm, basal septum thinning, or LVEF [left ventricular ejection fraction] ≤ 50%
    - Holter findings of sustained or nonsustained ventricular tachycardia
    - Cardiac MRI findings suggestive of CS
    - Unexplained palpitations or syncope
- Young patients (<60 y) with unexplained, new onset, significant conduction system disease (such as sustained second- or third-degree atrioventricular block)
- Patients with idiopathic sustained ventricular tachycardia, defined as not fulfilling any of the following criteria:
    - Typical outflow tract ventricular tachycardia
    - Fascicular ventricular tachycardia
    - Ventricular tachycardia secondary to other structural heart disease (coronary artery disease or any cardiomyopathy other than idiopathic)
- Patients with proven CS as adjunct to follow response to treatment"

American College of Cardiology et al

The American College of Cardiology (ACC) Foundation and American Heart Association (AHA) (2009) collaborated with 6 other imaging societies to develop Appropriate Use Criteria for cardiac radionuclide imaging.[53,] Their report stated:

"...use of cardiac radionuclide imaging for diagnosis and risk assessment in intermediate- and high-risk patients with coronary artery disease (CAD) was viewed favorably, while testing in low-risk patients, routine repeat testing, and general screenings in certain clinical scenarios were viewed less favorably. Additionally, use for perioperative testing was found to be inappropriate except for high selected groups of patients."

American College of Radiology

The American College of Radiology (ACR) Appropriateness Criteria (2016) considered both SPECT and PET to be appropriate for the evaluation of patients with a high probability of CAD.[54,] The ACR indicated that PET perfusion imaging has advantages over SPECT, including higher spatial and temporal resolution. Routine performance of both PET and SPECT are unnecessary. The 2017 update[55,] stated:

"Hybrid PET scanners use CT [computed tomography] for attenuation correction (PET/CT) following completion of the PET study. By coupling the PET perfusion examination findings to a

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CCTA [cardiac computed tomographic angiography], PET/CT permits the fusion of anatomic coronary arterial and functional (perfusion) myocardial information and enhances diagnostic accuracy. The fused examinations can accurately measure the atherosclerotic burden and identify the hemodynamic functional significance of coronary stenosis. The results of the combined examinations can more accurately identify patients for revascularization."

The ACR Appropriateness Criteria (2018) also recommended PET for the evaluation of patients with chronic chest pain that is unlikely to be from a noncardiac etiology and low-to-intermediate probability of CAD.[56,]

The ACR does not recommend PET for patients with acute nonspecific chest pain who have a low probability of CAD[57,] or for asymptomatic patients at risk for CAD.[58,]

Society of Nuclear Medicine and Molecular Imaging, et al
A joint guidance from SNMMI/ACC/ASNC/AHA/Canadian Cardiovascular Society/Canadian Society of Cardiovascular Nuclear and CT Imaging/Society of Cardiovascular CT/American College of Physicians/European Association of Nuclear Medicine (2020) developed appropriate use criteria for PET myocardial perfusion imaging for the most common scenarios encountered.[59,] The summary of recommendations for patients with suspected or known CAD with symptoms state that rest-stress PET myocardial perfusion imaging is appropriate for those with an intermediate-to-high pretest likelihood of disease regardless of whether the patient has a normal electrocardiogram result or can (or cannot) exercise. In ordering tests, both the diagnostic accuracy and prognostic value are considerations. In patients with a low pretest likelihood of disease, PET myocardial perfusion imaging is not appropriate. The document also stated: "[o]nly a few studies describe the effects of PET MPI [myocardial perfusion imaging] perfusion and flow quantification on the clinical decision-making process and clinical outcome, which thus warrants further evaluation in well-designed and large-scale clinical trials."

For the evaluation of patients with known or suspected cardiac sarcoidosis, "rest PET MPI [myocardial perfusion imaging] was rated by the experts as appropriate in patients undergoing assessment of myocardial inflammation with ^{18}F-FDG PET at baseline and during reevaluation for response to therapy or recurrent inflammation.[59,] In contrast, stress MPI was rated as may be appropriate in the evaluation of patients with suspected sarcoidosis who have not been previously evaluated for CAD, and as rarely appropriate in patients with suspected sarcoidosis who have been previously evaluated for CAD."

American Thoracic Society
The American Thoracic Society (2020) published guideline recommendations on detection and diagnosis of sarcoidosis.[46,] This guideline generally recommends cardiac MRI over PET or transthoracic echocardiography (TTE) for obtaining diagnostic or prognostic information in patients with sarcoidosis and potential cardiac involvement. In cases where cardiac MRI is unavailable or inconclusive, PET is recommended over TTE to obtain diagnostic or prognostic information. Both of these recommendations are conditional and based on very low-quality evidence.

U.S. Preventive Services Task Force Recommendations
No U.S. Preventive Services Task Force recommendations for the use of PET in cardiac imaging have been identified.

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Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01288560	Alternative Imaging Modalities in Ischemic Heart Failure (AIMI-HF) Project I-A of Imaging Modalities to Assist With Guiding Therapy and the Evaluation of Patients With Heart Failure (IMAGE-HF)	1511	Jun 2022
NCT00756379	Randomized Trial of Comprehensive Lifestyle Modifications, Optimal Pharmacological Treatment and PET Imaging for Detection and Management of Stable Coronary Artery Disease	1085	Mar 2022

NCT: national clinical trial.

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CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS

78429 Single metabolic evaluation with CT transmission.
78430 Myocardial imaging, PET; single; with CT transmission
78431 Myocardial imaging, PET; multiple; with CT transmission
78432 Myocardial imaging, PET, (perfusion with metabolic evaluation)
78433 Myocardial imaging, PET, (perfusion with metabolic evaluation); with CT transmission scan
78434 Absolute quantitation of myocardial blood flow, PET
78459 Myocardial imaging, positron emission tomography (PET), metabolic evaluation study (including ventricular wall motion[s] and/or ejection fraction[s], when performed), single study
78491 Myocardial imaging, positron emission tomography (PET), perfusion study (including ventricular wall motion[s] and/or ejection fraction[s], when performed); single study, at rest or stress (exercise or pharmacologic)
78492 Myocardial imaging, positron emission tomography (PET), perfusion study (including ventricular wall motion[s] and/or ejection fraction[s], when performed); multiple studies at rest and stress (exercise or pharmacologic)
A9526 Nitrogen N-13 ammonia, diagnostic, per study dose, up to 40 millicuries
A9552 Fluorodeoxyglucose F-18 FDG, diagnostic, per study does, up to 45 millicuries
A9555 Rubidium Rb-82, diagnostic, per study dose, up to 60 millicuries
A9598 Positron emission tomography radiopharmaceutical, diagnostic, for non-tumor identification, not otherwise classified
G0235 PET imaging, any site, not otherwise specified

- A PET scan essentially involves 3 separate activities:
  (1) manufacture of the radiopharmaceutical, which may be manufactured on site or at a regional center with delivery to the institution performing PET;
  (2) actual performance of the PET scan; and
  (3) interpretation of the results.

ICD-10 DIAGNOSES

A18.84 Tuberculosis of heart
D86.85 Sarcoid myocarditis
I20.0 Unstable angina
I20.1 Angina pectoris with documented spasm
I20.8 Other forms of angina pectoris

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ICD-10 DIAGNOSES

I20.9	Angina pectoris, unspecified
I21.01	ST elevation (STEMI) myocardial infarction involving left main coronary artery
I21.02	ST elevation (STEMI) myocardial infarction involving left anterior descending coronary artery
I21.09	ST elevation (STEMI) myocardial infarction involving other coronary artery of anterior wall
I21.11	ST elevation (STEMI) myocardial infarction involving right coronary artery
I21.19	ST elevation (STEMI) myocardial infarction involving other coronary artery of inferior wall
I21.21	ST elevation (STEMI) myocardial infarction involving left circumflex coronary artery
I21.29	ST elevation (STEMI) myocardial infarction involving other sites
I21.3	ST elevation (STEMI) myocardial infarction of unspecified site
I21.4	Non-ST elevation (NSTEMI) myocardial infarction
I21.9	Acute myocardial infarction, unspecified
I21.A1	Myocardial infarction type 2
I21.A9	Other myocardial infarction type
15A	Non-ischemic myocardial injury (non-traumatic) Effective 10-01-2021
I22.0	Subsequent ST elevation (STEMI) myocardial infarction of anterior wall
I22.1	Subsequent ST elevation (STEMI) myocardial infarction of inferior wall
I22.2	Subsequent non-ST elevation (NSTEMI) myocardial infarction
I22.8	Subsequent ST elevation (STEMI) myocardial infarction of other sites
I22.9	Subsequent ST elevation (STEMI) myocardial infarction of unspecified site
I24.0	Acute coronary thrombosis not resulting in myocardial infarction
I24.1	Dressler's syndrome
I24.8	Other forms of acute ischemic heart disease
I24.9	Acute ischemic heart disease, unspecified
I25.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
I25.110	Atherosclerotic heart disease of native coronary artery with unstable angina pectoris
I25.111	Atherosclerotic heart disease of native coronary artery with angina pectoris with documented spasm
I25.118	Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris
I25.119	Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris
I25.2	Old myocardial infarction
I25.3	Aneurysm of heart
I25.41	Coronary artery aneurysm
I25.42	Coronary artery dissection
I25.5	Ischemic cardiomyopathy
I25.6	Silent myocardial ischemia
I25.700	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris
I25.701	Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with documented spasm
I25.708	Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina pectoris

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ICD-10 DIAGNOSES

I25.709 Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina pectoris
I25.710 Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris
I25.711 Atherosclerosis of autologous vein coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.718 Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of angina pectoris
I25.719 Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina pectoris
I25.720 Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris
I25.721 Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.728 Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of angina pectoris
I25.729 Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified angina pectoris
I25.730 Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable angina pectoris
I25.731 Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.738 Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms of angina pectoris
I25.739 Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unspecified angina pectoris
I25.750 Atherosclerosis of native coronary artery of transplanted heart with unstable angina
I25.751 Atherosclerosis of native coronary artery of transplanted heart with angina pectoris with documented spasm
I25.758 Atherosclerosis of native coronary artery of transplanted heart with other forms of angina pectoris
I25.759 Atherosclerosis of native coronary artery of transplanted heart with unspecified angina pectoris
I25.760 Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable angina
I25.761 Atherosclerosis of bypass graft of coronary artery of transplanted heart with angina pectoris with documented spasm
I25.768 Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of angina pectoris
I25.769 Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified angina pectoris
I25.790 Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris
I25.791 Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.798 Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris

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ICD-10 DIAGNOSES

I25.799 Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris
I25.810 Atherosclerosis of coronary artery bypass graft(s) without angina pectoris
I25.811 Atherosclerosis of native coronary artery of transplanted heart without angina pectoris
I25.812 Atherosclerosis of bypass graft of coronary artery of transplanted heart without angina pectoris
I25.89 Other forms of chronic ischemic heart disease
I25.9 Chronic ischemic heart disease, unspecified
I42.0 Dilated cardiomyopathy
I42.3 Endomyocardial (eosinophilic) disease
I42.4 Endocardial fibroelastosis
I42.5 Other restrictive cardiomyopathy
I42.6 Alcoholic cardiomyopathy
I42.7 Cardiomyopathy due to drug and external agent
I42.8 Other cardiomyopathies
I42.9 Cardiomyopathy, unspecified
I43 Cardiomyopathy in diseases classified elsewhere
I47.0 Re-entry ventricular arrhythmia
I47.1 Supraventricular tachycardia
I49.2 Junctional premature depolarization
I50.1 Left ventricular failure, unspecified
I50.810 Right heart failure, unspecified
I50.811 Acute right heart failure
I50.812 Chronic right heart failure
I50.813 Acute on chronic right heart failure
I50.814 Right heart failure due to left heart failure
I50.82 Biventricular heart failure
I50.83 High output heart failure
I50.84 End stage heart failure
I50.89 Other heart failure
I51.5 Myocardial degeneration
I51.7 Cardiomegaly
I51.89 Other ill-defined heart diseases
I51.9 Heart disease, unspecified

REVISIONS	
10-30-2013	Cardiac Applications was originally part of the Positron Emission Tomography (PET) medical policy. Cardiac Applications was pulled out and placed into a separate medical policy, Positron Emission Tomography (PET) Scanning: Cardiac Applications. The medical policy language was unchanged.
	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Added ICD-10 Diagnosis codes *(Effective October 1,2014)*
	Updated Reference section.

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10-22-2015	Description section updated
	In Policy section: ▪ In Item A removed the example in the policy statement, "(e.g., obesity)" ▪ In Item B added "(See the Policy Guidelines section regarding the relative effectiveness of PET and SPECT scanning.)" ▪ In Item C revised wording by removing "the diagnosis of" and adding "diagnosing" to read "Cardiac PET scanning may be considered medically necessary for diagnosing cardiac sarcoidosis in patients…" ▪ Added Item D "Cardiac PET scanning is experimental / investigational for quantification of myocardial blood flow in patients diagnosed with CAD." ▪ Policy Guidelines updated to reflect current information on relative effectiveness of PET and SPECT scanning.
	Rationale section updated
	In Coding section: ▪ Removed CPT Code: 78399 ▪ Added HCPCS Code: A9555 ▪ Updated Coding notations
	References updated
10-01-2017	In Coding section: ▪ Removed ICD Code: I50.9 ▪ Added ICD Code: I21.9, I21.A1, I21.A9, I50.810, I50.811, I50.812, I50.813, I50.814, I50.82, I50.83, I50.84, I50.89 ▪ Revised nomenclature of ICD Code: I50.1
11-26-2018	Policy published October 26, 2018. Policy effective November 26, 2018.
	Description section updated
	In Policy section: Updates to the policy section did not change the intent of the policy. ▪ In Item A added verbiage for "PET" and "SPECT" to read "Cardiac positron emission tomography (PET) scanning…single-photon emission computed tomography (SPECT) scan…" ▪ In Item B revised "Policy Guidelines" to "Background" to read "…(See the Background Policy Guidelines section regarding the relative effectiveness of PET and SPECT scanning.)" ▪ In Item C removed "MRI" and replaced with "magnetic resonance imaging" and removed "(AICDs)" abbreviation. ▪ In Item D removed "CAD" to read "…diagnosed with coronary artery disease." ▪ Removed Policy Guidelines-myocardial perfusion and myocardial viability definitions.
	Rationale section updated
	In coding section: ▪ Added CPT Code: 0482T ▪ Add HCPCS Code: A9598, G0235 ▪ Added ICD Code: D86.85
	References updated
01-01-2020	In Coding section: ▪ Added CPT Codes: 78429, 78430, 78431, 78432, 78433, 78434 ▪ Revised CPT Codes: 78459, 78491, 78492 ▪ Removed CPT Code: 0482T
05-18-2020	Description section updated
	Rationale section updated
	References updated
10-01-2021	In Coding section (Effective 10-01-2021) Added ICD-10 code 15A
12-2-2021	Updated Description section

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	In Policy section ▪ Added Section E: All other indications for Cardiac positron emission tomography (PET) scanning are considered not medically necessary
	Updated Rationale Section
	Updated Reference Section

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