American College of Radiology ACR Appropriateness Criteria[®] Suspected New-Onset and Known Nonacute Heart Failure

<u>Variant 1:</u>

Suspected new-onset nonacute heart failure, not previously diagnosed. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US echocardiography transthoracic resting	Usually Appropriate	0
Radiography chest	Usually Appropriate	۲
CTA coronary arteries with IV contrast	May Be Appropriate (Disagreement)	���
MRI heart function and morphology without and with IV contrast	May Be Appropriate (Disagreement)	0
Arteriography coronary	Usually Not Appropriate	€€€
FDG-PET/CT heart	Usually Not Appropriate	♦€€€
MRI heart function and morphology without IV contrast	Usually Not Appropriate	0
MRI heart with function and inotropic stress without and with IV contrast	Usually Not Appropriate	0
MRI heart with function and inotropic stress without IV contrast	Usually Not Appropriate	0
MRI heart with function and vasodilator stress perfusion without and with IV contrast	Usually Not Appropriate	0
Rb-82 PET/CT heart	Usually Not Appropriate	∞∞∞∞
SPECT or SPECT/CT MPI rest and stress	Usually Not Appropriate	ଡ଼ଡ଼ଡ଼ଡ଼
Nuclear medicine ventriculography	Usually Not Appropriate	€€€
US echocardiography transthoracic stress	Usually Not Appropriate	0

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Variant 2:

Differentiating new-onset heart failure with reduced ejection fraction (HFrEF) from newonset heart failure with preserved ejection fraction (HFpEF).

Procedure	Appropriateness Category	Relative Radiation Level
US echocardiography transthoracic resting	Usually Appropriate	0
MRI heart function and morphology without and with IV contrast	Usually Appropriate	0
MRI heart function and morphology without IV contrast	Usually Appropriate	0
Nuclear medicine ventriculography	May Be Appropriate	€€
Arteriography coronary	May Be Appropriate	��€
CTA coronary arteries with IV contrast	May Be Appropriate	���
FDG-PET/CT heart	Usually Not Appropriate	€€€€
MRI heart with function and inotropic stress without and with IV contrast	Usually Not Appropriate	0
MRI heart with function and inotropic stress without IV contrast	Usually Not Appropriate	0
MRI heart with function and vasodilator stress perfusion without and with IV contrast	Usually Not Appropriate	0
Rb-82 PET/CT heart	Usually Not Appropriate	€€€€
SPECT or SPECT/CT MPI rest and stress	Usually Not Appropriate	€€€€
US echocardiography transthoracic stress	Usually Not Appropriate	0
Radiography chest	Usually Not Appropriate	•

Variant 3:

Confirmed new-onset heart failure with reduced ejection fraction of uncertain etiology: ischemic versus nonischemic.

Procedure	Appropriateness Category	Relative Radiation Level
CTA coronary arteries with IV contrast	Usually Appropriate	��€
MRI heart function and morphology without and with IV contrast	Usually Appropriate	0
MRI heart with function and vasodilator stress perfusion without and with IV contrast	Usually Appropriate	О
SPECT or SPECT/CT MPI rest and stress	Usually Appropriate	€€€€
Arteriography coronary	Usually Appropriate	€€
Rb-82 PET/CT heart	Usually Appropriate	€€€€
US echocardiography transthoracic stress	Usually Appropriate	0
MRI heart with function and inotropic stress without and with IV contrast	May Be Appropriate	0
MRI heart with function and inotropic stress without IV contrast	May Be Appropriate	0
FDG-PET/CT heart	May Be Appropriate (Disagreement)	$\textcircled{\begin{tabular}{lllllllllllllllllllllllllllllllllll$
MRI heart function and morphology without IV contrast	May Be Appropriate	0
Nuclear medicine ventriculography	Usually Not Appropriate	€€
US echocardiography transthoracic resting	Usually Not Appropriate	0
Radiography chest	Usually Not Appropriate	۲

SUSPECTED NEW-ONSET AND KNOWN NONACUTE HEART FAILURE

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Summary of Literature Review

Introduction/Background

Heart failure (HF) is a highly prevalent and complex clinical syndrome resulting from any structural or functional impairment of ventricular filling or ejection of blood [1]. HF may result from disorders of the pericardium, myocardium, valves, or great vessels as well as from certain systemic metabolic abnormalities [1].

It is estimated that approximately 5.7 million Americans ≥ 20 years of age already suffer from HF [2,3]. Unfortunately, it is projected that the prevalence of HF will increase by 46% between 2012 and 2030, with over 910,000 new HF cases appearing annually and resulting in >8 million people ≥ 18 years of age with HF [2,4]. By 40 years of age, the lifetime risk of developing HF in an adult is currently one in five, with 75% of HF cases having antecedent hypertension [5].

While survival after the initial manifestation of HF has improved because of greater evidence-based treatment of risk factors and complications [6,7], the death rate remains high, with approximately 50% of HF cases dying within 5 years of initial diagnosis [7,8]. One in 9 deaths had HF mentioned on the death certificate, and HF was the underlying cause in over 60,000 deaths in 2013 [9].

There is significant financial impact associated with HF, which is likely to increase in coming decades. In 2012, the total expense related to HF nationally was estimated to be \$30.7 billion, with 68% attributable to direct medical costs [4]. By 2030, the total annual expense of HF is projected to increase by almost 127% to \$69.7 billion [4].

There is no single diagnostic test for HF because it is largely a clinical diagnosis based on a careful history and physical examination [1]. Nevertheless, because most patients with HF become symptomatic because of impaired myocardial function of the left ventricle (LV) [1], imaging plays an important supportive role beginning with the confirmation of HF as the cause of the patients' presenting signs and symptoms, especially by detecting LV dysfunction (see Variant 1). This diagnostic phase overlaps with reported approaches to appropriate use of imaging in the setting of dyspnea of suspected cardiac origin (see the ACR Appropriateness Criteria[®] topic on "Dyspnea-Suspected Cardiac Origin" [10]).

Ejection fraction (EF) is considered important in the classification of HF cases because of differing patient demographics, comorbid conditions, prognosis, and response to therapies [11] and because of the fact that most clinical trials select patients based on EF [1]. Consequently, imaging plays a subsequent key role in the basic differentiation between HF with reduced EF (HFrEF) typically to $\leq 40\%$ on the one hand, and HF with preserved EF (HFpEF) typically at $\geq 50\%$ (borderline HFpEF LVEF = 41%–49%) on the other hand (see Variant 2) [1,12]. Randomized controlled trials have primarily enrolled patients with HFrEF, and it is only in these patients that efficacious therapies have been demonstrated to date [1]. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggesting HF [13]; consistently effective therapies for HFpEF have not been identified to date [1].

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HFrEF is typically found in the setting of a form of dilated cardiomyopathy, representing a large group of heterogeneous myocardial disorders characterized by ventricular dilation and depressed myocardial contractility in the absence of abnormal loading conditions (eg, hypertension or valvular disease) [1]. In clinical practice and multicenter HF trials, the etiology of HF has often been categorized into either ischemic cardiomyopathy or nonischemic cardiomyopathy [1,14]. Thus, once a case of HFrEF has been identified, the basic distinction between an ischemic etiology and a nonischemic etiology with the support from imaging (see Variant 3) facilitates further diagnostic assessment and therapeutic planning, with guidance in further imaging provided by other reports on appropriate use of imaging [15].

Overview of Imaging Modalities

Radiography Chest

Information provided by chest radiography about: (1) noncardiovascular (eg, lung parenchymal disease) and cardiovascular (eg, cardiomegaly) anatomy of the chest [16]; (2) pulmonary vascular and edema patterns (eg, stages of pulmonary venous hypertension) [17]; and (3) vascular (eg, chronic coronary atherosclerosis) [18] and nonvascular (eg, calcified pericardial thickening) [19] calcification has potential applications to evaluation of the aforementioned HF variants. The appropriateness of the chest radiograph in the setting of suspicion of acute or potentially unstable chronic cardiopulmonary disease by history or physical examination has been previously established [20].

US Echocardiography Transthoracic Stress or Resting

Echocardiography relies on ultrasonic waves to produce dynamic, usually tomographic versus volumetric images emphasizing a wide range of functional measures of cardiac chamber function and intravascular and intracavity flow in normal and various disease states, including HF, from which important hemodynamic measurements can be made in most patients noninvasively by transthoracic echocardiography (TTE) [21,22]. Despite its relatively weaker anatomic and histologic evaluation capabilities compared to some other cardiac imaging modalities, its risk-free nature, unless performed more invasively as transesophageal echocardiography (TEE), facilitates its use in the assessment of HF.

SPECT or SPECT/CT MPI Rest and Stress

Utilizing intravenously administered tracers, Single-photon emission computed tomography (SPECT) or SPECT/CT (ie, SPECT with CT attenuation correction) can provide insights into cardiac pathophysiology, including abnormalities of ventricular function (global and regional) and myocardial perfusion imaging (MPI) [23-25].

FDG-PET/CT Heart and Rb-82 PET/CT Heart

Utilizing rubidium-82 (Rb-82), PET/CT is capable of reflecting myocardial physiology, including perfusion, wall motion, and cardiac flow reserve; this can be valuable in assessing HF [23-25]. Evaluation of myocardial viability can be performed utilizing fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) as the PET agent [23-25].

MRI Heart

Cardiac MRI remains heavily reliant on electrocardiographic referencing of imaging data acquisition to the cardiac cycle and uses a magnetic field and radio waves to create detailed tomographic or volumetric images of high contrast. Depending upon the imaging acquisition employed and whether or not a gadolinium-based contrast agent was used and how and when administered relative to data acquisition, images demonstrating a range of abnormalities of (1) anatomy (eg, reduced thickness of ventricular wall, enlargement of atrial cavity, or increased thickness of pericardial sac); (2) histology (eg, myocardial edema, infiltration, deposition, or fibrosis); or (3) physiology (eg, depressed LVEF, restrictive transatrioventricular diastolic inflow, or reduced resting versus stress-induced myocardial strain or first-pass perfusion) [26-28]. These capabilities are potentially beneficial in assessing HF. Potential complications must be considered on a patient-by-patient basis before its use.

CTA Coronary Arteries

Referencing of image acquisition to the electrocardiographic recording facilitates high temporal and spatial resolution images of cardiovascular tissues that, when combined with intravenously administered iodinated contrast agents, permits primarily for the evaluation of coronary artery disease (CAD) as an etiology for newly diagnosed HF (coronary CT angiography [CTA]). Additionally, these advances can also be used for imaging during dynamic bolus contrast enhancement for the assessment of first-pass tissue perfusion (eg, myocardium) at rest or during pharmacologically induced stress, or the volumetric visualization of intraluminal/intracavity anatomy (eg, coronary artery, LV chamber) or arterial wall changes in static images (ie, CTA; or, without the use

of intravenous contrast for coronary calcification, calcium scoring for risk stratification). Delayed imaging helps further the detection of fibrous or fatty tissue replacement in cardiac structures (eg, LV wall) [26,29,30]. Despite marked improvements, prevailing concerns about potential complications are still limitations to the use of this modality.

Arteriography Coronary

Although a traditional gold standard for diagnosing disease of the coronary arteries or ventricles, conventional catheter-based selective coronary angiography is increasingly focused (eg, 38%) on patient-centric atherosclerotic CAD treatment planning or postrevascularization assessment [31]. It is supported by several complementary technologies allowing further characterization of plaque significance (eg, intravascular ultrasonography [US], fractional flow reserve) [32,33]. While concurrent LV ventriculography is dissuaded for LVEF determinations [34], direct hemodynamic measurements reflecting cardiac function maintain a distinct role in assessing a range of cardiovascular conditions in complicated clinical cases.

Stress Examinations

The objective of stress testing is typically to evaluate the extent and adequacy of the hyperemic response, thereby assessing the ability of the coronary circulation to augment flow to meet increasing work demand (ie, coronary flow reserve) [35]. When used in combination with imaging, depending on the degree and duration of induced ischemia, stress testing elicits and evaluates the ischemic endpoints that relate to coronary supply or demand imbalance characteristic of CAD. This ischemic cascade includes sequential abnormalities in the following order: perfusion, myocardial stiffening, wall motion abnormalities, electrocardiographic stress test segment changes, and chest pain.

When appropriate, exercise-based stress testing is preferred to pharmacologically induced stress testing; unfortunately, it is impractical in many imaging environments, moreover for patients unable to adequately exercise [35]. Thus, the pharmacologic stress perfusion endpoint (achieved with a coronary artery dilating agent, such as adenosine or regadenoson) of induced coronary flow heterogeneity is used with the various forms of MPI; the functional ischemic endpoint (achieved with a myocardial inotropic agent, such as dobutamine) of induced with a myocardial inotropic agent, such as dobutamine) of induced will motion abnormalities is detected and monitored during dynamic myocardial contraction imaging.

Discussion of Procedures by Variant

Prompt evidence-based diagnosis and treatment of new-onset nonacute HF may help decrease hospital stay, costs related to treatment, and mortality. Unfortunately, the accurate diagnosis of HF in the primary care setting is difficult and partly related to frequent suboptimal access to, and use of, cardiac imaging [36].

Variant 1: Suspected new-onset nonacute heart failure, not previously diagnosed. Initial imaging.

Radiography Chest

Historically, chest radiograph has been commonly used in the assessment of patients with suspected new-onset HF in the outpatient setting. Regardless of the acuity of new-onset HF, it is prudent to consider the impact of the training, experience, and focus of the chest radiography interpreter. For patients presenting to the emergency department (ED) with supportive clinical and laboratory evidence of HF, the accuracy in identifying HF on chest radiograph can vary from 78% for first-year emergency medicine residents, 85% for emergency medicine attendees, and 95% for radiologists [37].

A radiological score based on the sum of selected signs of congestion on chest radiograph correlates well with both findings on physical examination and lung impedance measurements during periods of sudden onset of HF [38]. Accordingly, in patients presenting to an ED with signs and symptoms of HF, those with sudden onset more likely demonstrate evidence of congestion on chest radiograph than those without sudden onset [39].

However, in ambulatory patients being evaluated in the community for suspected new-onset HF with standardized diagnostic evaluation, including chest radiography and TTE, a combination of 3 items from history plus 6 from physical examination have independent diagnostic value (c-statistic 0.83), increasing when supplemented by N-terminal pro-B-type natriuretic peptide (NT-proBNP) (c-statistic 0.86); chest radiography does not make a significant diagnostic contribution [40].

US Echocardiography Transthoracic Resting and Stress

Evaluation of cardiac structure and function for newly suspected or potential HF, with rest-only echocardiography for the assessment of cardiac structure and function can be made accurately to guide therapy. Multicenter studies

have demonstrated the value of various echocardiographic measures of cardiac structure and function as indicators of subclinical HF and risk for subsequent HF events [41-46].

A simple clinical rule based on gender, history of myocardial infarction, presence of ankle edema, and presence of basal lung crepitations discriminates between people with suspected HF who should be referred straight to TTE and those for whose referral should depend upon the NT-proBNP results [36]. Using a two-round RAND appropriateness method, general practitioners with or without specialty interests in cardiology determined in patients presenting with suspected HF that an abnormal electrocardiogram or NT-proBNP level justifies referral to TTE, especially in the presence of dyspnea [47]. Along with bedside lung US, TTE appears to be the most useful test for affirming the presence of sudden-onset HF, although not as valuable in excluding the diagnosis [48]. Although now generally endorsed that a complete HF evaluation includes TTE [49], not all evidence supports its universal use across these particular settings. Specifically in the ED setting, TTE allows rapid identification of sudden-onset left-sided HF with an overall accuracy of 90% (95% CI, 84%–95%), significantly better than 67% (95% CI, 57%–75%; P = .0001) for clinical examination, and trending better than 81% (95% CI, 72%–88%; P = .04) for the combination clinical examination NT-proBNP and chest radiography [50].

Independent of and incremental to basic parameters (eg, LV mass, left atrial [LA] size, and mitral regurgitation) provided by TTE, the following insights can be gained from more advanced echocardiographic techniques in the setting of suddenly decompensated ventricular function: (1) need for HF hospitalization based on LV global longitudinal strain derived using speckle-tracking technology [51]; (2) risk of all-cause 1-year mortality based on Doppler-determined transmitral to mitral annular early diastolic velocity ratio reflecting LV filling pressure [52]; and (3) risk for in-hospital mortality, rehospitalization, and cardiovascular mortality by early mitral inflow velocity to early diastolic mitral annular velocity reflecting LV filling pressure estimated with Doppler [53]. Cardiac filling pressures can be estimated from physical examination with modest accuracy, and exposure to echocardiographic data may not significantly enhance accuracy beyond bedside examination alone, both for left-heart and right-heart pressures [54].

However, in ambulatory patients being evaluated in the community for suspected of nonacute new-onset HF using standardized diagnostic evaluation, TTE was shown to not make a significant diagnostic contribution [40].

Nuclear Medicine Ventriculography

Radionuclide ventriculography (RNV) is an additional alternative that may be applied to the evaluation of cardiac function [41]. One of its benefits is its significant reproducibility, which has been used to track the efficacy of a variety of therapeutic interventions for patients with HF [41,55-57].

SPECT or SPECT/CT MPI Rest and Stress

There is no evidence to support the use of rest and stress SPECT/CT MPI as an initial imaging modality for suspected new-onset nonacute HF.

FDG-PET/CT Heart and Rb-82 PET/CT Heart

There are only minimal data on the use of PET/CT for evaluation of newly suspected or potential HF [23-25].

MRI Heart

In addition to the evaluation of cardiac structure and function by rest-only MRI, myocardial perfusion, viability, and fibrosis imaging can assist in identification of etiology and assess prognosis [41,58]. There is no evidence to support the use of rest and stress MRI.

CTA Coronary Arteries

There is limited evidence to support the use of cardiac CTA as initial imaging for the evaluation of patients with newly suspected or potential HF.

Arteriography Coronary

The invasive nature of coronary angiography limits its use for the assessment of patients with newly suspected or potential HF.

Variant 2: Differentiating new-onset heart failure with reduced ejection fraction (HFrEF) from new-onset heart failure with preserved ejection fraction (HFpEF).

Although LVEF has not been found to be a consistent risk marker [51], the distinction between reduced ($\leq 40\%$) and relatively preserved (borderline 41%–49% and totally $\geq 50\%$) LVEF is considered an important clinical and pathophysiologic distinction in the evaluation of patients presenting with suspected HF. However, this distinction

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is confounded by the following [1]: (1) in most symptomatic HF patients, variable balances of systolic and diastolic dysfunction coexist; and (2) derived LVEF values are dependent on the imaging modality used, method of analysis, and operator performance.

HFpEF is now the most common form of HF (approximately 50%; range 40%–71%), and it constitutes a growing health care burden worldwide [59,60]. Unfortunately, the diagnosis of HFpEF is particularly challenging for outpatient clinic practices [61].

Radiography Chest

While radiography may play a role in diagnosing HF, there is no evidence to support the use of chest radiographs for differentiating HFrEF from HFpEF.

US Echocardiography Transthoracic Resting and Stress

At the time of presentation of patients to the ED with new-onset symptomatic HF, the differentiation between HFpEF and HFrEF using TTE has prognostic significance, with HFpEF having higher noncardiovascular mortality but lower cardiovascular mortality compared to HFrEF [62].

Beyond conventional 2-D TTE or TEE evaluations, the use of new more sensitive and more specific technologies, such as tissue Doppler imaging (TDI), strain rate, speckle tracking, or 3-D imaging, has facilitated the identification of other high-risk parameters associated with adverse outcomes, which are useful in guiding therapy and follow-up management of HFrEF patients [63]. In outpatients with new-onset HF examined with TTE, including conventional Doppler and TDI, LA strain rate is significantly reduced in both HFrEF and HFpEF groups (without differences between them) compared with the non-HF group, with LA strain rate and indexed volume showing significant accuracy for HF diagnosis in receiver operating characteristic curves; however, LV strain rate shows no differences between non-HF and HFpEF groups, while both differed from the HFrEF group [64].

In patients with suddenly decompensated HF and presenting to the ED, point-of-care TTE has diagnostic sensitivity of 74% and specificity of 74% for HFrEF, changing to 36% and 100%, respectively, when combined with inferior vena cava collapsibility index and pleural sampling for B-lines; sensitivity and specificity of NT-proBNP >500 are 75% and 83%, respectively [65]. With the determination of HFrEF using TTE, LV filling pressure can be estimated well by LA expansion index, which predicts subsequent adverse events [66]. While early mitral inflow velocity to early diastolic mitral annular velocity on TTE with TDI is significantly higher in the elderly, compared to nonelderly, patients presenting with newly diagnosed suddenly decompensated HFrEF, there are no significant differences in in-hospital mortality, rehospitalization, and cardiovascular mortality during the following 45 months [53]. However, right ventricular (RV) systolic dysfunction, assessed using TTE with TDI of peak systolic velocity at the lateral tricuspid annulus, has prognostic significance in newly diagnosed HFrEF patients [67].

Diastolic dysfunction is widely considered a key pathophysiologic mediator of HFpEF. It is implicated as a major cause of shortness of breath on exertion in elderly primary-care patients who often are suffering from unrecognized HF (16%), more often from HFpEF (12%) than from either HFrEF (3%) or isolated right-sided HF (1%) as determined on TTE evaluation [68]. In dyspneic patients presenting to an ED, a basic bedside TTE diastolic evaluation performed by an emergency physician-sonographer with limited diastology-specific training (3 hours of didactic and hands-on training by a cardiologist) can accurately identify clinically significant diastolic dysfunction, although correct grading of dysfunction may be only moderately accurate [69].

Several TTE parameters, including ratio of early mitral inflow velocity to TDI velocity at lateral mitral annulus, LA volume index, and the difference between duration of reversed pulmonary vein LA systole flow and duration of mitral A wave flow, have the greatest value in diagnosing HFpEF (sensitivity of 77% and specificity of 81%) [70]. However, for the initial diagnosis of HFpEF, the association of NT-proBNP measurement and TTE with TDI is superior to the use of either one alone [61].

Certainly, echocardiography technologies have provided greater understanding of the complex pathophysiology related to HFpEF. From the application of TTE with speckle tracking [71], it is now known that HFpEF patients (1) demonstrate significantly lower longitudinal and circumferential strains compared to both normal patients and hypertensive heart disease patients, indicating the presence of underlying impaired LV systolic function [72]; (2) have significantly lower myocardial systolic and diastolic LV performance compared to patients with asymptomatic LV diastolic dysfunction, and this combined dysfunction is associated with increased LV filling

pressures, decreased cardiac output, and worse New York Heart Association functional class [73]; (3) showing LV mechanical dyssynchrony have significantly higher rates of LV longitudinal systolic (64%) and diastolic (70%) dysfunction than those without dyssynchrony, suggesting that restoration of asynchronous contractions could improve systolic and diastolic longitudinal LV dysfunction, as well as associated symptoms [74]; (4) have significantly more impaired RV longitudinal diastolic (RV global longitudinal early-diastolic strain rate) and systolic (RV global longitudinal systolic strain) function than matched asymptomatic patients with LV diastolic dysfunction, suggesting that RV longitudinal systolic and diastolic dysfunction could contribute to symptoms [75]; and (5) demonstrate significantly reduced LA longitudinal systolic (LA late diastolic strain rate) and diastolic dysfunction, suggesting that LA longitudinal systolic and diastolic dysfunction could be related to reduced functional capacity during effort [76]; accordingly, resting global peak LA longitudinal strain during LV systole has significant incremental diagnostic value over clinical and conventional TTE parameters (early diastolic mitral annular velocity ratio, LV mass index, and maximum LA volume index), and diagnostic value is further improved by adding leg-lifting during global peak LA longitudinal strain measurements (global chi-square = 72.2 versus 49.6; P < .0001) [77].

Peak mitral annular systolic velocity on TEE with TDI is a significant independent predictor of HFpEF, and when used in combination with exercise, it may increase the diagnostic value of models using the variables recommended by the European Society of Cardiology guidelines [78]. In addition, the assessment of longitudinal systolic and diastolic LV and RV function during a submaximal exercise stress TTE can confirm LV dysfunction related to HFpEF and might be used as a diagnostic test for difficult clinical situations [79]. In addition, it is known that within individual HFpEF cases, TTE with Doppler indexes of LV filling pressures (ie, early diastolic mitral annular velocity and E/Vp) do not reliably track directly measured filling pressures as these pressures vary, precluding the use of these techniques in the titration of medical therapy for HFpEF [80,81].

In HFpEF patients, global LV longitudinal strain measured using TTE with speckle tracking can help predict readmission within 30 days [51]. While global longitudinal strain is abnormal in HFpEF and is associated with a worse prognosis, it is not a powerful independent predictor of outcome [82]. However, exercise TTE may contribute to the identification of HFpEF patients, especially high-risk ones [83], and abnormal indices of LA mechanics, especially LA reservoir strain, are powerful clinical and prognostic factors in HFpEF [84].

Nuclear Medicine Ventriculography

Because RNV can be performed to assess LVEF and volumes [41], it has potential in differentiating between HFrEF and HFpEF.

SPECT or SPECT/CT MPI Rest and Stress

While there is no evidence to support the use of rest and stress SPECT/CT specifically for differentiating between HFrEF and HFpEF, gated SPECT/CT has potential in differentiating between these forms of HF.

FDG-PET/CT Heart and Rb-82 PET/CT Heart

While there is no evidence to support the use of PET/CT specifically for differentiating between HFrEF and HFpEF, cardiac gated PET/CT has potential in differentiating between these forms of HF.

MRI

In addition to the evaluation of cardiac structure and function using rest-only MRI, myocardial focal fibrosis quantified by late gadolinium enhanced (LGE)-MRI in patients with HFpEF is an independent predictor of future events after the adjustment for prognostic factors (ie, age, diabetes mellitus, New York Heart Association classification, history of HF hospitalization, and LVEF) previously identified in the Irbesartan in Heart Failure with Preserved Ejection Fraction study [85].

CTA Coronary Arteries

There is limited evidence to support the use of cardiac CTA for the differentiating patients with HFrEF from HFpEF.

Arteriography Coronary

While echocardiography is commonly used to diagnose and stage diastolic dysfunction, uncertainty in characterizing borderline cases may persist, and direct hemodynamic measurements may still be needed to establish a definitive diagnosis of HFpEF [86-88]. However, such invasive hemodynamic assessment is made without the need for concurrent coronary angiography or contrast LV ventriculography.

Variant 3: Confirmed new-onset heart failure with reduced ejection fraction of uncertain etiology: ischemic versus nonischemic.

Because of reversible or irreversible ischemic injury to the LV myocardium, CAD with or without a history of antecedent myocardial infarction remains a major source of HFrEF nationally [1]. Prompt differentiation of ischemic HFrEF from nonischemic HFrEF is important because patients with ischemic cardiomyopathy can potentially have dramatic improvement with specific therapy, including revascularization [14,89]. Thus, in the setting of new-onset nonacute HFrEF, it is important to distinguish between ischemic and nonischemic (eg, remote diffuse myocarditis, alcoholic cardiomyopathy) etiologies in order to guide further evaluation and treatment [15].

Radiography Chest

While radiography may play a role in diagnosing HF, there is no evidence to support the use of chest radiography for differentiating ischemic versus nonischemic etiology of HF.

US Echocardiography Transthoracic Resting and Stress

Several studies have demonstrated the utility of stress echocardiography to identify both resting and poststress systolic wall motion abnormalities [90-92]. Additionally, these findings correlate to clinical outcomes.

SPECT or SPECT/CT MPI Rest and Stress

With SPECT/CT MPI, sensitivity and negative predictive value are both excellent for detecting CAD in patients with HF with either reduced or preserved LVEF; however, the distinction between ischemic and nonischemic etiologies is more characteristic of the evaluation of HFrEF [93,94]. In dyspneic patients with HFrEF without concomitant chest pain, the nonglobal resting LV dysfunction and high-summed stress MPI-deficiency score on gated rest and stress SPECT serve as independent predictors of an ischemic etiology; although low in sensitivity, specificity is acceptable [95].

While standard MPI (more often performed with SPECT than PET) is often deficient in making that distinction because a nonischemic cardiomyopathy can have focal defects in tracer uptake and CAD with global balanced ischemia can result in a normal-appearing perfusion pattern, new developments in measuring quantitative blood flow have potential to provide a more accurate determination of HFrEF etiology [94].

Nuclear Medicine Ventriculography

RNV is used for the evaluation of cardiac function [41].

FDG-PET/CT Heart and Rb-82 PET/CT Heart

An advantage of the use of stress MPI with PET is its improved accuracy for the detection of severe, multivessel CAD when compared to SPECT alone. Additionally, PET markers of absolute peak stress LVEF measurements and myocardial perfusion reserve may improve detection of patients with CAD [41,96,97].

MRI Heart

For the differentiation between ischemic and nonischemic etiologies of new-onset nonacute HFrEF using MRI, the presence of myocardial LGE alone has good discriminative power (c-statistic 0.85; 95% CI, 0.76–0.94) for the detection of an ischemic cause; the presence of an ischemic pattern on both LGE and cine imaging has specificity of 87%, while the absence of both has specificity of 94% for a nonischemic cause (addition of resting first-pass perfusion imaging does not improve diagnosis) [98]. In patients presenting with new-onset HFrEF of uncertain etiology, LGE MRI has diagnostic sensitivity of 67% to 100%, positive predictive value of 100%, specificity of 96% to 100%, negative predictive value of 90%, and diagnostic accuracy of 97% for detecting ischemic LV myocardial damage, which is comparable to coronary angiography (sensitivity 93%, specificity 96%, and diagnostic accuracy 95%) in implicating CAD, which suggests that MRI with LGE is a safe, clinically effective, and potentially economical gatekeeper to coronary angiography in patients presenting with HFrEF [99] but cannot completely exclude an ischemic etiology when LGE is absent [100].

CTA Coronary Arteries

For the differentiation between ischemic and nonischemic etiologies in new-onset nonacute HFrEF, CT coronary calcium score = 0 alone may be used to exclude CAD, but this technique is typically used to determine the need for further evaluation with coronary CTA [101-104].

A CT algorithm, including coronary CTA when the initial CT coronary calcium score >0, has sensitivity of 100%, specificity of 95%, positive predictive value of 67%, and negative predictive value of 100% for detecting an

ischemic etiology in cases of new-onset HFrEF. HFrEF patients with CT coronary calcium score = 0 or no significant CAD on coronary CTA are not expected to have subsequent coronary events, thereby potentially obviating the need for coronary angiography [101].

Arteriography Coronary

The role of coronary angiography in evaluating HFrEF is not always clear [99]. In patients presenting with newonset HFrEF with only risk factors (without angina) suggesting CAD, coronary angiography is not beneficial in the process of differentiation between ischemic and nonischemic etiologies [105]. In patients in whom CAD has been excluded as the cause of HFrEF, coronary angiography is generally not indicated unless a change in clinical status suggests interim development of ischemic disease [1].

Summary of Recommendations

- Variant 1: For suspected new-onset nonacute HF, initial imaging with both resting TTE and chest radiography are usually appropriate.
- Variant 2: For differentiation of new-onset HF with ejection fraction reduced (HFrEF) versus preserved (HFpEF), more comprehensive anatomic/functional evaluation by resting TTE and/or MRI (including functional, without absolute need for contrast) is usually appropriate.
- Variant 3: If HFrEF is confirmed, its ischemic versus nonischemic etiology is identified by judicious patientby-patient use of usually appropriate imaging as follows: (1) Coronary CTA or coronary arteriography (if high pretest probability/symptoms for ischemic disease) for coronary assessment; (2) Rest/vasodilator stress SPECT/CT, PET/CT, or MRI for myocardial perfusion assessment; (3) Rest/exercise or inotropic stress TTE for myocardial contraction assessment; or (4) MRI (including morphologic with contrast) for myocardial characterization.

Summary of Evidence

Of the 106 references cited in the *ACR Appropriateness Criteria*[®] Suspected New-Onset and Known Nonacute *Heart Failure* document, 106 references are categorized as diagnostic references including 5 well-designed studies, 33 good-quality studies, and 18 quality studies that may have design limitations. There are 48 references that may not be useful as primary evidence. There are 2 references that are meta-analysis studies.

The 106 references cited in the ACR Appropriateness Criteria[®] Suspected New-Onset and Known Nonacute Heart Failure document were published from 1978 to 2018.

Although there are references that report on studies with design limitations, 38 well-designed or good-quality studies provide good evidence.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk- benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria[®] Radiation Dose Assessment Introduction document [106].

Relative Radiation Level Designations			
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range	
0	0 mSv	0 mSv	
۲	<0.1 mSv	<0.03 mSv	
€€	0.1-1 mSv	0.03-0.3 mSv	
��€	1-10 mSv	0.3-3 mSv	
$\mathbf{\mathfrak{S}}\mathbf{\mathfrak{S}}\mathbf{\mathfrak{S}}$	10-30 mSv	3-10 mSv	
	30-100 mSv	10-30 mSv	

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to <u>www.acr.org/ac</u>.

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.