2013 ACCF/ACR/ASE/ASNC/SCCT/SCMR Appropriate Utilization of Cardiovascular Imaging in Heart Failure: A Joint Report of the American College of Radiology Appropriateness Criteria Committee and the American College of Cardiology Foundation Appropriate Use Criteria Task Force

Literature Review

A Report of the American College of Radiology, American College of Cardiology Foundation

---

HEART FAILURE WRITING PANEL

Manesh R. Patel, MD, FACC Co-Chair

Richard D. White, MD, FACR, FACC, FAHA Co-Chair

Suhny Abbara, MD
Robert J. Herfkens, MD
Michael Picard, MD, FACC
Leslee J. Shaw, PhD, FACC, FAHA

David A. Bluemke, MD, PhD, FACR
Marc Silver, MD, FACC
Arthur E. Stillman, MD, PhD, FACR, FAHA
James Udelson, MD, FACC

Contents

Clinical Scenario #1 – Evaluation for Newly Suspected or Potential Heart Failure

Literature Review

Summary Statement

The literature review does not support routine use of stress imaging with Echo, CMR, SPECT or PET for initial evaluation of HF symptoms.

Echo

The strongest recommendations in favor of imaging of patients with newly suspected HF are echocardiography to include two-dimensional transthoracic ultrasound and Doppler(25). Among its most attractive attributes are its wide spread availability, lack of ionizing radiation and the reality of assessment in real-time. Assessments of cardiac structure and function can be made accurately to guide therapy. Multi-center 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 (26-30). Additionally, assessment of LV systolic function using echo in patients with suspected HF improved the disease identification by general practitioners as well as the application of appropriate medical care(31). Resting echocardiography has also been shown to identify patients with heart failure with preserved systolic function (32,33)and to predict subsequent poor outcomes (34-36)

CMR

Studies over the last decade support the use of CMR for this cohort of patients, as note in a recently published ACC expert consensus statement. While LV volume and EF measurements are as accurate as those obtained with echo (37), myocardial perfusion, viability and fibrosis imaging can assist in identification of etiology and assess prognosis (38). LV mass quantitation by CMR predicts future risk in patients with HF (39). A key strength of the technique is the high resolution of the anatomy of all aspects of the heart and surrounding structures (40). This has lead to recommendations for use in patients with known or suspected complex congenital heart disease (41). The accuracy of CMR and its utility in the initial assessment of valve function appear substantial, although some questions are not yet entirely answered.

SPECT

While the primary use of SPECT imaging is for myocardial perfusion assessment, LV systolic global and regional function can be quantified from the resultant images. It is most useful for assessment of LV function when concomitant evaluation for CAD is necessary.

PET

There are relatively few data to support the use of PET as an initial test but reports do note the utility of peak stress LVEF measurements(42).

CCT

Cardiac computed tomography (CCT) can provide accurate assessment of cardiac structure and function. A strong point of the technique is the high anatomic resolution of all aspects of the heart and surrounding structures, including the coronary arteries. One current limitation is the

loss of accuracy with variable or very high heart rate. An advantage of CCT over echo may be its ability to characterize the myocardium but studies have yet to demonstrate the importance of this factor. Currently, CCT studies specifically in patients with suspected HF are limited.

Cath

The invasive assessment of hemodynamics and valvular and ventricular function by catheterization with ventriculography is considered the traditional reference standard (43). However the radiation exposure, invasive nature of the test, and necessary geometric assumptions in calculations have gradually reduced reliance on this approach as an initial diagnostic test for LV function, especially in subjects who are deemed low risk.

Guidelines

The relevant guideline recommendations for this clinical scenario are:
Initial clinical assessment of patients presenting with HF:

ACC/AHA Heart Failure Guidelines
Class I

1. 2-dimensional Echo with Doppler should be performed during initial evaluation of patients presenting with HF to assess LVEF, LV size, LV wall thickness, and valve function. Radionuclide ventriculography can also be performed to assess LVEF and volumes. (*Level of Evidence: C*)

Assessment of patients at risk for developing heart failure:

ACC/AHA Heart Failure Guidelines
Class I

1. Healthcare providers should perform a noninvasive evaluation of LV function (i.e., LVEF) in patients with a strong family history of cardiomyopathy or in those receiving cardiotoxic interventions. (*Level of Evidence: C)*

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
Echo					
1. Hunt, S. A., et al. "ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society." Circulation 112.12 (2005): e154-e235.	15		Guideline		4

[1] See appendix A
[2] See appendix A

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
2. Gardin JM, McClelland R, Kitzman D, et al. M-mode echocardiographic predictors of six- to seven-year incidence of coronary heart disease, stroke, congestive heart failure, and mortality in an elderly cohort (the Cardiovascular Health Study). Am J Cardiol. 2001; 87:1051-7.	3a	Biracial cohort of 5,888 men and women (mean age 73 years) underwent 2-dimensional M-mode echocardiographic measurements of left ventricular (LV) internal dimensions, wall thickness, mass and geometry, as well as measurement of left atrial dimension and assessment for mitral annular calcium. Participants were followed for 6 to 7 years for incident events; analyses excluded subjects with prevalent disease.	Determine whether M-mode echocardiographic variables predicted all-cause mortality, incident coronary heart disease (CHD), congestive heart failure (CHF), and stroke in a large prospective, multicenter, population-based study.	LV mass was significantly related to incident CHD, CHF, and stroke. The highest quartile of LV mass conferred a hazards ratio of 3.36, compared with the lowest quartile, for incident CHF. Furthermore, incident CHF-free survival was significantly lower for participants with LV mass in the highest versus the 2 lowest quartiles (86% vs 97%, respectively, at 2,500 days). Thus, in an elderly biracial population, selected 2-dimensional M-mode echocardiographic measurements were important markers of subclinical disease and conferred independent prognostic information for incident CVD events, especially CHF and CHD.	2
3. Aurigemma GP, Gottdiener JS, Shemanski L, et al. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the cardiovascular health study. J Am Coll Cardiol. 2001;37:1042-8.	3	Studied 2,671 participants in the Cardiovascular Health Study who were free of coronary heart disease, CHF or atrial fibrillation. Clinical and quantitative echocardiographic data were obtained in all participants.	Assess the ability of echocardiographic indices of systolic and diastolic function to predict incident congestive heart failure (CHF).	At a mean follow-up of 5.2 years (range 0 to 6 years), 170 participants (6.4% of the cohort) developed CHF. Both high and low Doppler E/A ratios were predictive of incident CHF. CONCLUSIONS: Roughly half the occurrences of CHF in this population are associated with normal or borderline EF. Echocardiographic findings suggestive of subclinical contractile dysfunction and diastolic filling abnormalities are both predictive of subsequent CHF.	1
4. Lim TK, Ashrafian H, Dwivedi G, et al. Increased left atrial volume index is an independent predictor of raised serum natriuretic peptide in patients with suspected heart failure but normal left ventricular ejection fraction: Implication for diagnosis of diastolic heart failure. Eur J Heart Fail. 2006;8:38-45.	9	137 patients with suspected heart failure (HF), referred from the community for echocardiography, prospectively underwent Doppler echocardiography, LAVI and NTproBNP estimation. Raised LAVI and reduced LV systolic function were defined as >26 ml/m2 and LV EF <50% respectively.	Assess the capacity of LAVI to predict LV diastolic dysfunction in comparison with N-terminal pro B-type natriuretic peptide (NTproBNP) in patients with suspected heart failure and a normal ejection fraction (EF).	Of the remaining 116 subjects, 92 showed normal LV systolic function. The univariate predictors of serum log NTproBNP were age ($p < 0.001$), LA dimension ($p = 0.001$), LAVI ($p < 0.001$), A wave ($p = 0.001$), E:A ($p = 0.07$) and septal wall thickness ($p = 0.004$). However on multivariate analysis, LAVI was found to be the most consistent and significant predictor of NTproBNP.	2

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
5. Chen AA, Wood MJ, Krauser DG, et al. NT-proBNP levels, echocardiographic findings, and outcomes in breathless patients: results from the ProBNP Investigation of Dyspnoea in the Emergency Department (PRIDE) echocardiographic substudy. Eur Heart J. 2006;27:839-45.	8	Of 599 emergency department patients enrolled in a clinical study of NT-proBNP at a tertiary-care hospital, 134 (22%) had echocardiographic results available for analysis. Echocardiographic parameters correlating with NT-proBNP levels were determined using multivariable linear regression analysis.	Determine the integrative utility of measuring plasma NT-proBNP levels with echocardiography in the evaluation of dyspnoeic patients.	NT-proBNP levels correlate with, and provide important prognostic information beyond, echocardiographic parameters of cardiac structure and function. Routine NT-proBNP testing may thus be useful to triage patients to more timely or deferred echocardiographic evaluation.	2
6. Grayburn PA, Appleton CP, DeMaria AN, et al. Echocardiographic predictors of morbidity and mortality in patients with advanced heart failure: the Beta-blocker Evaluation of Survival Trial (BEST). J Am Coll Cardiol. 2005;45:1064-71.	3A	Complete echocardiograms were performed in 336 patients at 26 sites and analyzed by a core laboratory. A Cox proportional-hazards regression model was used to determine which echocardiographic variables predicted the primary end point of death or the secondary end point of death, HF hospitalization, or transplant. Significant variables were then entered into a multivariable model adjusted for clinical and demographic covariates.	The aim of this study was to determine echocardiographic predictors of outcome in patients with advanced heart failure (HF) due to severe left ventricular (LV) systolic dysfunction in the Beta-blocker Evaluation of Survival Trial (BEST).	On multivariable analysis adjusted for clinical covariates, only LV end-diastolic volume index predicted death (events = 75), with a cut point of 120 ml/m(2). Three echocardiographic variables predicted the combined end point of death (events = 75), HF hospitalization (events = 97), and transplant (events = 9): LV end-diastolic volume index, mitral deceleration time, and the vena contracta width of MR. Optimal cut points for these variables were 120 ml/m(2), 150 ms, and 0.4 cm, respectively.	1

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
7. Francis CM, Caruana L, Kearney P, et al. Open access echocardiography in management of heart failure in the community. BMJ. 1995;310:634-6.	3	Studied the presence or absence of left ventricular systolic dysfunction and consequent changes in clinical management of 259 consecutive patients.	To assess the value of an open access echocardiography service.	119 treated patients, 99 untreated patients, and nine asymptomatic patients were referred over five months. 32 were considered to be inappropriately referred. Among the treated patients, 31 had impaired left ventricular systolic function and five had valvular disease; angiotensin converting enzyme inhibitors were recommended for 34 of these patients. In addition, 53 were thought not to need diuretics. Eight untreated patients had impaired systolic function and six valvular disease. The service was well used by general practitioners and led to advice to change management in more than two thirds of patients.	1
8. Whalley GA, Wright SP, Pearl A, Gamble GD, Walsh HJ, Richards M, Doughty RN. Prognostic role of echocardiography and brain natriuretic peptide in symptomatic breathless patients in the community. Eur Heart J. 2008 Feb;29(4):509-16.	8	Two hundred and twenty-eight elderly symptomatic general practice patients (dyspnoea/oedema) were recruited and underwent clinical evaluation, NT-proBNP assay, and comprehensive echocardiography. The Kaplan-Meier analysis of time to first CV hospitalization or CV death was performed for 1 year after presentation according to nominated thresholds of LV systolic function, NT-proBNP, MFP, and E/Ea ratio.	Evaluate the potential role of E/Ea for predicting cardiovascular (CV) events in patients with suspected HF.	Time to first CV event predicted by NT-proBNP ($P < 0.0001$), MFP ($P = 0.009$), and E:Ea ($P = 0.0076$), but not EF ($P = 0.098$). When NT-proBNP was elevated, E:Ea >15 identified a group of patients with lower survival ($P < 0.0001$). Both E/Ea and NT-proBNP predicted hospitalization and when used in a two-step approach (NT-proBNP first, followed by E/Ea), the combination of both (elevated NT-proBNP and elevated E/Ea) identified those patients at highest risk, thus supporting a complementary approach for echocardiography and NT-proBNP in patients with HF symptoms.	1

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
9. Melenovsky V, Borlaug BA, Rosen B, et al. Cardiovascular features of heart failure with preserved ejection fraction versus nonfailing hypertensive left ventricular hypertrophy in the urban Baltimore community: the role of atrial remodeling/dysfunction. J Am Coll Cardiol. 2007;49:198-207	3b	A cross-sectional study comparing HFpEF patients (n = 37), HLVH subjects without HF (n = 40), and normotensive control subjects without LVH (n = 56). All subjects had an EF of >50%, sinus rhythm, and insignificant valvular or active ischemic disease, and groups were matched for age, gender, and ethnicity. Comprehensive echo-Doppler and pressure analysis was performed.	The purpose of this study was to identify cardiovascular features of patients with heart failure with preserved ejection fraction (HFpEF) that differ from those in individuals with hypertensive left ventricular hypertrophy (HLVH) of similar age, gender, and racial background but without failure.	The HFpEF patients were predominantly African-American women with hypertension, LVH, and obesity. They had vascular and systolic-ventricular stiffening and abnormal diastolic function compared with the control subjects. However, most of these parameters either individually or combined were similarly abnormal in the HLVH group and poorly distinguished between these groups. The HFpEF group had quantitatively greater concentric LVH and estimated mean pulmonary artery wedge pressure (20 mm Hg vs. 16 mm Hg) and shorter isovolumic relaxation time than the HLVH group. They also had left atrial dilation/dysfunction unlike in HLVH and greater total epicardial volume. The product of LV mass index and maximal left atrial (LA) volume best identified HFpEF patients (84% sensitivity, 82% specificity).	4
10. Persson H, Lonn E, Edner M, Baruch L, Lang CC, Morton JJ, Ostergren J, McKelvie RS; Investigators of the CHARM Echocardiographic Substudy-CHARMES. Diastolic dysfunction in heart failure with preserved systolic function: need for objective evidence: results from the CHARM Echocardiographic Substudy-CHARMES. J Am Coll Cardiol. 2007 Feb 13;49(6):687-94. Epub 2007 Jan 26.	1	312 patients mean age 66 +/- 11 years, EF was 50 +/- 10%, and 34% were women. Patients underwent Doppler echocardiographic examination that included assessment of pulmonary venous flow or determination of plasma NT-pro-brain natriuretic peptide > or months after randomization to candesartan or placebo. The patients were classified into 1 of 4 diastolic function groups: normal, relaxation abnormality (mild dysfunction), pseudonormal (moderate dysfunction), and restrictive (severe dysfunction).	To test the hypothesis that diastolic dysfunction (DD) was an important predictor of cardiovascular (CV) death or heart failure (HF) hospitalization in a subset of patients (ejection fraction [EF] >40%) in the CHARM-Preserved study.	Diastolic dysfunction was found in 67% of classified patients (n = 293), and moderate and severe DD were identified in 44%. Moderate and severe DD had a poor outcome compared with normal and mild DD (18% vs. 5%, $p < 0.01$). Diastolic dysfunction, age, diabetes, previous HF, and atrial fibrillation were univariate predictors of outcome. In multivariate analysis, moderate (hazard ratio [HR] 3.7, 95% confidence interval [CI] 1.2 to 11.1) and severe DD (HR 5.7, 95% CI 1.4 to 24.0) remained the only independent predictors ($p = 0.003$).	1

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
CMR					
11. Davis BR, Kostis JB, Simpson LM, Black HR, Cushman WC, Einhorn PT, Farber MA, Ford CE, Levy D, Massie BM, Nawaz S; ALLHAT Collaborative Research Group. Heart failure with preserved and reduced left ventricular ejection fraction in the antihypertensive and lipid-lowering treatment to prevent heart attack trial. Circulation. 2008 Nov 25;118(22):2259-67. Epub 2008 Nov 10.	1	Men and women ≤ 55 years of age with hypertension and 1 additional risk factor for CHD were included. Participants were randomly assigned to step 1 drugs of chlorthalidone, amlodipine, lisinopril, or doxazosin in a ratio of 1.7:1:1:1. Patients were treated in a double-blind fashion to achieve a goal blood pressure (BP) of ≤ 140/90 mm Hg by titrating the step 1 randomized drug and adding step 2 (atenolol, clonidine, or reserpine) or step 3 (hydralazine) open-label agents supplied by the study as clinically indicated.	Study to determine whether treatment initiated with a calcium channel blocker (amlodipine), an angiotensin-converting enzyme inhibitor (lisinopril), or an _-adrenergic blocker (doxazosin) would reduce the incidence of fatal coronary heart disease (CHD) or nonfatal myocardial infarction more than treatment with a thiazide-type diuretic (chlorthalidone) in high-risk patients ≥55 years of age with hypertension.	HF case fatality rates were examined. Of those with EF data, 44.4% had HFPEF and 55.6% had HFREF. Chlorthalidone reduced the risk of HFPEF compared with amlodipine, lisinopril, or doxazosin; the hazard ratios were 0.69 (95% confidence interval [CI], 0.53 to 0.91; *P*_0.009), 0.74 (95% CI, 0.56 to 0.97; *P*_0.032), and 0.53 (95% CI, 0.38 to 0.73; *P*_0.001), respectively. Chlorthalidone reduced the risk of HFREF compared with amlodipine or doxazosin; the hazard ratios were 0.74 (95% CI, 0.59 to 0.94;*P*_0.013) and 0.61 (95% CI, 0.47 to 0.79; *P*_0.001), respectively. Chlorthalidone was similar to lisinopril with regard to incidence of HFREF (hazard ratio, 1.07; 95% CI, 0.82 to 1.40; *P*_0.596). After HF onset, death occurred in 29.2% of participants (chlorthalidone/amlodipine/lisinopril) with new-onset HFPEF versus 41.9% in those with HFREF (*P*_0.001; median follow-up, 1.74 years); and in the chlorthalidone/doxazosin comparison that was terminated early, 20.0% of HFPEF and 26.0% of HFREF patients died (*P*_0.185; median follow-up, 1.55 years).	1

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
12. St John SM, Pfeffer MA, Moye L, et al. Cardiovascular death and left ventricular remodeling two years after myocardial infarction: baseline predictors and impact of long-term use of captopril: information from the Survival and Ventricular Enlargement (SAVE) trial. Circulation. 1997;96:3294-9.	2	Two-dimensional echocardiograms were obtained in 512 patients at 11+/-3 days and 1 and 2 years postinfarction to assess LV size, percentage of the LV that was akinetic/dyskinetic (%AD), and LV shape index. LV function was assessed by radionuclide ejection fraction. Two hundred sixty-three patients (51.4%) sustained cardiovascular death and/or LV diastolic dilatation; 279 (54.5%) had cardiovascular death and/or systolic dilatation.	Quantified cardiovascular death and/or left ventricular (LV) dilatation in patients from the SAVE trial to determine whether dilatation continued beyond 1 year, whether ACE inhibitor therapy attenuated late LV dilatation, and whether any baseline descriptors predicted late dilatation.	In 373 patients with serial echocardiograms, LV end-diastolic and end-systolic sizes increased progressively from baseline to 2 years (both P<.01). More patients with LV dilatation had a decrease in ejection fraction: 24.8% versus 6.8% (P<.001) (diastole) and 25.7% versus 5.3% (P<.001) (systole). Captopril attenuated diastolic LV dilatation at 2 years (P=.048), but this effect was carried over from the first year of therapy because changes in LV size with captopril beyond 1 year were similar to those with placebo. Predictors of cardiovascular death and/or dilatation were age (P=.023), prior infarction (P<.001), lower ejection fraction (P<.001), angina (P=.007), heart failure (P=.002), LV size (P<.001), and infarct size (%AD) (P<.001).	1
13. Jenkins C, Moir S, Chan J, et al. Left ventricular volume measurement with echocardiography: a comparison of left ventricular opacification, three-dimensional echocardiography, or both with magnetic resonance imaging. Eur Heart J. 2009;30:98-106.	9	Studied 50 patients (46 men, mean age 63+/-10 years) with past myocardial infarction who underwent echocardiographic assessment of LV volume and function. All patients sequentially underwent NC-2DE followed by NC-3DE. CE-2DE and CE-3DE were acquired during contrast infusion. Resting echocardiographic image quality was evaluated on the basis of NC-2DE.	Both contrast enhanced (CE) two-dimensional echocardiography (2DE) and three-dimensional echocardiography (3DE) have been proposed as techniques to improve the accuracy of left ventricular (LV) volume measurements. Study sought to examine the accuracy of non-contrast (NC) and CE-2DE and 3DE for calculation of LV volumes and ejection fraction (EF), relative to cardiac magnetic resonance imaging (MRI).	CE-2DE is analogous to NC-3DE in accurate categorization of LV function. However, CE-3DE is feasible and superior to other NC- and CE-techniques in patients with previous infarction.	2

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
14. Valle-Munoz A, Estornell-Erill J, Soriano-Navarro CJ, et al. Late gadolinium enhancement-cardiovascular magnetic resonance identifies coronary artery disease as the aetiology of left ventricular dysfunction in acute new-onset congestive heart failure. Eur J Echocardiogr. 2009;10:968-74.	3a	Hundred consecutive patients admitted with acute new-onset decompensated HF and EF <40%, with no clinical or electrocardiographic data suggestive of CAD. The patients were classified according to the presence or absence of significant CAD (stenosis > or =70% in at least one major vessel).	Evaluate the ability of late gadolinium enhancement (LGE) using cardiovascular magnetic resonance (CMR) to identify acute new-onset heart failure (HF) with left ventricular systolic dysfunction (LVSD), whether or not in relation to underlying coronary artery disease (CAD), in patients with no clinical evidence of associated ischaemic cardiomyopathy.	In patients with new-onset HF and LVSD for whom there are no clinical and exploratory data suggestive of ischaemic heart disease, CMR with LGE is an excellent means of ruling out significant CAD and is a valid alternative to angiography.	2
15. Bluemke DA, Kronmal RA, Lima JA, et al. The relationship of left ventricular mass and geometry to incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study. J Am Coll Cardiol. 2008;52:2148-55.	8	5098 participants in the MESA study underwent cardiac MRI at the baseline examination and were followed for a median of 4 years. Cox proportional hazard models were constructed to predict the endpoints of coronary heart disease (CHD), stroke and heart failure (HF) after adjustment for cardiovascular risk factors.	Study was to evaluate the relationship of left ventricular mass and geometry measured with cardiac MRI to incident cardiovascular events in the Multi-Ethnic Study of Atherosclerosis (MESA) study.	Left ventricular size was related to incident HF, stroke and CHD in this multi-ethnic cohort. While body-size adjusted left ventricular mass alone predicted incident HF, concentric ventricular remodeling predicted incident stroke and CHD.	1

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
16.Bogaert J, Francone M. Cardiovascular magnetic resonance in pericardial diseases. J Cardiovasc Magn Reson. 2009; 11:14.	7	Review of evidence relating to CMR	Provides review focusing on the current state of knowledge on how CMR can be used to study the most common pericardial diseases.	The added value of CMR compared to the standard techniques used for assessment of patients with pericardial diseases has substantially increased in recent years, questioning whether this technique should not be considered the most appropriate non-invasive modality to study the pericardium. Strong points in favor of CMR are the integration of anatomic and functional information within a single examination, the ability for tissue characterization and to determine the presence and degree of inflammation and activity of disease, and the value of CMR to accurately assess the rest of the heart, in particular the myocardium, helpful in the differential diagnosis, which currently often remains a diagnostic challenge.	4

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
17. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in Collaboration With the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons.	15	-	Guideline	-	-

Reference	Study Type[1]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[2]
Clinical Scenario 1 – Evaluation for Newly Suspected or Potential Heart Failure					
PET					
18. Chander A, Brenner M, Lautamaki R, et al. Comparison of measures of left ventricular function from electrocardiographically gated 82Rb PET with contrast-enhanced CT ventriculography: a hybrid PET/CT analysis. J Nucl Med. 2008;49:1643-50.	10	A total of 24 patients underwent PET/CT, consisting of rest and dipyridamole (82)Rb perfusion studies and contrast-enhanced CT angiography, using a 64-slice scanner, for the workup of coronary artery disease. From gated PET images, LV ejection fraction (EF), end-diastolic volume (EDV), and end-systolic volume (ESV) were calculated using 2 commercial products. For functional CT analysis, commercial software using endocardial contour detection was applied.	Compared functional parameters from gated (82)Rb PET with simultaneous high-resolution contrast-enhanced CT ventriculography, obtained as a byproduct a CT coronary angiography during hybrid cardiac PET/CT.	Inter- and intraobserver agreement was good for all methods. On CT, EF was 66% +/- 13%, ESV was 41 +/- 29 mL, and EDV was 115 +/- 36 mL. On PET, EF during dipyridamole was 56% +/- 15% and 52% +/- 15% using the 2 commercial products ($P < 0.05$ vs. CT), ESV was 36 +/- 28 and 47 +/- 35 mL (P = not significant vs. CT), and EDV was 75 +/- 30 and 91 +/- 33 mL ($P < 0.05$ vs. CT). Correlations with CT were 0.85 and 0.87 for EF using commercial software, 0.76 and 0.88 for ESV, and 0.60 and 0.68 for EDV ($P < 0.01$ for all). Bland-Altman analysis confirmed systematic underestimation of EF and EDV by PET versus CT but did not show a significant deviation from linearity.	1
Cath					
19. Baim D, Grossman W. Grossman's Cardiac Catheterization, Angiography, and Intervention / Edition 7. Lippincott Williams & Wilkins, 2005	-	-	-	-	-

Clinical Scenario #2 – Ischemic Etiology in Patients with HF

Literature Review

Summary Statement
Available evidence regarding the optimal method for evaluation of patients with classical angina, ischemic equivalent pain, dyspnea-equivalent angina, or extensive proven or suspected silent myocardial ischemia and HF is characterized by observational studies with various imaging modalities that demonstrate diagnostic performance and some that provide prognostic information(48). The ongoing STITCH trial evaluating medical versus surgical revascularization (49) should provide evidence regarding the benefit of revascularization.

Review of the current literature does not support routine use of rest-only imaging with Echo, CMR, SPECT, or PET for ischemic evaluation of HF symptoms.

In patients with increasing renal dysfunction, modalities that use iodinated or gadolinium-based contrast agents pose increased risk and should be avoided when suitable alternatives exist.

Literature Review – By Imaging Test
Echo
Stress Echo has been shown to identify both resting and post-stress systolic wall motion abnormalities in many observational studies (50-52). In many of these observational studies ischemia was defined as new/worsening wall motion abnormality (WMA) or a biphasic response (defined as WMA augmentation at low dose with deterioration at high dose dobutamine stress echocardiography). These findings have been related to clinical outcomes.

CMR
Perfusion CMR studies have been performed in patients without systolic dysfunction for the identification of CAD, but have not been extensively studied in HF patients. CMR has been studied in small series used to evaluate wall motion with stress in patients with HF. (53). CMR with high resolution has more often been used to detect fibrosis, a technique that, in observational studies, has identified ischemic versus non-ischemic cardiomyopathy in HF patients. Recent reports have started to link fibrosis with clinical outcome (54,55).

SPECT
SPECT has been studied extensively in HF patients to determine both ischemia and prognosis. Moreover, observational evidence supports the concept that patients referred to stress MPI (myocardial perfusion imaging) with dyspnea are high risk (56). A benefit to the use of SPECT imaging is the addition of rest and post-stress gated LVEF and wall motion information in addition to MPI measurements, including both visual (qualitative) and quantitative measurements(57). For patients referred for evaluation of symptoms suggestive of HF, the results of stress MPI have been applied to differentiate ischemic from non-ischemic cardiomyopathy. Significant and extensive angiographic CAD occurs frequently in patients with higher risk stress MPI findings. Finally, reports on the use of stress MPI have focused on the utility of ischemia as a marker of downstream improvement in left ventricular function. In the CHRISTMAS trial, a total of 305 patients with HF were enrolled and randomized to carvedilol

versus placebo (58). There was a gradient relationship, with the number of ischemic segments and improvement in left ventricular function noted at approximately 6 months of follow-up. In a recent prospective controlled clinical trial, 201 patients following index hospitalization for HF underwent stress MPI(59). This cohort included a broad range of LVEF measurements including 36% of patients with preserved systolic function. When the stress MPI (i.e., summed stress score >3, indicating at least mildly abnormal) results were compared to invasive coronary angiography in 75 patients, the sensitivity and specificity of stress MPI for detection of any significant CAD stenosis were 82% and 57%, respectively. For extensive CAD in the proximal left anterior decending (LAD) or left main (LM) or multivessel CAD, the sensitivity and specificity were 96% and 56%, respectively.

PET

Data regarding the use of PET in this setting are largely derived from studies that includee patients undergoing evaluation of myocardial viability. An advantage of the addition of stress MPI with PET is its improved accuracy for the detection of severe, multivessel CAD, which may appear as balanced reduction and normal SPECT findings. Moreover, PET markers of absolute peak stress LVEF measurements and myocardial perfusion reserve may improve detection of patients with CAD (60,61). Some recent small series have noted the advantage of quantifying the extent of myocardial scarring and insulin resistance as important prognostic findings from PET (62). Finally, altered glucose metabolism and myocardial efficiency have also been studied in small series and may offer an added means to identify high risk patients with HF using PET (63,64).

CCT

CCT has been examined in some preliminary studies of patients with HF and has been shown to have a high negative predictive value, in confirming the absence of CAD (65-67). In a small study, EBCT showed promise in identifying CAD in HF patients when compared to cath (68,69).

Cath

Cardiac catheterization has shown obstructive CAD in patients with HF with and without ischemic equivalent in observational studies (70-72) and is considered a central study by the ACC/AHA guidelines.

Guidelines

The relevant guideline recommendations for this clinical scenario are:

ACC/AHA Heart Failure Guidelines:

Patient with Ischemic equivalent Syndrome / Angina

Class I

- Coronary arteriography should be performed in patients presenting with HF who have angina or significant ischemia unless the patient is not eligible for revascularization of any kind. (Level of Evidence B)

Class – IIa

- Coronary arteriography is reasonable for patients presenting with HF who have ischemic equivalent that may or may not be of cardiac origin who have not had evaluation of their coronary anatomy and who have no contraindications to coronary revascularization. (Level of Evidence: C)

Class – IIb

- Noninvasive imaging may be considered to define the likelihood of CAD in patients with HF and LV dysfunction. (Level of Evidence: C)

Patient without Ischemic equivalent Syndrome/Angina

Class IIa

- Coronary arteriography is reasonable for patients presenting with HF who have known or suspected CAD but who do not have angina unless the patient is not eligible for revascularization of any kind. (Level of Evidence: C)
- Noninvasive imaging to detect myocardial ischemia and viability is reasonable in patients presenting with HF who have known CAD and no angina unless the patient is not eligible for revascularization of any kind (20). (Level of Evidence: B)

Class IIb

- Noninvasive imaging may be considered to define the likelihood of CAD in patients with HF and LV dysfunction. (Level of Evidence: C)

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
20. Abidov A, Rozanski A, Hachamovitch R, et al. Prognostic significance of dyspnea in patients referred for cardiac stress testing. N Engl J Med. 2005;353:1889-98.	3a	Studied 17,991 patients undergoing myocardial-perfusion single-photon-emission computed tomography during stress and at rest. Patients were divided into five categories on the basis of symptoms at presentation (none, nonanginal chest pain, atypical angina, typical angina, and dyspnea). Multivariable analysis was used to assess the incremental prognostic value of symptom categories in predicting the risk of death from cardiac causes and from any cause. In addition, the prognosis associated with various symptoms at presentation was compared in subgroups selected on the basis of propensity analysis.	Assess the prognostic significance of dyspnea.	After a mean (+/-SD) follow-up of 2.7+/-1.7 years, the rate of death from cardiac causes and from any cause was significantly higher among patients with dyspnea (both those previously known to have coronary artery disease and those with no known history of coronary artery disease) than among patients with other or no symptoms at presentation. Among patients with no known history of coronary artery disease, those with dyspnea had four times the risk of sudden death from cardiac causes of asymptomatic patients and more than twice the risk of patients with typical angina. Dyspnea was associated with a significant increase in the risk of death among each clinically relevant subgroup and remained an independent predictor of the risk of death from cardiac causes ($P<0.001$) and from any cause ($P<0.001$) after adjustment for other significant factors by multivariable and propensity analysis.	2

[3] See appendix A
[4] See appendix A

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
21 Velazquez EJ, Lee KL, O'Connor CM, et al. The rationale and design of the Surgical Treatment for Ischemic Heart Failure (STICH) trial. J Thorac Cardiovasc Surg. 2007; 134:1540-7.	-	Not yet completed	National Heart, Lung, and Blood Institute-funded multicenter international randomized trial addressing 2 specific primary hypotheses: (1) coronary artery bypass grafting with intensive medical therapy improves long-term survival compared with survival with medical therapy alone, and (2) in patients with anterior left ventricular dysfunction, surgical ventricular reconstruction to a more normal left ventricular size plus coronary artery bypass grafting improves survival free of subsequent hospitalization for cardiac cause when compared with that with coronary artery bypass grafting alone.	Not yet completed	-

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
Echo					
22. Elhendy A, Sozzi F, van Domburg RT, et al. Effect of myocardial ischemia during dobutamine stress echocardiography on cardiac mortality in patients with heart failure secondary to ischemic cardiomyopathy. Am J Cardiol. 2005; 96:469-73.	3	528 patients (62 +/- 11 years of age, 402 men) who had heart failure and previous myocardial infarction or known coronary artery disease and underwent DSE. Measured cardiac death at follow up.	Assess the effect of ischemia during dobutamine stress echocardiography (DSE) on cardiac mortality in patients with heart failure.	Angina was not predictive of death. In patients who had ischemia, revascularization within 4 months after DSE was associated with decreased risk of cardiac death (RR 0.43, 95% confidence interval 0.3 to 0.8). In conclusion, myocardial ischemia that is detected by DSE is associated with increased risk of cardiac death among patients who have heart failure, after adjustment for left ventricular function. Patients who had ischemia and received revascularization within 4 months had a better survival than did patients who had ischemia and did not receive revascularization. Angina had no effect on prognosis. Therefore, patients who do not have angina should not be considered a lower-risk population if they have inducible ischemia.	2
23.. Maskoun W, Mustafa N, Mahenthiran J, et al. Wall motion abnormalities with low-dose dobutamine predict a high risk of cardiac death in medically treated patients with ischemic cardiomyopathy. Clin Cardiol. 2009;32:403-9.	3a	Low- and peak-dose dobutamine echocardiography was performed in 235 patients with ischemic cardiomyopathy (ejection fraction 31% +/- 8%) who were treated with medical therapy. The survival of patients with low-dose SWMA (n = 33) was compared with the survival of patients without ischemia (n = 85) and those with peak-dose SWMA (n = 117).	Assess the prognostic value of low-dose stress-induced wall motion abnormalities (SWMA) in medically treated patients with ischemic cardiomyopathy.	Low-dose SWMA is an independent predictor of cardiac mortality in medically treated patients with ischemic cardiomyopathy. Patients with low-dose SWMA are at equivalent risk to those with peak-dose SWMA.	3

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
24.. Sozzi FB, Elhendy A, Rizzello V, et al. Prognostic significance of akinesis becoming dyskinesis during dobutamine stress echocardiography. J Am Soc Echocardiogr. 2007;20:257-61.	3a	A total of 731 patients (age 62 +/- 15 years, 628 men) with two or more akinetic left ventricular segments at rest underwent DSE and were followed up for a mean period of 5 +/- 2.7 years.	Assess the long-term outcome of patients with Akinesis becoming dyskinesis (AKBD) AKBD during dose dobutamine stress echocardiography (DSE).	Ischemia occurred in 197 patients (27%). During follow-up, 254 patients (35%) developed hard cardiac events and 204 patients (28%) developed heart failure. In all, 226 patients (31%) died of various causes (cardiac death in 172 patients). The annualized hard cardiac event rate was 11% in patients with AKBD and 6% in patients without (P = .03). The incidence of heart failure was significantly higher in patients with AKBD than without (47% vs 26%, P < .001). AKBD at peak DSE is associated with increased risk of cardiac events in patients with akinetic segments at baseline echocardiogram.	3
CMR					
25.. Dall'Armellina E, Morgan TM, Mandapaka S, et al. Prediction of cardiac events in patients with reduced left ventricular ejection fraction with dobutamine cardiovascular magnetic resonance assessment of wall motion score index. J Am Coll Cardiol. 2008;52:279-86.	3a	Two hundred consecutive patients ages 30 to 88 (average 64) years with an LVEF <or=55% that were poorly suited for stress echocardiography underwent DCMR in which left ventricular wall motion score index (WMSI), was assessed at rest, during low-dose, and after peak intravenous infusion of dobutamine/atropine.	Assess the utility of dobutamine cardiovascular magnetic resonance (DCMR) results for predicting cardiac events in individuals with reduced left ventricular ejection fraction (LVEF).	Stress-induced increase in WMSI during DCMR was associated with future cardiac events (p < 0.001).In individuals with mild to moderate reductions in LVEF (40% to 55%), dobutamine-induced increases in WMSI forecast MI and cardiac death to a greater extent than an assessment of resting LVEF. In those with an LVEF <40%, a dobutamine-induced increase in WMSI does not predict MI and cardiac death beyond the assessment of resting LVEF.	1

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
26. Yokokawa M, Tada H, Koyama K, Naito S, Oshima S, Taniguchi K. Nontransmural Scar Detected by Magnetic Resonance Imaging and Origin of Ventricular Tachycardia in Structural Heart Disease. *Pacing and Clinical Electrophysiology* 2009; 32(s1):S52-S56.	3a	CMR was performed in 34 patients with monomorphic, sustained VT and dilated cardiomyopathy (DCM, n = 18), ischemic cardiomyopathy (ICM, n = 10), or idiopathic VT (IVT, n = 6). The VT exit site was assessed by a detailed analysis of the QRS morphology, including bundle branch block type, limb lead polarity, and precordial R-wave transition. On CMR imaging, the transmural score of each of the 17 segments was assigned, using a computer-assisted, semiautomatic technique, to measure the DE areas. Segmental scars were classified as nontransmural when DE was 1-75% and transmural when DE was 76-100% of the left ventricular mass in each segment.	To study the relationship between the occurrence of VT and the characteristics of scar tissue.	A scar was detected in all patients with DCM or ICM. Nontransmural scar tissue was often found at the VT exit site, in patients with DCM or ICM. In contrast, no scar was found in patients with IVT. CMR clarified the characteristics and distribution of scar tissue in patients with structural heart disease, and the presence and location of scar tissue might predict the VT exit site in these patients.	2

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
27.. Krittayaphong R, Maneesai A, Chaithiraphan V, et al. Comparison of diagnostic and prognostic value of different electrocardiographic criteria to delayed-enhancement magnetic resonance imaging for healed myocardial infarction. Am J Cardiol. 2009;103:464-70.	9	Twelve-lead electrocardiography and CMR were performed the same day. A standard CMR protocol including a delayed-enhancement (DE) technique was performed. The prognostic value of using various ECG criteria and DE-CMR was assessed for the occurrence of cardiac death, nonfatal MI, or major adverse cardiac events. We studied 1,366 patients. Average follow-up was 31.4 +/- 15.8 months. Myocardial scar was detected in 507 patients (37.1%) using DE-CMR.	Determine the accuracy and prognostic value of standard ECG criteria for the diagnosis of healed MI compared with cardiac magnetic resonance (CMR). Consecutive patients with known or suspected coronary artery disease who were referred for CMR were studied.	Healed MI using various ECG criteria had sensitivity, specificity, and accuracy of 44% to 59%, 91% to 95%, and 75% to 79% compared with DE-CMR, respectively. Multivariable Cox regression analysis showed that myocardial scar using DE-CMR was the most powerful predictor for cardiac events, followed by left ventricular ejection fraction. In the absence of DE-CMR data, MI using European Society of Cardiology/American College of Cardiology (ESC/ACC) 2000 criteria was the most powerful predictor. In conclusion, various ECG criteria had limited sensitivity, but high specificity, for the diagnosis of healed MI compared with myocardial scar using DE-CMR. Myocardial scar, left ventricular ejection fraction, and MI using ESC/ACC 2000 criteria were important predictors for cardiac events.	2
SPECT					
28. Abidov, A., et al. "Prognostic significance of dyspnea in patients referred for cardiac stress testing." N.Engl.J Med. 353.18 (2005): 1889-98.	3a	Studied 17,991 patients undergoing myocardial-perfusion single-photon-emission computed tomography during stress and at rest. Patients divided into five categories on the basis of symptoms. Multivariate analysis was used to assess the incremental prognostic value of symptom categories in predicting the risk of death from cardiac causes and from any cause.	To study the prognostic significance among patients referred for cardiac evaluation who present with symptoms of dyspnea.	In a large series of patients, self-reported dyspnea identified a subgroup of otherwise asymptomatic patients at increased risk for death from cardiac causes and from any cause.	2

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
29. Vaduganathan P, He ZX, Vick GW, III, et al. Evaluation of left ventricular wall motion, volumes, and ejection fraction by gated myocardial tomography with technetium 99m-labeled tetrofosmin: a comparison with cine magnetic resonance imaging. J Nucl Cardiol. 1999;6:3-10.	9	Twenty-five patients with an acute myocardial infarction underwent 99mTc-labeled tetrofosmin (99mTc-tetrofosmin) gated SPECT and cine magnetic resonance imaging (MRI). Wall motion was assessed in 13 left ventricular segments using a 5-point scoring system ranging from 3 (normal) to -1 (dyskinetic).	Study whether left ventricular function can be assessed accurately by gated single photon emission computed tomography (SPECT) in patients with myocardial infarction and severe perfusion defects is not well known.	Exact agreement for wall motion scores between gated SPECT and MRI was excellent (92%, kappa = 0.82). Furthermore, correlations between the two techniques were also good for end-diastolic volume ($r = 0.81$, $P < .0001$), end-systolic volume ($r = 0.92$, $P < .0001$), and ejection fraction ($r = 0.93$, $P < .0001$).	2
30. Cleland JG, Pennell DJ, Ray SG, et al. Myocardial viability as a determinant of the ejection fraction response to carvedilol in patients with heart failure (CHRISTMAS trial): randomised controlled trial. Lancet. 2003;362:14-21.	1	Double-blind, randomized trial to compare placebo and carvedilol for 6 months in individuals with stable, chronic heart failure due to ischaemic left-ventricular systolic dysfunction (N= 489), of whom 387 were randomised. The primary endpoint was change in LVEF, measured by radionuclide ventriculography, in hibernators versus non-hibernators, on carvedilol compared with placebo. Analysis was by intention to treat.	Investigate whether improvement in LVEF was associated with the volume of hibernating myocardium (viable myocardium with contractile failure)	LVEF was unchanged with placebo (mean change -0.4 [SE 0.9] and -0.4 [0.8] for non-hibernators and hibernators, respectively) but increased with carvedilol (2.5 [0.9] and 3.2 [0.8], respectively; $p<0.0001$ compared with baseline).Some of the effect of carvedilol on LVEF might be mediated by improved function of hibernating or ischaemic myocardium, or both. Medical treatment might be an important adjunct or alternative to revascularisation for patients with hibernating myocardium.	1

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
31.Soman P, Lahiri A, Mieres JH, et al. Etiology and pathophysiology of new-onset heart failure: evaluation by myocardial perfusion imaging. J Nucl Cardiol. 2009;16:82-91.	3a	Recruited 201 patients (age 65.3 +/- 14.5 years, 43% women) hospitalized with their first episode of heart failure. Rest/stress gated SPECT Tc-99m sestamibi MPI was performed during or within 2 weeks of the index hospitalization, in addition to standard care.	The IMAGING in Heart Failure study was a prospective, multi-national trial designed to explore the role of single-photon emission computed tomographic (SPECT) myocardial perfusion imaging (MPI) as an initial investigative strategy in patients hospitalized with new-onset heart failure.	SPECT MPI revealed a broad range of ejection fractions with preserved systolic function in 36% of patients. Forty-one percent of patients had normal perfusion. In the remaining patients, perfusion abnormalities were predominantly due to prior myocardial infarction, with extensive ischemia seen only in 6%. Among patients who underwent coronary angiography, SPECT performance characteristics revealed excellent negative predictive value (96%) for extensive coronary artery disease (CAD). In multivariable analyses, the extent of perfusion abnormality and advancing age predicted the presence of extensive CAD.	2
PET					
32.. Range FT, Paul M, Schafers KP, et al. Myocardial perfusion in nonischemic dilated cardiomyopathy with and without atrial fibrillation. J Nucl Med. 2009; 50:390-6.	5	Twelve men (age +/- SD, 55 +/- 12 y) who had DCM and persistent AF were compared with a group of 18 men (mean age, 43 +/- 15 y, P = not statistically significant) who had DCM and sinus rhythm and with 22 healthy controls (mean age, 47 +/- 13 y, P = not statistically significant). Myocardial blood flow (MBF) was noninvasively quantified at rest and during adenosine infusion using PET and radioactive-labeled water (H(2)(15)O PET).	Compared myocardial perfusion between patients with nonischemic DCM with and without AF.	Compared with controls, DCM patients without AF showed impaired hyperemic perfusion (2.52 +/- 1.29 vs. 3.57 +/- 0.88 mL/min/mL, P = 0.014) and perfusion reserve (2.10 +/- 1.01 vs. 3.37 +/- 0.97, P = 0.003). However, compared with DCM patients without AF, DCM patients with AF showed an additional impairment in resting perfusion (0.82 +/- 0.31 mL/min/mL, P = 0.010) and hyperemic perfusion (1.32 +/- 0.93 mL/min/mL, P = 0.022), and compared with controls, DCM patients with AF showed a further diminishment of perfusion reserve (1.68 +/- 0.94 vs. 3.37 +/- 0.97, P < 0.001) accompanied by the highest coronary vascular resistance of all groups.	4

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
33. Chander A, Brenner M, Lautamaki R, et al. Comparison of measures of left ventricular function from electrocardiographically gated 82Rb PET with contrast-enhanced CT ventriculography: a hybrid PET/CT analysis. J Nucl Med. 2008;49:1643-50.	10	A total of 24 patients underwent PET/CT, consisting of rest and dipyridamole (82)Rb perfusion studies and contrast-enhanced CT angiography, using a 64-slice scanner, for the workup of coronary artery disease. From gated PET images, LV ejection fraction (EF), end-diastolic volume (EDV), and end-systolic volume (ESV) were calculated using 2 commercial products. For functional CT analysis, commercial software using endocardial contour detection was applied.	Compared functional parameters from gated (82)Rb PET with simultaneous high-resolution contrast-enhanced CT ventriculography, obtained as a byproduct a CT coronary angiography during hybrid cardiac PET/CT.	Inter- and intraobserver agreement was good for all methods. On CT, EF was 66% +/- 13%, ESV was 41 +/- 29 mL, and EDV was 115 +/- 36 mL. On PET, EF during dipyridamole was 56% +/- 15% and 52% +/- 15% using the 2 commercial products ($P < 0.05$ vs. CT), ESV was 36 +/- 28 and 47 +/- 35 mL (P = not significant vs. CT), and EDV was 75 +/- 30 and 91 +/- 33 mL ($P < 0.05$ vs. CT). Correlations with CT were 0.85 and 0.87 for EF using commercial software, 0.76 and 0.88 for ESV, and 0.60 and 0.68 for EDV ($P < 0.01$ for all). Bland-Altman analysis confirmed systematic underestimation of EF and EDV by PET versus CT but did not show a significant deviation from linearity.	1

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
34.. Feola M, Biggi A, Chauvie S, et al. Myocardial scar and insulin resistance predict cardiovascular events in severe ischaemic myocardial dysfunction: a perfusion-metabolism positron emission tomography study. Nucl Med Commun. 2008; 29:448-54.	3a	All patients had previous myocardial infarction (>6 months previously) and left ventricular ejection fraction (LVEF) <40%. Metabolism-perfusion PET, echocardiogram and coronary angiography were provided. All subjects underwent short euglycaemic-hyperinsulinaemic clamp before the metabolism study. The dysfunctioning segment was defined as hibernating myocardium when metabolism was normal-moderately reduced with impaired perfusion (mismatch flow-metabolism). Cardiac death, hospital admission for myocardial infarction or heart failure were considered cardiovascular events.	Determined whether the amount of viable or non-viable myocardium detected with a PET scan or clinical-functional parameters might predict cardiovascular events.	Ninety-three patients (71 males, aged 64.2 years) were studied. The LVEF was 30.2+/-7.7%; 48 (51.6%) suffered an anterior myocardial infarction. Fifty-three (54.1%) subjects were treated with coronary revascularization; all had optimal medical therapy. Cardiovascular events occurred in 20/93 patients at 1-year follow-up (event group). Age (P=0.7), diabetes mellitus (P=0.6) and rate of coronary revascularization (P=0.3) were not different in the two groups. Patients who experienced cardiovascular events had larger non-viable myocardium (5.8+/-2.7 vs. 4.1+/-2.6, P=0.01), lower metabolic rate glucose (1.3+/-0.6 vs. 1.7+/-0.7 ml /kg . min, P=0.04) but similar hibernating myocardium (1.6+/-1.6 vs. 1.7+/-2, P=0.8) and baseline LVEF (28.1+/-4.8 vs. 30.7+/-8.3%, P=0.08). Having more then five non-viable segments and a metabolic rate for glucose of <0.9 mg /kg . min predicted a worse prognosis (P=0.04, log rank, 3.89; and P=0.004, log rank, 8.1, respectively).	2

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
35. Tuunanen H, Engblom E, Naum A, et al. Free fatty acid depletion acutely decreases cardiac work and efficiency in cardiomyopathic heart failure. Circulation. 2006; 114:2130-7.	3	Eighteen fasting nondiabetic patients with IDCM (14 men, 4 women, aged 58.8+/-8.0 years, ejection fraction 33+/-8.8%) and 8 matched healthy controls underwent examination of myocardial perfusion and oxidative and FFA metabolism, before and after acute reduction of serum FFA concentrations by acipimox, an inhibitor of lipolysis. Metabolism was monitored by positron emission tomography and [15O]H2O, [11C]acetate, and [11C]palmitate. Left ventricular function and myocardial work were echocardiographically measured, and efficiency of forward work was calculated.	Studied the effect of acute FFA withdrawal on cardiac function in patients with heart failure caused by idiopathic dilated cardiomyopathy (IDCM).	Acutely decreased serum FFA depresses cardiac work. In healthy hearts, this is accompanied by parallel decrease in oxidative metabolism, and myocardial efficiency is preserved. In failing hearts, FFA depletion did not downregulate oxidative metabolism, and myocardial efficiency deteriorated. Thus, failing hearts are unexpectedly more dependent than healthy hearts on FFA availability. We propose that both glucose and fatty acid oxidation are required for optimal function of the failing heart.	3

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
36.. Thompson K, Saab G, Birnie D, et al. Is septal glucose metabolism altered in patients with left bundle branch block and ischemic cardiomyopathy? J Nucl Med. 2006; 47:1763-8.	3	Fifty-three patients with LV dysfunction and ICM were identified: 34 with LBBB, 19 with normal QRS (</=100, control patients). PET using (18)F-FDG and (82)Rb was used to measure myocardial glucose metabolism and perfusion, respectively. Perfusion-metabolism differences were determined. Scar scores (matched decreases in (18)F-FDG and (82)Rb), mismatch scores (hibernating myocardium with decreased (82)Rb relative to (18)F-FDG), and reverse-mismatch (R-MM) scores (reduced (18)F-FDG relative to (82)Rb) were assessed in the septum and lateral wall.	Determine the effect of LBBB on septal metabolism in patients with ICM, LV dysfunction, and LBBB.	(18)F-FDG uptake in the septum was reduced in patients with LBBB (64.0% +/- 15.4%) compared with control patients (74.9% +/- 14.3%; P < 0.05). Mean septal R-MM was greater in patients with LBBB (19.1% +/- 15.3%) versus control patients (4.7% +/- 10.6%; P < 0.05). However, 32% (11/34) of patients with LBBB did not demonstrate septal R-MM, 91% (10/11) of whom demonstrated lateral wall perfusion defects. Of the 68% (23/34) of patients with LBBB and septal R-MM, 52% (12/23) demonstrated lateral wall perfusion defects (P < 0.05). There was a significant difference in the percentage of the lateral wall with scar between those with septal R-MM (9.3% +/- 10.5%) and those without (19.9% +/- 14.3%; P < 0.05).	3
CCT					
37.. Budoff MJ, Shavelle DM, Lamont DH, et al. Usefulness of electron beam computed tomography scanning for distinguishing ischemic from nonischemic cardiomyopathy. J Am Coll Cardiol. 1998; 32:1173-8.	9	One hundred and twenty-five patients with cardiomyopathy (ejection fraction <0.40) and known coronary anatomy underwent EBCT coronary scanning to evaluate for CCs within 3 months of coronary angiography.	Evaluate the ability of electron beam computed tomography (EBCT) to distinguish ischemic from nonischemic causes of cardiomyopathy by evaluating heart failure patients for coronary calcification (CC).	Of the 72 patients who were found to have ischemic cardiomyopathy, 71 patients had CC by EBCT (sensitivity 99%, p < 0.001), mean score 798+/-899. In comparison, among the 53 patients without significant coronary artery disease (CAD) (nonischemic cardiomyopathy), the mean score was significantly lower (17+/-51; p < 0.0001), and 44 patients had a CC score of 0 (no CC present). The specificity of EBCT to exclude CAD in patients with cardiomyopathy was 83%, using a threshold CC score of 0, and 92% for scores <80 (p < 0.001). Overall accuracy for determining the etiology of cardiomyopathy (differentiating ischemic from nonischemic) was 92% for this technique.	2

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
38. Andreini D, Pontone G, Pepi M, et al. Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with dilated cardiomyopathy. J Am Coll Cardiol. 2007;49:2044-50.	8	Studied 61 unknown origin DCM patients (ejection fraction: 33.9 +/- 8.6%, group 1) and 139 patients with normal cardiac function with indications for coronary angiography (group 2, control population). All underwent coronary MDCT and angiography. Multidetector computed tomography images were acquired by light speed 16-slice computed tomography.	Assess the safety, feasibility, and diagnostic accuracy of multidetector computed tomography (MDCT) in dilated cardiomyopathy (DCM) of unknown etiology.	In group 1, no MDCT-related complications were found, while 10 complications were associated with conventional angiography ($p = 0.001$). Multidetector computed tomography is feasible, safe, and accurate for identification of idiopathic versus ischemic DCM, and may represent an alternative to coronary angiography.	2
39.. Cornily, J. C., et al. "Accuracy of 16-detector multislice spiral computed tomography in the initial evaluation of dilated cardiomyopathy." Eur.J Radiol. 61.1 (2007): 84-90.	9	36 patients with DCM underwent cardiac MSCT before conventional coronary angiography with ventriculography. Analysis was performed on arterial calcium score (Agatston score equivalent: ASE), coronary stenosis, left ventricular parameters and venous network.	Sought to validate a Multislice Computed Tomography (MSCT) -based strategy in the initial evaluation of patients with dilated cardiomyopathy (DCM).	In patients undergoing an initial evaluation of DCM, MSCT appears to be an effective alternative to conventional angiography. The following attitude may be proposed: when ASE >1.000, conventional coronary angiography is mandatory due to MSCT's poor interest in such cases; when ASE <1.000, a contrast-enhanced MSCT may, when normal, replace coronary angiography.	2
40. Budoff MJ, Shavelle DM, Lamont DH, et al. Usefulness of electron beam computed tomography scanning for distinguishing ischemic from nonischemic cardiomyopathy. J Am Coll Cardiol. 1998;32:1173-8.	9	One hundred and twenty-five patients with cardiomyopathy (ejection fraction <0.40) and known coronary anatomy underwent EBCT coronary scanning to evaluate for CCs within 3 months of coronary angiography.	This study was undertaken to evaluate the ability of electron beam computed tomography (EBCT) to distinguish ischemic from nonischemic causes of cardiomyopathy by evaluating heart failure patients for coronary calcification (CC).	Of the 72 patients who were found to have ischemic cardiomyopathy, 71 patients had CC by EBCT (sensitivity 99%, $p < 0.001$), mean score 798+/-899. In comparison, among the 53 patients without significant coronary artery disease (CAD) (nonischemic cardiomyopathy), the mean score was significantly lower (17+/-51; $p < 0.0001$), and 44 patients had a CC score of 0 (no CC present). The specificity of EBCT to exclude CAD in patients with cardiomyopathy was 83%, using a threshold CC score of 0, and 92% for scores <80 ($p < 0.001$). Overall accuracy for determining the etiology of cardiomyopathy (differentiating ischemic from nonischemic) was 92% for this technique.	2

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
41. Bluemke DA, Kronmal RA, Lima JA, et al. The relationship of left ventricular mass and geometry to incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study. J Am Coll Cardiol. 2008;52:2148-55.	2	A total of 5,098 participants in the MESA study underwent cardiac MRI at the baseline examination and were followed up for a median of 4 years. Cox proportional hazard models were constructed to predict the end points of coronary heart disease (CHD), stroke, and heart failure (HF) after adjustment for cardiovascular risk factors.	The purpose of this study was to evaluate the relationship of left ventricular (LV) mass and geometry measured with cardiac magnetic resonance imaging (MRI) to incident cardiovascular events in the MESA (Multi-Ethnic Study of Atherosclerosis) study.	A total of 216 incident events were observed during the follow-up period. In adjusted models, the end points of incident CHD and stroke were positively associated with increased LV mass-to-volume ratio (CHD, hazard ratio [HR]: 2.1 per g/ml, p = 0.02; stroke, HR: 4.2 per g/ml, p = 0.005). In contrast, LV mass showed the strongest association with incident HF events (HR: 1.4 per 10% increment, p < 0.0001). The HF events occurred primarily in participants with LV hypertrophy, that is, >or=95th percentile of LV mass (HR: 8.6, 95% confidence interval: 3.7 to 19.9, reference group <50th percentile of LV mass).	1
CATH					
42. Alderman EL, Fisher LD, Litwin P, et al. Results of coronary artery surgery in patients with poor left ventricular function (CASS). Circulation. 1983;68:785-95.	1	Compared 420 medically treated and 231 surgically treated patients (coronary graft plus myocardial surgery in 30%) who had severe left ventricular dysfunction manifest by an ejection fraction below 0.36 and markedly abnormal wall motion.	Compare the benefits of medical treatment versus surgical treatment for heart failure patients.	Compared with medically treated patients, those treated surgically had more severe angina (56.7% vs 29.0% class III or IV; p less than .001), less heart failure as predominant symptom (11.1% vs 18.8%; p less than .003), more severe coronary disease (66.7% vs 50.2% three-vessel disease; p less than .001), a greater concentration of left main coronary artery lesions greater than 70% (12.6% vs 3.8%: p less than .001), and a greater estimated extent of jeopardized myocardium (p less than .001). Surgically treated patients experienced substantial symptomatic benefit compared with medically treated.	1
43. Fox KF, Cowie MR, Wood DA, et al. Coronary artery disease as the cause of incident heart failure in the population. Eur Heart J. 2001;22:228-36.	3a	Studied 292 000 patients in South London, U.K. by monitoring those admitted to hospital or a a rapid access heart failure clinic. The presence and severity of coronary artery disease was identified by coronary angiography in patients under 75 years.	Investigate the frequency of coronary artery disease in incident cases of heart failure in the population given.	Coronary artery disease is the cause of 52% (95% CI 43-61%) of incident heart failure in the general population under 75 years. Clinical assessment without angiography under-estimates the proportion of patients with coronary artery disease, and fails to identify those patients who may benefit from revascularization.	3

Reference	Study Type[3]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[4]
Clinical Scenario 2 – Ischemic Etiology in Patients with HF					
44. Arques S, Ambrosi P, Gelisse R, et al. Prevalence of angiographic coronary artery disease in patients hospitalized for acute diastolic heart failure without clinical and electrocardiographic evidence of myocardial ischemia on admission. Am J Cardiol. 2004;94:133-5.	5	The prevalence of coronary artery disease was investigated in 18 patients hospitalized for acute diastolic heart failure without clinical and electrocardiographic evidence of myocardial ischemia on admission.	Retrospective review of cases to determine cause of HF.	On the basis of coronary angiography, 7 patients had coronary artery disease and 4 had ischemic heart disease. In addition, besides uncontrolled hypertension and several systemic factors, silent myocardial ischemia potentially contributed to acute exacerbation of heart failure for at least 5 patients with coronary artery disease, according to either elevation in troponin I or segmental wall motion abnormalities.	4

Clinical Scenario #3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization

Literature Review

Summary Statement
Evidence for the use of viability imaging in patients with impaired LV dysfunction is currently available from several meta-analyses of observational studies that demonstrate recovery of function and clinical improvement in patients undergoing revascularization with evidence of viable myocardium (74,74,75). Large randomized trials now underway may clarify the role of revascularization in such patients.

Echo
Contractile reserve with echo can be imaged using dobutamine echo, and manifests in the dysfunctional region of interest as an increase in wall thickening and motion during low doses of dobutamine, with a subsequent impairment of contractility at higher doses, a finding termed "biphasic response". This technique has been shown in observational studies to identify myocardial segments with higher likelihood of functional recovery after coronary revascularization in patients with moderately reduced LVEF (median 31%)(76) Contractile reserve may be limited in patients with thinned LV walls. (77).

CMR
CMR identification of hibernating myocardium and potential reversibility of LV dysfunction is based on the use of late enhancement gadolinium imaging, in combination with information on regional function available with cine CMR techniques. Observational studies have demonstrated that "viability", defined by the relative absence of scarring, resulted in improvement in myocardial function following coronary revascularization in patients with preserved (78) and severely depressed LV function (79). Post-infarction risk stratification with pharmacologic stress CMR data is also available(80). Dobutamine stress CMR is also useful for diagnosing CAD (81). Additionally, CMR has been show to demonstrate subendocardial infarction with a greater sensitivity than SPECT in observational studies (82) (83).

SPECT
Studies with SPECT tracers involving biopsies of regional myocardium in patients undergoing CABG have demonstrated that the degree of uptake of the tracers (by quantitative analysis) correlates directly with the magnitude of regional myocyte tissue viability on biopsies, thus validating the use of this technique in this scenario. Observational studies of SPECT imaging in patients with HF have identified worse prognosis in patients without viable myocardium(84).

PET
In two randomized trials, a strategy of FDG PET-directed revascularization has been compared to standard care for decisions regarding revascularization (PARR 1 and PARR 2)(85,86). These studies demonstrated that patients with viability who underwent revascularization had evidence of improved myocardial function. In addition, when compared to SPECT, FDG-PET was able to identify viable myocardium with a higher sensitivity (87). Although PET is reported to have

greater sensitivity, the clinical relative value in comparison to SPECT with regards to decision making and clinical outcomes has not clearly been demonstrated (88)

CCT

Preliminary studies suggest that CCT imaging may provide similar information as CMR using contrast enhancement with regards to delineation of etiology of LV dysfunction and to identify areas of regional infarction, in combination with readily available information on regional function (89,90). However, this technique has not as yet been widely used for this purpose, and validation studies are more preliminary in nature compared to the robust literature on all of the other noninvasive imaging modalities.

Cath

There is limited initial evidence on the use of ventriculography for the determination of viability and response to revascularization. With the advent of newer non-invasive techniques this has not been subsequently studied.

Guidelines

The relevant guideline recommendations for this clinical scenario are:

ACC/AHA Chronic Stable Angina Guidelines

Class I

Percutaneous coronary intervention or CABG for patients with one- or two-vessel CAD without significant proximal LAD CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing *(Level of Evidence: B)*

Class IIa

Use of PCI or CABG for patients with one-or two-vessel CAD without significant proximal LAD disease but with a moderate area of viable myocardium and demonstrable ischemia on noninvasive testing *(Level of Evidence: B)*

Class III

Use of PCI or CABG for patients with one-or two-vessel CAD without significant proximal LAD disease who have mild symptoms that are unlikely to be due to myocardial ischemia, or who have not received an adequate trial of medical therapy and have only:

a. small area of viable myocardium or
b. have no demonstrable ischemia on noninvasive testing. *(Level of Evidence: C)*

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
45. Allman, K. C., et al. "Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis." J Am.Coll.Cardiol 39.7 (2002): 1151-58.	7	-	This study pools data from published series examining late survival with revascularization versus medical therapy after myocardial viability testing in patients with severe coronary artery disease (CAD) and left ventricular (LV) dysfunction.	This meta-analysis demonstrates a strong association between myocardial viability on noninvasive testing and improved survival after revascularization in patients with chronic CAD and LV dysfunction. Absence of viability was associated with no significant difference in outcomes, irrespective of treatment strategy.	3
46.. Bax JJ, Poldermans D, Elhendy A, et al. Improvement of left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine stress echocardiography. J Am Coll Cardiol. 1999; 34:163-9.	3a	Studied 68 patients with DSE before revascularization; 62 patients underwent resting echocardiography/radionuclide ventriculography before and three months after revascularization. Long-term follow-up data (New York Heart Association [NYHA] functional class, Canadian Cardiovascular Society [CCS] classification and events) were acquired up to two years.	This study was designed to address, in patients with severe ischemic left ventricular dysfunction, whether dobutamine stress echocardiography (DSE) can predict improvement of left ventricular ejection fraction (LVEF), functional status and long-term prognosis after revascularization.	Patients with > or =4 viable segments on DSE (group A, n = 22) improved in LVEF at three months (from 27+/-6% to 33+/-7%, p < 0.01), in NYHA functional class (from 3.2+/-0.7 to 1.6+/-0.5, p < 0.01) and in CCS classification (from 2.9+/-0.3 to 1.2+/-0.4, p < 0.01); in patients with <4 viable segments (group B, n = 40) LVEF and NYHA functional class did not improve, whereas CCS classification improved significantly (from 3.0+/-0.8 to 1.3+/-0.5, p < 0.01). A higher event rate was observed at long-term follow-up in group B versus group A (47% vs. 17%, p < 0.05).	2

[5] See appendix A
[6] See appendix A

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
Echo					
47.. Rizzello V, Poldermans D, Schinkel AF, et al. Long term prognostic value of myocardial viability and ischaemia during dobutamine stress echocardiography in patients with ischaemic cardiomyopathy undergoing coronary revascularisation. Heart. 2006;92:239-44.	8	Low-high dose dobutamine stress echocardiography (DSE) was performed before revascularisation in 128 consecutive patients with ischaemic cardiomyopathy (mean (SD) left ventricular ejection fraction (LVEF) 31 (8)%).	Evaluate the relative merits of viability and ischaemia for prognosis after revascularisation.	Univariable predictors of cardiac death were the presence of multivessel disease (hazard ratio (HR) 0.21, p < 0.001), baseline LVEF (HR 0.90, p < 0.0001), wall motion score index (WMSI) at rest (HR 4.02, p = 0.0006), low dose DSE (HR 7.01, p < 0.0001), peak dose DSE (HR 4.62, p < 0.0001), the extent of scar (HR 1.39, p < 0.0001), and the presence of CR in > or = 25% of dysfunctional segments (HR 0.34, p = 0.02). The best multivariable model to predict cardiac death included the presence of multivessel disease, WMSI at low dose DSE, and the presence of CR in > or = 25% of the severely dysfunctional segments (HR 9.62, p < 0.0001). Inclusion of ischaemia in the model did not provide additional predictive value.	1
48. Pedone C, Bax JJ, van Domburg RT, et al. Long-term prognostic value of ejection fraction changes during dobutamine-atropine stress echocardiography. Coron Artery Dis. 2005; 16:309-13	9	Study population comprised 106 consecutive patients (mean age 60+/-11 years, 73% men) with suspected or known coronary artery disease referred for DSE. Stress-induced ischemia was defined as new or worsening wall motion abnormalities. LVEF was measured at rest, peak stress and recovery. Follow-up was successful in 104 (98%) patients. Four patients who underwent revascularization within 60 days were excluded from the analysis. End-points during follow-up were cardiac death, non-fatal myocardial infarction and late revascularization.	Assess the additional prognostic value of left ventricular ejection fraction (LVEF) changes during DSE at different stages.	During a mean follow-up of 5.3+/-2.1 years, 26% of patients died: 13% due to cardiac death, 6% patients experienced non-fatal myocardial infarction and 38% underwent late revascularization. Rest-to-peak LVEF increase was lower in patients who experienced cardiac death or non-fatal myocardial infarction (4.9+/-8.6 compared with 9.2+/-7.5, P=0.04) and any cardiac events (6.0+/-8.5 compared with 10.5+/-6.7, P=0.004). An inverse correlation was found between left ventricular ejection increase and the number of ischemic segments (P<0.0001). A multivariable Cox proportional hazard model demonstrated that, in addition to clinical data and new wall motion abnormalities, lower LVEF increase had an incremental prognostic value in predicting hard cardiac events (hazard ratio 1.1, 95% confidence interval 1.0-1.2).	1

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
CMR					
49. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med. 2000;343:1445-53.	3a	Gadolinium-enhanced MRI was performed in 50 patients with ventricular dysfunction before they underwent surgical or percutaneous revascularization. The transmural extent of hyperenhanced regions was postulated to represent the transmural extent of nonviable myocardium. The extent of regional contractility at the same locations was determined by cine MRI before and after revascularization in 41 patients.	Assessed if results of contrast-enhanced MRI can be used to predict whether regions of abnormal ventricular contraction will improve after revascularization in patients with coronary artery disease.	Contrast-enhanced MRI showed hyperenhancement of myocardial tissue in 40 of 50 patients before revascularization. Concluded that reversible myocardial dysfunction can be identified by contrast-enhanced MRI before coronary revascularization.	3
50.. Selvanayagam, J. B., et al. "Value of delayed-enhancement cardiovascular magnetic resonance imaging in predicting myocardial viability after surgical revascularization." Circulation 110.12 (2004): 1535-41.	3a	Fifty-two patients undergoing multivessel CABG were studied by preoperative and early (day 6) and late (6 months) postoperative cine MRI for global and regional functional assessment and delayed-enhancement MRI for assessment of irreversible myocardial injury.	Assess utility of delayed-enhancement MRI in identifying irreversible myocardial injury in the setting of coronary artery bypass surgery (CABG).	Delayed-enhancement MRI is a powerful predictor of myocardial viability after surgery, suggesting an important role for this technique in clinical viability assessment.	2

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
51. Jahnke C, Nagel E, Gebker R, et al. Prognostic value of cardiac magnetic resonance stress tests: adenosine stress perfusion and dobutamine stress wall motion imaging. Circulation. 2007;115:1769-76.	2	In 513 patients (with known or suspected coronary disease, prior coronary artery bypass graft, or percutaneous coronary intervention), a combined single-session magnetic resonance stress examination (MRP and DSMR) was performed at 1.5 T. For first-pass perfusion imaging, the standard adenosine stress imaging protocol (140 microg x kg(-1) x min(-1) for 6 minutes, 3-slice turbo field echo-echo-planar imaging or steady-state free precession sequence, 0.05 mmol/kg Gd-DTPA) was applied, and for DSMR, the standard high-dose dobutamine/atropine protocol (steady-state free-precession cine sequence) was applied. Stress testing was classified as pathological if at MRP > or = 1 segment showed an inducible perfusion deficit > 25% transmurality or if at DSMR > or = 1 segment showed an inducible wall motion abnormality	Adenosine stress magnetic resonance perfusion (MRP) and dobutamine stress magnetic resonance (DSMR) wall motion analyses are highly accurate for the detection of myocardial ischemia. However, knowledge about the prognostic value of stress MR examinations is limited. We sought to determine the value of MRP and DSMR, as assessed during a single-session examination, in predicting the outcome of patients with known or suspected coronary artery disease.	During a median follow-up of 2.3 years (range, 0.06 to 4.55 years), 19 cardiac events occurred (4.1%; 9 cardiac deaths, 10 nonfatal myocardial infarctions). The 3-year event-free survival was 99.2% for patients with normal MRP and DSMR and 83.5% for those with abnormal MRP and DSMR. Univariate analysis showed ischemia identified by MRP and DSMR to be predictive of cardiac events (hazard ratio, 12.51; 95% confidence interval, 3.64 to 43.03; and hazard ratio, 5.42; 95% confidence interval, 2.18 to 13.50; P<0.001, respectively); other predictors were diabetes mellitus, known coronary artery disease, and the presence of resting wall motion abnormality. By multivariate analysis, ischemia on magnetic resonance stress testing (MRP or DSMR) was an independent predictor of cardiac events. In a stepwise multivariate model (Cox regression), an abnormal magnetic resonance stress test result had significant incremental value over clinical risk factors and resting wall motion abnormality (P<0.001).	1

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
52. Wahl A, Paetsch I, Gollesch A, et al. Safety and feasibility of high-dose dobutamine-atropine stress cardiovascular magnetic resonance for diagnosis of myocardial ischaemia: experience in 1000 consecutive cases. Eur Heart J. 2004;25:1230-6.	3a	From 1997 to 2002, 1000 consecutive stress-CMR examinations were performed. Images were acquired at rest and during a high-dose dobutamine-atropine protocol in 3 short-axis, a 4- and a 2-chamber view. Stress testing was discontinued when > or =85% of age-predicted heart rate was reached, on patient request, maximum pharmacologic infusion, or when new or worsening wall motion abnormalities, severe angina, dyspnoea, increase or decrease in blood pressure, or severe arrhythmias occurred. Stress-CMR was successfully performed in all but four patients (0.4%; insufficient ECG-triggering)	To determine the safety of high-dose dobutamine-atropine stress cardiovascular magnetic resonance (stress-CMR), which recently emerged as a highly accurate modality for diagnosis of inducible myocardial ischaemia.	Target heart rate was not reached in 95 cases (9.5%), due to maximum pharmacologic infusion in submaximal negative examinations in 21 cases (2.1%), and limiting side effects in 74 (7.4%). Side effects included one case (0.1%) of sustained and four cases (0.4%) of non-sustained ventricular tachycardia, 16 cases (1.6%) of atrial fibrillation, and two cases (0.2%) of transient second degree AV block.	2

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
53. Wagner, A., et al. "Contrast-enhanced MRI and routine single photon emission computed tomography (SPECT) perfusion imaging for detection of subendocardial myocardial infarcts: an imaging study." Lancet 361.9355 (2003): 374-79.	3c	Contrast-enhanced CMR and SPECT examinations in 91 patients with suspected or known coronary artery disease. All CMR and SPECT images were scored, using a 14-segment model, for the presence, location, and spatial extent of infarction. Acquired contrast-enhanced CMR and SPECT images in 12 dogs with, and three dogs without, myocardial infarction as defined by histochemical staining.	Myocardial infarcts are routinely detected by nuclear imaging techniques such as single photon emission computed tomography (SPECT) myocardial perfusion imaging. A newly developed technique for infarct detection based on contrast-enhanced cardiovascular magnetic resonance (CMR) has higher spatial resolution than SPECT. The study looked at this technique to see if it would detect infarcts missed by SPECT.	SPECT and CMR detect transmural myocardial infarcts at similar rates. However, CMR systematically detects subendocardial infarcts that are missed by SPECT.	2
54. Roes, S. D., et al. "Agreement and disagreement between contrast-enhanced magnetic resonance imaging and nuclear imaging for assessment of myocardial viability." Eur.J Nucl.Med.Mol.Imaging 36.4 (2009): 594-601	3a	60 patients with severe ischaemic left ventricular (LV) dysfunction who underwent contrast-enhanced MRI, (99m)Tc-tetrofosmin and (18)F-FDG SPECT.	To compare contrast-enhanced MRI and nuclear imaging with (99m)Tc-tetrofosmin and (18)F-fluorodeoxyglucose ((18)F-FDG) single photon emission computed tomography (SPECT) for assessment of myocardial viability.	Agreement between contrast-enhanced MRI and nuclear imaging for assessment of viability was high in segments without scar tissue and in segments with transmural scar tissue on contrast-enhanced MRI. However, evident disagreement was observed in segments with subendocardial scar tissue on contrast-enhanced MRI, illustrating that the nonenhanced epicardial rim can contain either normal or ischaemically jeopardized myocardium.	2

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
SPECT					
55..Inaba Y, Chen JA, Bergmann SR. Quantity of viable myocardium required to improve survival with revascularization in patients with ischemic cardiomyopathy: A meta-analysis. J Nucl Cardiol. 2010;17:646-54.	7	Searched five electronic databases to identify relevant studies through December 2008. Relative risks of cardiac death, both in patients with and without viability, were calculated in each study. In order to estimate the optimal threshold for the presence of viability, we assumed a linear relationship between the amount of viable myocardium and survival benefit of revascularization. Twenty-nine studies (4,167 patients) met the inclusion criteria. The optimal threshold for the presence of viability was estimated to be 25.8% (95% CI: 16.6-35.0%) by positron emission tomography using 18F-fluorodeoxyglucose-perfusion mismatch, 35.9% (95% CI: 31.6-40.3%) by stress echocardiography using contractile reserve or ischemic responses, and 38.7% (95% CI: 27.7-49.7%) by single photon emission computed tomography using thallium-201 or technetium-99m MIBI myocardial perfusion.	Determine optimal cutoff values for the assessment of viability using various imaging techniques for which revascularization would offer a survival benefit in patients with ischemic cardiomyopathy (ICM).	The calculated amount of viable myocardium determined to lead to improved survival was different among imaging techniques. Thus, separate cutoff values for imaging modalities may be helpful in determining which patients with ICM benefit from revascularization.	3

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
PET					
56. Beanlands RS, Ruddy TD, deKemp RA, et al. Positron emission tomography and recovery following revascularization (PARR-1): the importance of scar and the development of a prediction rule for the degree of recovery of left ventricular function. J Am Coll Cardiol. 2002; 40:1735-43.	1	A total of 82 patients with CAD and an ejection fraction (EF) < or =35% had FDG PET perfusion imaging before revascularization. Complete follow-up was available on 70 patients (86%). Patients had radionuclide angiograms at baseline and three months post-revascularization.	Determine whether the extent of viability or scar is important in the amount of recovery of left ventricular (LV) function, and to develop a model for predicting recovery after revascularization that could be tested in a randomized trial.	Diabetes (p = 0.029), time to operation (p = 0.008), and scar score (p = 0.001) were significant independent predictors of the change in EF. Previous coronary artery bypass graft confounded the effect of age. There was a significant interaction between the perfusion tracer used and mismatch score (p = 0.02). The multivariable prediction model incorporating PET and clinical variables had a goodness of fit with p = 0.001. Across tertiles of scar scores (I, small: 0% to 16%; II, moderate: 16% to 27.5%; III, large: 27.5% to 47%), the changes in EFs were 9.0 +/- 1.9%, 3.7 +/- 1.6%, and 1.3 +/- 1.5% (p = 0.003: I vs. III), respectively.	1
57. Beanlands, R. S., et al. "F-18-fluorodeoxyglucose positron emission tomography imaging-assisted management of patients with severe left ventricular dysfunction and suspected coronary disease: a randomized, controlled trial (PARR-2)." J Am.Coll.Cardiol 50.20 (2007): 2002-12.	8	Patients were stratified according to recent angiography or not, then randomized to management assisted by FDG PET (n = 218) or standard care (n = 212).	Assess the effectiveness of F-18-fluorodeoxyglucose (FDG) positron emission tomography (PET)-assisted management in patients with severe ventricular dysfunction and suspected coronary disease.	This study did not demonstrate a significant reduction in cardiac events in patients with LV dysfunction and suspected coronary disease for FDG PET-assisted management versus standard care. In those who adhered to PET recommendations and in patients without recent angiography, significant benefits were observed. The utility of FDG PET is best realized in this subpopulation and when adherence to recommendations can be achieved.	2

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
58. Slart RH, Bax JJ, de BJ, et al. Comparison of 99mTc-sestamibi/18FDG DISA SPECT with PET for the detection of viability in patients with coronary artery disease and left ventricular dysfunction. Eur J Nucl Med Mol Imaging. 2005; 32:972-9.	2, 9	Fifty-eight patients with chronic coronary artery disease and LV dysfunction (LV ejection fraction 33+/-12%) were studied. Patients underwent a 1-day dipyridamole stress 99mTc-sestamibi/18F-fluorodeoxyglucose (18FDG) DISA SPECT and 13N-ammonia/18FDG PET protocol. Within 1 week, resting MRI was performed to assess contractile function. Comparison of PET and SPECT data was performed using both visual and quantitative analysis.	DISA SPECT was compared with positron emission tomography (PET) for the detection of myocardial viability in normal and dysfunctional left ventricular (LV) myocardium.	The correlation of normalised activities of the flow tracers 99mTc-sestamibi and 13N-ammonia was good ($r = 0.82$; $p < 0.001$). The correlation between the two 18FDG studies was also good ($r = 0.83$; $p < 0.001$). The agreement for the assessment of viability for all segments between DISA SPECT and PET was 82%, with a kappa-statistic of 0.59 (95% CI 0.53-0.64), without a significant difference; in dysfunctional segments only, the agreement was 82%, with a kappa-statistic of 0.63 (95% CI 0.56-0.70), without a significant difference. When the DISA SPECT data were analysed visually, the agreement between DISA SPECT and PET was 83%, with a kappa-statistic of 0.58 (95% CI 0.52-0.63), without a significant difference. Moreover, there was no significant difference between visual and quantitative DISA SPECT analysis for the detection of viability.	1
59. Siebelink HM, Blanksma PK, Crijns HJ, et al. No difference in cardiac event-free survival between positron emission tomography-guided and single-photon emission computed tomography-guided patient management: a prospective, randomized comparison of patients with suspicion of jeopardized myocardium. J Am Coll Cardiol. 2001;37:81-8.	9	Patients with evidence of jeopardized (i.e., ischemic or viable) myocardium may benefit from revascularization, whereas patients without it should be treated with drugs. Both PET and SPECT imaging have been proven to delineate jeopardized myocardium. When patient management is based on identification of jeopardized myocardium, it is unknown which technique is most accurate for long-term prognosis.	Sought to prospectively compare nitrogen-13 (13N)-ammonia/18fluorodeoxyglucose (18FDG) positron emission tomography (PET)-guided management with stress/rest technetium-99m (99mTc)-sestamibi single-photon emission computed tomography (SPECT)-guided management.	In a clinical setting, 103 patients considered for revascularization with left ventricular wall motion abnormalities and suspicion of jeopardized myocardium underwent both PET and SPECT imaging. The imaging results were used in a randomized fashion to determine management (percutaneous transluminal coronary angioplasty [PTCA], coronary artery bypass graft surgery [CABG] or drug treatment). Follow-up for cardiac events (cardiac death, myocardial infarction and revascularization) was recorded for 28 +/- 1 months. The study was designed to have a power of 80% to detect a 20% difference in the event rate between PET- and SPECT-based management.	2

Reference	Study Type[5]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[6]
Clinical Scenario 3 – Therapy – Consideration of Revascularization (PCI or CABG) in Patients with Ischemic HF and Known Coronary Anatomy Amenable to Revascularization					
CCT					
60. Mendoza DD, Joshi SB, Weissman G, Taylor AJ, Weigold WG. Viability imaging by cardiac computed tomography. J Cardiovasc Comput Tomogr. 2010; 4:83-91.	7	First-pass perfusion and delayed enhancement cardiac imaging have been shown to be feasible by cardiac CT. However, questions remain about its reliability, and ideal scanning parameters have yet to be fully established. In general, scar imaging with cardiac CT typically requires 2 scans, with first-pass perfusion information derived from the same data set used to visualize the coronary arteries. Reduced contrast enhancement on first-pass cardiac CT images represents reduced perfusion. Higher doses of contrast are required to perform viability imaging by cardiac CT. Approximately 10 minutes after contrast administration, viability information is obtained by performing a second (noncontrast) scan. In addition to the concepts of perfusion and viability imaging by cardiac CT, we review parameters such as scan timing, tube settings, contrast delivery, reconstruction, and postprocessing techniques, as well as the associated pitfalls and technical limitations in perfusion and viability imaging by cardiac CT.			3
61. le Polain de Waroux JB, Pouleur AC, Goffinet C, et al. Combined coronary and late-enhanced multidetector-computed tomography for delineation of the etiology of left ventricular dysfunction: comparison with coronary angiography and contrast-enhanced cardiac magnetic resonance imaging. Eur Heart J. 2008;29:2544-51.	9	Seventy-one consecutive patients (50 males, 59 +/- 16 years) with LVD (ejection fraction: 26 +/- 11%) of unknown etiology underwent MDCT, LGE (late Gd-DTPA-enhanced)-CMR and CA. Patients were classified into four groups according to coronary artery disease (CAD) by CA and LGE-CMR patterns.	To evaluate whether comprehensive evaluation of coronary anatomy and delayed enhancement (DE) by multidetector-computed tomography (MDCT) would allow determination of etiology of left ventricular dysfunction (LVD) as compared with coronary angiography (CA) and DE-magnetic resonance (CMR).	Patients (n = 24) with CAD and transmural or sub-endocardial DE by CMR were considered having definite ischaemic LVD (group 1). Patients (n = 36) without CAD by CA and with no/atypical LGE-CMR were considered non-ischaemic LVD (group 2). Further we identified four patients with transmural DE but no CAD (group 3) and seven patients with CAD but no DE (group 4). On per-patient basis, combined coronary and DE-MDCT had excellent agreement (kappa = 0.89; P < 0.001) with CA/LGE-CMR to classify patients into the same four groups. Sensitivity, specificity and accuracy of MDCT were 97, 92 and 94%, respectively for detecting patients with definite (group 1) or likely (groups 3 and 4) ischaemic LVD.	2

Clinical Scenario #4 – Therapy –Consideration and Follow-up for Implantable Cardioverter-Defibrillator (ICD) / Cardiac Resynchronization Therapy (CRT)

Literature Review

ICD

Cardiovascular imaging for consideration of ICD implantation is mainly based on the evaluation of left ventricular systolic function. In the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), the distribution of LVEF values measured by echo, contrast left ventriculography, and radionuclide angiography differed, but clinical outcomes did not (106). Repeat imaging for ICD implantation may be done to determine if a course of therapy (either revascularization or medical) has improved the ventricular function or if the patient still meets LVEF criteria. Therefore, again the goals of imaging are dependent on LV systolic function as described above.

CRT

Cardiovascular imaging for consideration of CRT implantation also is mainly based on the evaluation of left ventricular systolic function. The majority of the large randomized CRT studies have used echo to evaluate LV systolic function before and after implantation. Other imaging modalities have been used to evaluate LV systolic function, but with limited studies in patients undergoing CRT. Identification of cardiac vein anatomy for CRT implantation has been shown with CCT and in some smaller studies, with CMR, and invasive cardiac catheterization. CCT does provide the means to assess LV dysynchrony and pulmonary vein anatomy with a single study, as, in theory, does CMR. Despite several observational studies that evaluated different imaging modalities for identifying potential predictors of clinical response to CRT, however, available randomized trial data do not demonstrate improved outcomes. Up to 30% of carefully selected HF candidates do not show benefit from CRT and possibly progressive worsening despite CRT (107,108).

Post-Implantation – Follow Up Imaging

Studies with repeat imaging after ICD implantation for clinically stable patients without a change in status have not been conducted. For patients with clinical deterioration or change in arrhythmia status, evaluation of a change in ventricular function or in CAD / ischemia may be warranted based on guideline recommendations for standard care of symptomatic HF.
In patients with improved HF class and LV systolic function following CRT implantation, routine clinical imaging has not been studied.

Echo

Echo has been studied in the assessment of LVEF prior to ICD implantation such as in the SCD-HeFT (42). Several observational studies have evaluated the value of echo in identifying and predicting response to CRT(109-112) Tissue Doppler imaging is superior to strain rate imaging and postsystolic shortening on the prediction of reverse remodeling in both ischemic and nonischemic heart failure after cardiac resynchronization therapy(113) (114). A large randomized trial using echo-based parameters to identify patients that will respond to CRT did not show a clinical benefit(115).

In patients with failure to respond to CRT or with worsening clinical status, studies with echo have been used to maximize A-V intervals and programming of the CRT device while monitoring LV systolic function and mitral regurgitation(116,117). Echo has also been shown to identify patients with dysynchrony who are missed by ECG criteria alone(118,119).

CMR

CMR has been demonstrated to reliably image left ventricular systolic function, but with limited studies to date in patients being considered for ICD placement. CMR has been shown to identify fibrosis that may lead to future VT/VF in patient with (120) and those without an ICD(121) (122). CMR has also shown the ability to demonstrate LV thrombus and pulmonary vein anatomy and relationships.

Repeat imaging with CMR is not routinely performed in patients with an intra-cardiac device due to both safety concerns and limitations in the ability to acquire diagnostic images. Observational studies with CMR in patients under consideration for CRT, have shown areas of fibrosis, specifically near potential lead placement areas, and do not demonstrate clinical improvement with CRT (123). One study found CMR to be more sensitive for fibrosis than SPECT in prospective CRT patients.

SPECT

Radionuclide angiography for LVEF is highly reproducible when compared to echo and has been used as an inclusion test for randomized trials demonstrating the benefit of ICD implantation (106,124). Rest and post-stress gated LVEF measurements are routinely applied and are highly reproducible as part of a CAD evaluation (57). Various SPECT measures of dyssynchrony in patients undergoing CRT have been studied with some studies correlating with echocardiographic measures. Observational studies have evaluated SPECT measures of dyssynchrony in patients undergoing CRT to determine patients that will respond to the therapy (125).

PET

Data for the use of PET in patient being considered for ICD implantation are limited. Initial PET studies have identified potential areas of fibrosis in patients with CRT, and attempted to differentiate responders from non-responders to CRT..

CCT

CCT has had promising initial studies evaluating LV systolic function. Recent reports have noted the utility of CCT for ICD placement, including venous imaging prior to ICD, quantitation of dyssynchrony, and EF assessment.

Guidelines

The relevant guideline recommendations for this clinical scenario are:
ACC/AHA Heart Failure Guidelines [1,2,4]

Class I

ICD
Primary prevention of sudden cardiac death in HF are for patients with:
1. non-ischemic dilated cardiomyopathy or ischemic heart disease $\geq$ 40 days post-MI;
2. LVEF $\leq$ 35%;

3. NYHA functional class II or III despite optimal medical therapy; and
4. a reasonable expectation of survival with a good functional status for more than 1 year.

Class I
ICD
Secondary prevention [1,2] in order to prolong survival in HF patients with:
1. current or prior HF symptoms;
2. reduced LVEF; and
3. a history of cardiac arrest, ventricular fibrillation, or hemodynamically destabilizing ventricular tachycardia.

Class I
CRT (with or without ICD) [1,2,4] use in patients with HF are:
1. LVEF $\leq$ 35%;
2. Sinus rhythm;
3. NYHA functional class III or ambulatory class IV symptoms despite optimal medical therapy; and
4. Cardiac dyssynchrony (defined as QRS duration $\geq$ 0.12 seconds), CRT (with or without combined ICD).

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
Implantable Cardioverter-Defibrillator (ICD) Use					
62.. Gula LJ, Klein GJ, Hellkamp AS, et al. Ejection fraction assessment and survival: an analysis of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). *Am Heart J* 2008; 156(6):1196-1200.	1	2,521 patients enrolled in SCD-HeFT, EF was measured by RNA in 616 (24%), echocardiography in 1,469 (58%), and contrast angiography in 436 (17%). Mean EF as measured by RNA was 25.1% ± 6.9%; by echocardiography, 23.8 ± 6.9%; and by angiography, 21.9 ± 6.9%.	Assess whether the use of echocardiography, radionuclide angiography (RNA), or contrast angiography is more accurate in detection of Ejection Fractions (EF).	Distribution of ejection fractions measured by radionuclide angiography differed from those measured by echocardiography or contrast angiograms. Survival did not differ according to modality of EF assessment.	1
CRT					
63.. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002; 346:1845-53.	7	While numerous pathophysiologic mechanisms may lead to the onset and progression of chronic systolic heart failure, a variety of electrophysiologic abnormalities seen in the setting of chronic left ventricular dysfunction may also contribute to the natural history of the disease. Atrial, atrial-ventricular, and inter- and intraventricular conduction disturbances may place the failing ventricle at a further mechanical disadvantage, thus contributing to the functional impairment and poor outcomes associated with chronic heart failure. In the early 1990s, attempts at treating patients with end-stage systolic heart failure using conventional pacing strategies met with equivocal results. However, this work did provide further insight into the electromechanical consequences of advanced heart failure and suggested that atrial-synchronized biventricular pacing, or cardiac resynchronization therapy, might provide better and more consistent symptomatic and hemodynamic improvement. Several landmark clinical trials have evaluated the safety and efficacy of cardiac resynchronization therapy in New York Heart Association (NYHA) class III and IV heart failure. These studies have consistently shown statistically significant improvements in quality of life, NYHA functional class ranking, exercise tolerance, and left ventricular reverse remodeling. Some studies have suggested reductions in morbidity and mortality. This latter observation has been confirmed by a recent large-scale outcomes study. Thus, cardiac resynchronization therapy should be routinely considered in eligible NYHA class III and IV heart failure patients with ventricular dyssynchrony.			3

[7] See appendix A
[8] See appendix A

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
64.. Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005; 352(15):1539-1549.	1	A total of 813 patients were enrolled and followed for a mean of 29.4 months. There were 82 deaths in the cardiac-resynchronization group (n=159), as compared with 120 in the medical-therapy group (n=224).	To evaluate the effects of Cardiac resynchronization on morbidity and mortality in patients with heart failure.	In patients with heart failure and cardiac dyssynchrony, cardiac resynchronization improves symptoms and the quality of life and reduces complications and the risk of death. These benefits are in addition to those afforded by standard pharmacologic therapy. The implantation of a cardiac-resynchronization device should routinely be considered in such patients.	1
Echo					
65. Bax JJ, Bleeker GB, Marwick TH, et al. Left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronization therapy. J Am Coll Cardiol 2004; 44(9):1834-1840.	9	Eighty-five patients with end-stage HF, QRS duration 120 ms, and left bundle-branch block were evaluated by tissue Doppler imaging before CRT. At baseline and six months follow-up, New York Heart Association functional class, quality of life and 6-min walking distance, LV volumes, and LV ejection fraction were determined. Events (death, hospitalization for decompensated HF) were obtained during one-year follow-up.	This study was designed to predict the response and prognosis after cardiac resynchronization therapy (CRT) in patients with end-stage heart failure (HF). Response to CRT was predicted by the presence of LV dyssynchrony assessed by tissue Doppler imaging. Moreover, the prognostic value of LV dyssynchrony in patients undergoing CRT was assessed.	1) all baseline characteristics are comparable in responders and nonresponders to CRT, except for the LV dyssynchrony, which was larger in responders; 2) baseline LV dyssynchrony of 65 ms or more has a sensitivity and specificity of 80% to predict clinical response and 92% to predict reverse LV remodeling; 3) patients with extensive dyssynchrony who undergo CRT have an excellent prognosis (6% event rate), whereas patients who do not have dyssynchrony and undergo CRT have a poor prognosis (event rate 50%).	2

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
66.. Penicka M, Bartunek J, De BB, et al. Improvement of left ventricular function after cardiac resynchronization therapy is predicted by tissue Doppler imaging echocardiography. Circulation. 2004;109:978-83.	3a	Forty-nine consecutive patients with CHF and a wide QRS complex (182+/-32 ms) were studied by echocardiography before resynchronization. Intraventricular and interventricular asynchrony and their combination were assessed by pulsed-wave tissue Doppler imaging from measurements of regional electromechanical coupling times in basal segments of the right and left ventricle	To investigate predictive factors of LV functional recovery and reversed remodeling after biventricular pacing.	At 6-month follow-up, responders were defined by a relative increase in LV ejection fraction > or =25% compared with baseline (n=27). Receiver operating curve analysis revealed the degree of intraventricular asynchrony (area under the curve=0.77), interventricular asynchrony (area under the curve=0.69), and their combination (area under the curve=0.84) as the best predictors of functional recovery after resynchronization.	3
67.. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. Circulation. 2008;117:2608-16.	2	Fifty-three centers in Europe, Hong Kong, and the United States enrolled 498 patients with standard CRT indications (New York Heart Association class III or IV heart failure, left ventricular ejection fraction < or = 35%, QRS > or = 130 ms, stable medical regimen). Twelve echocardiographic parameters of dyssynchrony, based on both conventional and tissue Doppler-based methods, were evaluated after site training in acquisition methods and blinded core laboratory analysis.	Study whether echocardiographic parameters of mechanical dyssynchrony can improve patient selection for cardiac resynchronization therapy (CRT).	Indicators of positive CRT response were improved clinical composite score and > or = 15% reduction in left ventricular end-systolic volume at 6 months. Clinical composite score was improved in 69% of 426 patients, whereas left ventricular end-systolic volume decreased > or = 15% in 56% of 286 patients with paired data. The ability of the 12 echocardiographic parameters to predict clinical composite score response varied widely, with sensitivity ranging from 6% to 74% and specificity ranging from 35% to 91%; for predicting left ventricular end-systolic volume response, sensitivity ranged from 9% to 77% and specificity from 31% to 93%. For all the parameters, the area under the receiver-operating characteristics curve for positive clinical or volume response to CRT was < or = 0.62. There was large variability in the analysis of the dyssynchrony parameters.	1

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
68.. Ypenburg C, Van Bommel RJ, Delgado V, et al. Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy. J Am Coll Cardiol. 2008;52:1402-9.	9	The site of latest mechanical activation was determined by speckle tracking radial strain analysis and related to the LV lead position on chest X-ray in 244 CRT candidates. Echocardiographic evaluation was performed after 6 months. Long-term follow-up included all-cause mortality and hospitalizations for heart failure.	To evaluate echocardiographic parameters after 6 months of cardiac resynchronization therapy (CRT) as well as long-term outcome in patients with the left ventricular (LV) lead positioned at the site of latest activation (concordant LV lead position) as compared with that seen in patients with a discordant LV lead position.	Significant LV reverse remodeling (reduction in LV end-systolic volume from 189 +/- 83 ml to 134 +/- 71 ml, p < 0.001) was noted in the group of patients with a concordant LV lead position (n = 153, 63%), whereas patients with a discordant lead position showed no significant improvements. In addition, during long-term follow-up (32 +/- 16 months), less events (combined for heart failure hospitalizations and death) were reported in patients with a concordant LV lead position. Moreover, a concordant LV lead position appeared to be an independent predictor of hospitalization-free survival after long-term CRT (hazard ratio: 0.22, p = 0.004)	2
69.. Sogaard P, Egeblad H, Kim WY, et al. Tissue Doppler imaging predicts improved systolic performance and reversed left ventricular remodeling during long-term cardiac resynchronization therapy. *J Am Coll Cardiol* 2002; 40(4):723-730.	3a	Twenty-five consecutive patients with severe heart failure and bundle branch block who underwent biventricular pacemaker implantation were included. Before and after implantation of the pacemaker, three-dimensional echocardiography and TDI were performed. These examinations were repeated at outpatient visits every six months.	To evaluate the long-term impact of cardiac resynchronization therapy (CRT) on left ventricular (LV) performance and remodeling using three-dimensional echocardiography and tissue Doppler imaging (TDI).	Five patients (20%) died during one-year follow-up. In the remaining 20 patients, significant reductions in LV end-diastolic volume and LV end-systolic volume of 9.6 $\pm$14% and 16.5 $\pm$ 15%, respectively (p < 0.01), could be demonstrated during long-term follow-up. Accordingly, LV ejection fraction increased by 21.7 $\pm$ 18% (p < 0.01). According to a newly developed TDI technique—tissue tracking—all regional myocardial segments improved their longitudinal systolic shortening (p _ 0.01). The extent of the LV base displaying delayed longitudinal contraction, as detected by TDI before pacemaker implantation, predicted long-term efficacy of CRT. The QRS duration failed to predict resynchronization efficacy.	2

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
Other Relevant Literature					
70. Yu CM, Fung JW, Zhang Q, et al. Tissue Doppler imaging is superior to strain rate imaging and postsystolic shortening (PSS) on the prediction of reverse remodeling in both ischemic and nonischemic heart failure after cardiac resynchronization therapy. *Circulation* 2004; 110(1):66-73.	9	Fifty-four heart failure patients (mean age, 65±11 years; 36 male) who received CRT and were followed up for at least 3 months were analyzed.	To compare the relative predictive values of tissue Doppler imaging (TDI) and strain-rate imaging (SRI) parameters for LV reverse remodeling in patients who received CRT and examined for potential differences in ischemic (n=22) and nonischemic (n=32) heart failure.	Ts-SD is the most powerful predictor of LV reverse remodeling and was consistently useful for ischemic and nonischemic heart failure. However, PSS is useful only for nonischemic pathogenesis, whereas the role of SRI parameters was not supported by the present study.	3
71. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med 2007; 357(24):2461-2471.	1	Enrolled 172 patients who had a standard indication for an implantable cardioverter–defibrillator. Patients received the CRT device and were randomly assigned to the CRT group or to a control group (no CRT) for 6 months. The primary end point was the proportion of patients with an increase in peak oxygen consumption of at least 1.0 ml per kilogram of body weight per minute during cardiopulmonary exercise testing at 6 months.	To evaluate the efficacy of CRT in patients with a standard indication for an implantable cardioverter–defibrillator (ischemic or nonischemic cardiomyopathy and an ejection fraction of 35% or less), NHYA class III heart failure, a QRS interval of less than 130 msec, and evidence of mechanical dyssynchrony as measured on echocardiography.	At 6 months, the CRT group and the control group did not differ significantly in the proportion of patients with the primary end point (46% and 41%, respectively). In a prespecified subgroup with a QRS interval of 120 msec or more, the peak oxygen consumption increased in the CRT group (P = 0.02), but it was unchanged in a subgroup with a QRS interval of less than 120 msec (P = 0.45). There were 24 heartfailure events requiring intravenous therapy in 14 patients in the CRT group (16.1%) and 41 events in 19 patients in the control group (22.3%), but the difference was not significant.	1

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
72 Parreira L, Santos JF, Madeira J, et al. Cardiac resynchronization therapy with sequential biventricular pacing: impact of echocardiography guided VV delay optimization on acute results. Rev Port Cardiol. 2005;24:1355-65.	3a	15 consecutive patients with severe heart failure and left bundle branch block underwent CRT by BiV device implantation. They were studied with conventional and TDI echo the day before implantation. Left ventricular ejection fraction (LVEF) was determined, and the electromechanical delay (QS), defined as the time interval from the beginning of the QRS to the S wave in pulsed TDI, was assessed in each of the four left ventricular basal segments. The dyssynchrony index was calculated as the difference between the longest and shortest electromechanical delay (QS(max-min)). The parameters were re-evaluated the day after implantation during simultaneous BiV pacing and with seven different VV delays. The optimal VV delay was determined by finding the VV interval corresponding to the maximum aortic velocity time interval (VTI).	ardiac resynchronization therapy (CRT) improves left ventricular synchrony as evaluated by tissue Doppler imaging (TDI), leading to improved left ventricular performance and reverse remodeling. New CRT devices enable programming of left and right VV delay. The aim of this study was to determine whether sequential biventricular (BiV) pacing by echo-guided programming of VV delay would enhance the response to CRT.	QS(max-min) decreased from 85.3 +/- 27.0 msec to 46.7 +/- 23.0 msec (p = 0.0002), LVEF increased from 21.7 +/- 7.3% to 30.0 +/- 7.7% (p = 0.0001) and aortic VTI increased from 12.7 +/- 3.6 cm to 15.2 +/- 4.0 cm (p < 0.0001), with simultaneous BiV pacing. The VV intervals were programmed as follows: LV pre-excitation by 10 msec in five patients, 20 msec in three, 30 msec in two, and 40 msec in three; and RV pre-excitation by 10 msec in one and by 20 msec in one. The maximal aortic VTI obtained with VV delay programming increased from 15.2 +/- 4.0 cm to 17.7 +/- 4.0 cm (p = 0.0005). During optimized sequential BiV pacing, QS(max-min) further decreased from 46.7 +/- 23.0 msec to 30.6 +/- 21.0 msec (p = 0.02) and LVEF further increased from 30.0 +/- 7.7% to 35.0 +/- 7.7% (p = 0.0003).	3

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
73. Sawhney NS, Waggoner AD, Garhwal S, et al. Randomized prospective trial of atrioventricular delay programming for cardiac resynchronization therapy. Heart Rhythm. 2004;1:562-7.	2	A randomized, prospective, single-blind clinical trial was performed to compare two methods of AV delay programming in 40 patients with severe heart failure referred for CRT. Patients were randomized to either an optimized AV delay determined by Doppler echocardiography (group 1, n = 20) or an empiric AV delay of 120 ms (group 2, n = 20) with both groups programmed in the atriosynchronous biventricular pacing (VDD) mode. Optimal AV delay was defined as the AV delay that yielded the largest aortic VTI at one of eight tested AV intervals (between 60 and 200 ms). New York Heart Association (NYHA) functional classification and quality-of-life (QOL) score were compared 3 months after randomization.	The purpose of this study was to determine if AV delay optimization with continuous-wave Doppler aortic velocity-time integral (VTI) is clinically superior to an empiric program in patients treated with cardiac resynchronization therapy (CRT) for severe heart failure.	Immediately after CRT initiation with AV delay programming, VTI improved by 4.0 +/- 1.7 cm vs 1.8 +/- 3.6 cm (P < .02), and ejection fraction (EF) increased by 7.8 +/- 6.2% vs 3.4 +/- 4.4% (P < .02) in group 1 vs group 2, respectively. After 3 months, NYHA classification improved by 1.0 +/- 0.5 vs 0.4 +/- 0.6 class points (P < .01), and QOL score improved by 23 +/- 13 versus 13 +/- 11 points (P < .03) for group 1 vs group 2, respectively.	1

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
74. Perry R, De Pasquale CG, Chew DP, Aylward PE, Joseph MX. QRS duration alone misses cardiac dyssynchrony in a substantial proportion of patients with chronic heart failure. *J Am Soc Echocardiogr* 2006; 19(10):1257-1263	2	A total of 100 patients with significant LV Dysfunction (Simpson's ejection fraction < 35%) referred for echocardiography underwent TSI. Dyssynchrony was defined as a difference in time to peak contraction of greater than 105 milliseconds between opposing ventricular segments.	To determine the prevalence of dyssynchrony in a cardiomyopathic population referred for echocardiography irrespective of QRS duration, to validate the novel technique of TSI in evaluation of mechanical LV dyssynchrony and to determine the accuracy of QRS duration in predicting significant LV dyssynchrony.	61 patients (61%) demonstrated significant dyssynchrony, whereas 52% had a QRS duration of greater than 120 milliseconds. Among those with a prolonged QRS duration, significant dyssynchrony was evident in 30 (58%). However, dyssynchrony was also common among those with a narrow QRS duration (<120 milliseconds) (31 patients [65%]). Of the 61 patients with dyssynchrony, 31 (51%) would have been missed if QRS criteria were used alone.	1
75. Yu CM, Lin H, Zhang Q, Sanderson JE. High prevalence of left ventricular systolic and diastolic asynchrony in patients with congestive heart failure and normal QRS duration. *Heart* 2003; 89(1):54-60	3a	200 subjects were studied by echocardiography. 67 patients had HF and narrow QRS complexes (< 120 ms), 45 patients had HF and wide QRS complexes (> 120 ms), and 88 served as normal controls.	To study the possible occurrence of left ventricular (LV) systolic and diastolic asynchrony in patients with systolic heart failure (HF) and narrow QRS complexes.	LV systolic and diastolic mechanical asynchrony is common in patients with HF with narrow QRS complexes. As QRS complex duration is not a determinant of systolic asynchrony, it implies that assessment of intraventricular synchronicity is probably more important than QRS duration in considering cardiac resynchronisation treatment.	2
CMR					

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
76. Roes SD, Borleffs CJ, van der Geest RJ, et al. Infarct tissue heterogeneity assessed with contrast-enhanced MRI predicts spontaneous ventricular arrhythmia in patients with ischemic cardiomyopathy and implantable cardioverter-defibrillator. Circ Cardiovasc Imaging 2009; 2(3):183-190.	3a	Ninety-one patients (age, 65±11 years) with previous myocardial infarction scheduled for ICD implantation underwent cine MRI to evaluate left ventricular function and volumes and contrast-enhanced MRI for characterization of scar tissue (infarct gray zone as measure of infarct tissue heterogeneity, infarct core, and total infarct size). Appropriate ICD therapy was documented in 18 patients (20%) during a median follow-up of 8.5 months (interquartile range, 2.1 to 20.3).	To evaluate the predictive value of infarct tissue heterogeneity assessed with contrast-enhanced MRI on the occurrence of spontaneous ventricular arrhythmia with subsequent implantable cardioverter-defibrillator (ICD) therapy (as surrogate of sudden cardiac death) in patients with previous myocardial infarction.	Multivariable Cox proportional hazards analysis revealed that infarct gray zone was the strongest predictor of the occurrence of spontaneous ventricular arrhythmia with subsequent ICD therapy (hazard ratio, 1.49/10 g; CI, 1.01 to 2.20; _2_4.0; *P*_0.04). Infarct tissue heterogeneity on contrast-enhanced MRI is the strongest predictor of spontaneous ventricular arrhythmia with subsequent ICD therapy (as surrogate of sudden cardiac death) among other clinical and MRI variables, that is, total infarct size and left ventricular function and volumes, in patients with previous myocardial infarction.	2
77 Assomull RG, Prasad SK, Lyne J, et al. Cardiovascular magnetic resonance, fibrosis, and prognosis in dilated cardiomyopathy. *J Am Coll Cardiol* 2006; 48(10):1977-1985.	3	Consecutive DCM patients (n = 101) with the presence or absence of midwall fibrosis were followed up prospectively for 658 ± 355 days for events.	To study the prognostic implications of midwall fibrosis in dilated cardiomyopathy (DCM) in a prospective longitudinal study.	Midwall fibrosis was present in 35% of patients and was associated with a higher rate of the predefined primary combined end point of all-cause death and hospitalization for a cardiovascular event (hazard ratio 3.4, p _ 0.01). Multivariate analysis showed midwall fibrosis as the sole significant predictor of death or hospitalization. However, there was no significant difference in all-cause mortality between the 2 groups. Midwall fibrosis also predicted secondary outcome measures of sudden cardiac death (SCD) or ventricular tachycardia (VT) (hazard ratio 5.2, p _ 0.03). Midwall fibrosis remained predictive of SCD/VT after correction for baseline differences in left ventricular ejection fraction between the 2 groups.	2

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
78. Yokokawa M, Tada H, Koyama K, et al. Nontransmural scar detected by magnetic resonance imaging and origin of ventricular tachycardia in structural heart disease. Pacing Clin Electrophysiol. 2009;32 Suppl 1:S52-S56.	3a	MR was performed in 34 patients with monomorphic, sustained VT and dilated cardiomyopathy (DCM, n = 18), ischemic cardiomyopathy (ICM, n = 10), or idiopathic VT (IVT, n = 6). The VT exit site was assessed by a detailed analysis of the QRS morphology, including bundle branch block type, limb lead polarity, and precordial R-wave transition. On CMR imaging, the transmural score of each of the 17 segments was assigned, using a computer-assisted, semiautomatic technique, to measure the DE areas. Segmental scars were classified as nontransmural when DE was 1-75% and transmural when DE was 76-100% of the left ventricular mass in each segment.	Contrast-enhanced magnetic resonance imaging (CMR) identifies scar tissue as an area of delayed enhancement (DE). The scar region might be the substrate for ventricular tachycardia (VT). However, the relationship between the occurrence of VT and the characteristics of scar tissue has not been fully studied.	A scar was detected in all patients with DCM or ICM. Nontransmural scar tissue was often found at the VT exit site, in patients with DCM or ICM. In contrast, no scar was found in patients with IVT.	2

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
79. Bilchick KC, Dimaano V, Wu KC, et al. Cardiac magnetic resonance assessment of dyssynchrony and myocardial scar predicts function class improvement following cardiac resynchronization therapy. *JACC Cardiovasc Imaging* 2008; 1(5):561-568	9	MR-MT was performed in patients with cardiomyopathy, divided into: 1) a CRT-HF cohort (n=20) with mean (SD) LVEF 0.23 (0.057) in order to evaluate the clinical use of MR-MT and DEMRI prior to CRT; and 2) a multimodality cohort (n=27) with mean (SD) LVEF 0.20 (0.066) in order to compare MR-MT and tissue Doppler imaging (TDI) assessments of mechanical dyssynchrony. MR-MT was also performed in 9 healthy control subjects.	To test a circumferential mechanical dyssynchrony index (circumferential uniformity ratio estimate, or CURE; 0–1, 1=synchrony) derived from magnetic resonance myocardial tagging (MR-MT) for predicting	MR-MT showed that control subjects had highly synchronous contraction (mean [SD] CURE 0.96 [0.01]) while TDI septal-lateral delay indicated dyssynchrony in 44% of normal controls. Using a cutoff of <0.75 for CURE based on ROC analysis (AUC 0.889), 56% of patients tested positive for mechanical dyssynchrony, and the MR-MT CURE predicted improved function class in CRT-HF patients with 90% accuracy (PPV 87%; NPV 100%). Adding DEMRI (% total scar<15%) data improved accuracy further to 95% (PPV 93%; NPV 100%). The correlation between CURE and QRSd was modest in all cardiomyopathy subjects (r=0.58, p<0.001), and somewhat less in the CRTHF group (r=0.40, p=0.08). The multimodality cohort showed a 30% discordance rate between CURE and TDI septal-lateral delay.	3
SPECT					

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
80. van RN, Jaffe CC, Krumholz HM, et al. Comparison and reproducibility of visual echocardiographic and quantitative radionuclide left ventricular ejection fractions. . Am J Cardiol. 1996;77:843-50.	3a	Seventy-three clinically stable patients had both equilibrium radionuclide angiography and echocardiography performed within a 4-day period. LVEF by both techniques was compared after blinded analysis by 3 echocardiographers and 3 nuclear technologists. Reproducibility was assessed by blinded repeat analysis after a 1-week interval. The frequency of differences in repeat assessments of EF that the authors considered to be of potential clinical relevance (i.e., difference > or = 10% EF units) was assessed for both techniques. Correlation of LVEF determined by both methods was good (r = 0.81, SEE = 3.5) but with substantial differences in individual patients (limits of agreement, 23.6%).	This study (1) compares quantification of LVEF by equilibrium radionuclide angiography with visual estimation of LVEF by echocardiography, (2) determines the reproducibility of both methods, and (3) evaluates whether differences in determinations of LVEF are of clinical relevance.	Intra- and inter-observer reproducibility was good for both methods, but better for radionuclide LVEF than for echocardiographic LVEF. Limits of agreement were substantially better for radionuclide LVEF than for echocardiographic LVEF (1.8% to 3.6% versus 13.4% to 17.4%, respectively). Clinically relevant differences did not occur on repeat processing of equilibrium radionuclide angiography. In contrast, potentially clinically relevant differences occurred in 8% to 26% of studies on repeat analysis of echocardiography. Thus, LVEF determined by equilibrium radionuclide angiography and echocardiography show good agreement. Both methods provide clinically valuable measurements for LV function. However, when a precisely reproducible measurement is required for patient management decisions, equilibrium radionuclide angiography is the method of choice.	2

Reference	Study Type[7]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[8]
Clinical Scenario 4 – ICD & CRT					
81. Boogers MM, Van Kriekinge SD, Henneman MM, et al. Quantitative gated SPECT-derived phase analysis on gated myocardial perfusion SPECT detects left ventricular dyssynchrony and predicts response to cardiac resynchronization therapy. *J Nucl Med* 2009; 50(5):718-725.	1	Patients (n 5 40) with severe heart failure (New York Heart Association class III–IV), an LV ejection fraction of no more than 35%, and a QRS complex greater than or equal to 120 ms were evaluated for LV dyssynchrony using GMPS and echocardiography with TDI. At baseline and after 6 mo of CRT, clinical status, LV volumes, and LV ejection fraction were evaluated. Patients with functional improvement were classified as CRT responders.	To validate the QGS algorithm for phase analysis on GMPS in a direct comparison with echocardiography using tissue Doppler imaging (TDI) for LV dyssynchrony assessment. Also, prediction of response to CRT using GMPS and phase analysis was evaluated.	Both histogram bandwidth and phase SD derived from GMPS correlated significantly with TDI for assessment of LV dyssynchrony. At baseline, CRT responders showed a significantly larger histogram bandwidth and a larger phase SD than did nonresponders. For phase SD, sensitivity and specificity similar to those for histogram bandwidth were obtained at a cutoff value of 19.6±. QGS phase analysis on GMPS correlated significantly with TDI for the assessment of LV dyssynchrony. Moreover, a high accuracy for prediction of response to CRT was obtained using either histogram bandwidth or phase SD.	1

Clinical Scenario #5 – Repeat Imaging Evaluation of HF

Literature Review

Summary Statement

Although a common clinical situation, little published literature exists regarding repeat imaging and evaluation of patients with HF. The majority of literature is associated with re-evaluation for consideration of implantable defibrillator therapy or efficacy of resynchronization therapy. Both of these clinical situations and their relevant literature are reviewed in Scenario 4.

Regarding stable patients without a change in clinical status, a few studies have demonstrated that radionuclide imaging, echo, and CMR can reliably demonstrate a change in LVEF after medical therapy (126-130). However, there were no studies found that identified a clinical benefit in routine serial imaging in patients without a change in clinical status. Measures of rest and stress LVEF measures with SPECT have been shown to be highly reproducible (56,131).

Guidelines

The relevant guideline recommendations for this clinical scenario are:

ACC/AHA Heart Failure Guidelines

CLASS IIa

1. Repeat measurement of EF and the severity of structural remodeling can be useful to provide information in patients with HF who have had a change in clinical status or who have experienced or recovered from a clinical event or received treatment that might have had a significant effect on cardiac function. (Level of Evidence: C)

Reference	Study Type[9]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[10]
Clinical Scenario #5 – Repeat Imaging Evaluation of HF					
82. Konstam MA, Rousseau MF, Kronenberg MW, et al. Effects of the angiotensin converting enzyme inhibitor enalapril on the long-term progression of left ventricular dysfunction in patients with heart failure. SOLVD Investigators. Circulation. 1992;86:431-8.	1	One hundred eight patients enrolled in the Studies of Left Ventricular Dysfunction (SOLVD) Prevention Trial, with left ventricular ejection fraction < or = 0.35 but without clinical heart failure, underwent radionuclide ventriculograms, and 49 underwent left heart catheterizations. Measurements were made before and after double-blinded randomization to enalapril (2.5 to 20 mg/d) or placebo.	Patients with heart failure and reduced left ventricular (LV) ejection fraction (EF) manifest progressive LV dilatation, which is prevented by angiotensin converting enzyme (ACE) inhibitors. In patients with asymptomatic LV systolic dysfunction, in whom there is less activation of the renin-angiotensin system, ventricular remodeling might be less rapid and the benefit of ACE inhibitors less discernible.	Repeated-measures analysis of all time points showed significant differences for change in end-diastolic volume (EDV) between enalapril and placebo groups. Significant difference between the enalapril and placebo groups (P < .05) was present for change in EDV at 1 year within the catheterization study and at a mean of 25 months within the radionuclide study. Radionuclide EDV increased in placebo patients (119 +/- 28 to 124 +/- 33 mL/m2, mean +/- SD) and decreased in enalapril patients (120 +/- 25 to 113 +/- 25 mL/m2). Differences between the two groups were significantly less than previously described in patients with symptomatic heart failure (P < .02), with less increase in LV volumes in the placebo group and less decrease in volumes in the enalapril group.	1
83. Doherty NE, III, Seelos KC, Suzuki J, et al. Application of cine nuclear magnetic resonance imaging for sequential evaluation of response to angiotensin-converting enzyme inhibitor therapy in dilated cardiomyopathy. J Am Coll Cardiol. 1992;19:1294-302.	-	Cine nuclear magnetic resonance (NMR) imaging was used to serially measure cardiovascular function in 17 patients with New York Heart Association class II or III heart failure and left ventricular ejection fraction less than or equal to 45% who were treated for 3 months with benazepril hydrochloride, a new angiotensin-converting enzyme inhibitor, while continuing treatment with diuretic agents and digoxin. Interobserver reproducibilities for ejection fraction (r = 0.94, SEE 3.3%), end-systolic volume (r = 0.98, SEE 10.6 ml), end-diastolic volume (r = 0.99, SEE 8.29 ml), end-systolic mass (r = 0.96, SEE 15.4 g), end-systolic wall stress (r = 0.91, SEE 10 dynes.s.cm-5) and end-systolic stress/volume ratio (r = 0.85, SEE 0.13) demonstrated applicability of cine NMR imaging for the serial assessment of cardiovascular function in response to pharmacologic interventions in patients with heart failure. During 12 weeks of treatment with benazepril, ejection fraction increased progressively from 29.7 +/- 2.2% (mean +/- SEM) to 36 +/- 2.2% (p less than 0.05), end-diastolic volume decreased from 166 +/- 14 to 158 +/- 12 ml (p = NS), end-systolic volume decreased from 118 +/- 12 to 106 +/- 11 ml (p less than 0.05), left ventricular mass decreased from 235 +/- 13 to 220 +/- 12 g (p less than 0.05), end-systolic wall stress decreased 29% from 90 +/- 5 to 64 +/- 5 dynes.s.cm-5 (p less than 0.05), end-systolic pressure decreased from 92.6 +/- 3.7 to 78.8 +/- 5.3 (p less than 0.05) and end-systolic stress/volume ratio, a load-independent index of contractility, decreased from 0.83 +/- 0.05 to 0.67 +/- 0.06 (p less than 0.05), demonstrating that improved ejection fraction is due to afterload reduction.			-

[9] See appendix A
[10] See appendix A

Reference	Study Type[9]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[10]
Clinical Scenario #5 – Repeat Imaging Evaluation of HF					
84. Kasama S, Toyama T, Sumino H, et al. Prognostic value of serial cardiac 123I-MIBG imaging in patients with stabilized chronic heart failure and reduced left ventricular ejection fraction. J Nucl Med. 2008;49:907-14.	9	A total of 208 patients with CHF (left ventricular ejection fraction [LVEF] < 45%) and with no cardiac events for at least 5 mo were identified on the basis of a history of decompensated acute heart failure requiring hospitalization. The delayed percentage of denervation (% denervation), delayed heart-to-mediastinum count (H/M) ratio, and washout rate (WR) were determined from the patients' 123I-MIBG images just before they left the hospital and after they had received 6 mo of treatment. The left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and LVEF were also determined by echocardiography at the same time points.	Many studies have shown that a one-time 123I-metaiodobenzylguanidine (123I-MIBG) scintigraphic study during a stable period is useful for determining the prognosis of patients with chronic heart failure (CHF). However, the findings from this imaging modality are well known to be improved by medical treatment for heart failure. Accordingly, this study was performed to determine whether serial 123I-MIBG scintigraphic studies represent a reliable prognostic marker for patients with CHF.	Of the 208 patients, 56 experienced fatal cardiac events during the study. The mean follow-up period was 4.45 +/- 1.82 y. The baseline H/M ratio and WR; follow-up % denervation, H/M ratio, and WR; Delta-% denervation, H/M ratio, and WR; baseline LVEF; follow-up LVEDV, LVESV, and LVEF; and Delta-LVEDV, Delta-LVESV, and Delta-LVEF were significantly worse in the cardiac death group. A Cox regression analysis showed that the Delta-WR was an independent predictor of cardiac death. Moreover, sudden death occurred in 13 of the 56 patients with cardiac death. A Cox regression analysis also showed that the Delta-WR was an incremental predictor of sudden death. The cardiac death-free rate and sudden death-free rate were significantly higher in patients with Delta-WR less than -5% and Delta-WR less than -2% than in patients with Delta-WR greater than or equal to -5% and Delta-WR greater than or equal to -2%.	2

Reference	Study Type[9]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[10]
Clinical Scenario #5 – Repeat Imaging Evaluation of HF					
85. Grothues F, Moon JC, Bellenger NG, et al. Interstudy reproducibility of right ventricular volumes, function, and mass with cardiovascular magnetic resonance. Am Heart J. 2004;147:218-23.	3a	Sixty subjects (47 men; 20 healthy volunteers, 20 patients with heart failure, 20 patients with ventricular hypertrophy) underwent 2 CMR studies for assessment of RV measurements with a minimum time interval between each study.	Cardiovascular magnetic resonance (CMR) has shown excellent results for interstudy reproducibility in the assessment of left ventricular (LV) parameters. However, interstudy reproducibility data for the more complex-shaped right ventricle in a large study group have not yet been reported. We sought to determine the interstudy reproducibility of measurements of right ventricular (RV) volumes, function, and mass with CMR and compare it with correspondent LV values.	The overall interstudy reproducibility (range between groups) for the RV was 6.2% (4.2%-7.8%) for end-diastolic volume, 14.1% (8.1%-18.1%) for end-systolic volume, 8.3% (4.3%-10.4%) for ejection fraction (EF), and 8.7% (7.8%-9.4%) for RV mass. RV reproducibility was not as good as for the LV for all measures in all 3 groups, but this was only statistically significant for EF (P <.01).	2

Reference	Study Type[9]	Patient/Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence[10]
Clinical Scenario #5 – Repeat Imaging Evaluation of HF					
86. Grothues F, Smith GC, Moon JC, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol. 2002;90:29-34.	2	A total of 60 subjects (normal volunteers [n = 20], or patients with heart failure [n = 20] or LV hypertrophy [n = 20]) underwent 2 CMRs and 2 echocardiographic studies for assessment of LV volumes, function, and mass.	Fast breath-hold cardiovascular magnetic resonance (CMR) shows excellent results for interstudy reproducibility of left ventricular (LV) volumes, ejection fraction, and mass, which are thought to be superior to results of 2-dimensional echocardiography. However, there is no direct comparison of the interstudy reproducibility of both methods in the same subjects.	The interstudy reproducibility coefficient of variability was superior for CMR in all groups for all parameters. Statistical significance was reached for end-systolic volume (4.4% to 9.2% vs 13.7% to 20.3%, p <0.001), ejection fraction (2.4% to 7.3% vs 8.6% to 19.4%, p <0.001), and mass (2.8% to 4.8% vs 11.6% to 15.7% p <0.001), with a trend for end-diastolic volume (2.9% to 4.9% vs 5.5% to 10.5%, p = 0.17). The superior interstudy reproducibility resulted in considerably lower calculated sample sizes (reductions of 55% to 93%) required by CMR compared with echocardiography to show clinically relevant changes in LV dimensions and function. Thus, CMR has excellent interstudy reproducibility in normal, dilated, and hypertrophic hearts, and is superior to 2-dimensional echocardiography.	1
87. McGowan JH, Cleland JG. Reliability of reporting left ventricular systolic function by echocardiography: a systematic review of 3 methods. Am Heart J. 2003;146:388-97.	7	A systematic review was performed of the evidence for the accuracy of 3 echocardiographic methods--Simpson's rule, wall motion index (WMI), and subjective visual assessment--compared with radionuclide or contrast ventriculography for the assessment of LV ejection fraction (LVEF).	An accurate assessment of left ventricular (LV) systolic function is of central importance to the diagnosis and management of heart failure. Echocardiography is currently the technique most widely used for this purpose.	Twenty-five studies were identified in which data on agreement between echocardiography and reference methods were obtainable. A further 18 studies provided correlation data alone. For Simpson's rule, Bland-Altman limits of agreement (95% CI) ranged from LVEF +/-7% to +/-25% (median +/-18%); for WMI +/-13% to +/-20% (median +/-16%); and for subjective visual assessment +/-16% to +/-24% (median +/-19%). Subject echogenicity, the nature of underlying disease, and the use of additional imaging technology, including secondary harmonic imaging and contrast agents, is likely to influence the accuracy of different methods. No method appears to systematically under- or overestimate LVEF to any major extent.	2

Appendix A Evidence Table Key

Study Type Key

Numbers 1-7 are for studies of therapies while numbers 8-15 are used to describe diagnostic studies.

1. Randomized Controlled Trial — Treatment
2. Controlled Trial
3. Observation Study
    a. Cohort
    b. Cross-sectional
    c. Case-control
4. Clinical Series
5. Case reviews
6. Anecdotes
7. Reviews
8. Randomized Controlled Trial — Diagnostic
9. Comparative Assessment
10. Clinical Assessment
11. Quantitative Review
12. Qualitative Review
13. Descriptive Study
14. Case Report
15. Other (Described in text)

Strength of Evidence Key

- Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.
- Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.
- Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.
- Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

References

1. Hunt SA, Abraham WT, Chin MH, et al. 2009 Focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration With the International Society for Heart and Lung Transplantation. J Am Coll Cardiol. 2009;53:e1-e90.

2. Gardin JM, McClelland R, Kitzman D, et al. M-mode echocardiographic predictors of six- to seven-year incidence of coronary heart disease, stroke, congestive heart failure, and mortality in an elderly cohort (the Cardiovascular Health Study). Am J Cardiol. 2001;87:1051-7.

3. Aurigemma GP, Gottdiener JS, Shemanski L, et al. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the cardiovascular health study. J Am Coll Cardiol. 2001;37:1042-8.

4. Lim TK, Ashrafian H, Dwivedi G, et al. Increased left atrial volume index is an independent predictor of raised serum natriuretic peptide in patients with suspected heart failure but normal left ventricular ejection fraction: Implication for diagnosis of diastolic heart failure. Eur J Heart Fail. 2006;8:38-45.

5. Chen AA, Wood MJ, Krauser DG, et al. NT-proBNP levels, echocardiographic findings, and outcomes in breathless patients: results from the ProBNP Investigation of Dyspnoea in the Emergency Department (PRIDE) echocardiographic substudy. Eur Heart J. 2006;27:839-45.

6. Grayburn PA, Appleton CP, DeMaria AN, et al. Echocardiographic predictors of morbidity and mortality in patients with advanced heart failure: the Beta-blocker Evaluation of Survival Trial (BEST). J Am Coll Cardiol. 2005;45:1064-71.

7. Francis CM, Caruana L, Kearney P, et al. Open access echocardiography in management of heart failure in the community. BMJ. 1995;310:634-6.

8. Whalley GA, Wright SP, Pearl A, et al. Prognostic role of echocardiography and brain natriuretic peptide in symptomatic breathless patients in the community. Eur Heart J. 2008;29:509-16.

9. Melenovsky V, Borlaug BA, Rosen B, et al. Cardiovascular features of heart failure with preserved ejection fraction versus nonfailing hypertensive left ventricular hypertrophy in the urban Baltimore community: the role of atrial remodeling/dysfunction. J Am Coll Cardiol. 2007;49:198-207.

10. Persson H, Lonn E, Edner M, et al. Diastolic dysfunction in heart failure with preserved systolic function: need for objective evidence:results from the CHARM Echocardiographic Substudy-CHARMES. J Am Coll Cardiol. 2007;49:687-94.

11. Davis BR, Kostis JB, Simpson LM, et al. Heart failure with preserved and reduced left ventricular ejection fraction in the antihypertensive and lipid-lowering treatment to prevent heart attack trial. Circulation. 2008;118:2259-67.

12. St John SM, Pfeffer MA, Moye L, et al. Cardiovascular death and left ventricular remodeling two years after myocardial infarction: baseline predictors and impact of long-term use of captopril: information from the Survival and Ventricular Enlargement (SAVE) trial. Circulation. 1997;96:3294-9.

13. Jenkins C, Moir S, Chan J, et al. Left ventricular volume measurement with echocardiography: a comparison of left ventricular opacification, three-dimensional echocardiography, or both with magnetic resonance imaging. Eur Heart J. 2009;30:98-106.

14. Valle-Munoz A, Estornell-Erill J, Soriano-Navarro CJ, et al. Late gadolinium enhancement-cardiovascular magnetic resonance identifies coronary artery disease as the aetiology of left ventricular dysfunction in acute new-onset congestive heart failure. Eur J Echocardiogr. 2009;10:968-74.

15. Bluemke DA, Kronmal RA, Lima JA, et al. The relationship of left ventricular mass and geometry to incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study. J Am Coll Cardiol. 2008;52:2148-55.

16. Bogaert J, Francone M. Cardiovascular magnetic resonance in pericardial diseases. J Cardiovasc Magn Reson. 2009;11:14.

17. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in Collaboration With the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2008;52:e1-121.

18. Chander A, Brenner M, Lautamaki R, et al. Comparison of measures of left ventricular function from electrocardiographically gated 82Rb PET with contrast-enhanced CT ventriculography: a hybrid PET/CT analysis. J Nucl Med. 2008;49:1643-50.

19. Baim D, Grossman W. Grossman's Cardiac Catheterization, Angiography, and Intervention / Edition 7. Lippincott Williams & Wilkins, 2005.

20. Abidov A, Rozanski A, Hachamovitch R, et al. Prognostic significance of dyspnea in patients referred for cardiac stress testing. N Engl J Med. 2005;353:1889-98.

21. Velazquez EJ, Lee KL, O'Connor CM, et al. The rationale and design of the Surgical Treatment for Ischemic Heart Failure (STICH) trial. J Thorac Cardiovasc Surg. 2007;134:1540-7.

22. Elhendy A, Sozzi F, van Domburg RT, et al. Effect of myocardial ischemia during dobutamine stress echocardiography on cardiac mortality in patients with heart failure secondary to ischemic cardiomyopathy. Am J Cardiol. 2005;96:469-73.

23. Maskoun W, Mustafa N, Mahenthiran J, et al. Wall motion abnormalities with low-dose dobutamine predict a high risk of cardiac death in medically treated patients with ischemic cardiomyopathy. Clin Cardiol. 2009;32:403-9.

24. Sozzi FB, Elhendy A, Rizzello V, et al. Prognostic significance of akinesis becoming dyskinesis during dobutamine stress echocardiography. J Am Soc Echocardiogr. 2007;20:257-61.

25. Dall'Armellina E, Morgan TM, Mandapaka S, et al. Prediction of cardiac events in patients with reduced left ventricular ejection fraction with dobutamine cardiovascular magnetic resonance assessment of wall motion score index. J Am Coll Cardiol. 2008;52:279-86.

26. Yokokawa M, Tada H, Toyama T, et al. Magnetic resonance imaging is superior to cardiac scintigraphy to identify nonresponders to cardiac resynchronization therapy. Pacing Clin Electrophysiol. 2009;32 Suppl 1:S57-S62.

27. Krittayaphong R, Maneesai A, Chaithiraphan V, et al. Comparison of diagnostic and prognostic value of different electrocardiographic criteria to delayed-enhancement magnetic resonance imaging for healed myocardial infarction. Am J Cardiol. 2009;103:464-70.

28. Abidov A, Rozanski A, Hachamovitch R, et al. Prognostic significance of dyspnea in patients referred for cardiac stress testing. N Engl J Med. 2005;353:1889-98.

29. Vaduganathan P, He ZX, Vick GW, III, et al. Evaluation of left ventricular wall motion, volumes, and ejection fraction by gated myocardial tomography with technetium 99m-labeled tetrofosmin: a comparison with cine magnetic resonance imaging. J Nucl Cardiol. 1999;6:3-10.

30. Cleland JG, Pennell DJ, Ray SG, et al. Myocardial viability as a determinant of the ejection fraction response to carvedilol in patients with heart failure (CHRISTMAS trial): randomised controlled trial. Lancet. 2003;362:14-21.

31. Soman P, Lahiri A, Mieres JH, et al. Etiology and pathophysiology of new-onset heart failure: evaluation by myocardial perfusion imaging. J Nucl Cardiol. 2009;16:82-91.

32. Range FT, Paul M, Schafers KP, et al. Myocardial perfusion in nonischemic dilated cardiomyopathy with and without atrial fibrillation. J Nucl Med. 2009;50:390-6.

33. Chander A, Brenner M, Lautamaki R, et al. Comparison of measures of left ventricular function from electrocardiographically gated 82Rb PET with contrast-enhanced CT ventriculography: a hybrid PET/CT analysis. J Nucl Med. 2008;49:1643-50.

34. Feola M, Biggi A, Chauvie S, et al. Myocardial scar and insulin resistance predict cardiovascular events in severe ischaemic myocardial dysfunction: a perfusion-metabolism positron emission tomography study. Nucl Med Commun. 2008;29:448-54.

35. Tuunanen H, Engblom E, Naum A, et al. Free fatty acid depletion acutely decreases cardiac work and efficiency in cardiomyopathic heart failure. Circulation. 2006;114:2130-7.

36. Thompson K, Saab G, Birnie D, et al. Is septal glucose metabolism altered in patients with left bundle branch block and ischemic cardiomyopathy? J Nucl Med. 2006;47:1763-8.

37. Budoff MJ, Shavelle DM, Lamont DH, et al. Usefulness of electron beam computed tomography scanning for distinguishing ischemic from nonischemic cardiomyopathy. J Am Coll Cardiol. 1998;32:1173-8.

38. Andreini D, Pontone G, Pepi M, et al. Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with dilated cardiomyopathy. J Am Coll Cardiol. 2007;49:2044-50.

39. Cornily JC, Gilard M, Le GG, et al. Accuracy of 16-detector multislice spiral computed tomography in the initial evaluation of dilated cardiomyopathy. Eur J Radiol. 2007;61:84-90.

40. Budoff MJ, Shavelle DM, Lamont DH, et al. Usefulness of electron beam computed tomography scanning for distinguishing ischemic from nonischemic cardiomyopathy. J Am Coll Cardiol. 1998;32:1173-8.

41. Bluemke DA, Kronmal RA, Lima JA, et al. The relationship of left ventricular mass and geometry to incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study. J Am Coll Cardiol. 2008;52:2148-55.

42. Alderman EL, Fisher LD, Litwin P, et al. Results of coronary artery surgery in patients with poor left ventricular function (CASS). Circulation. 1983;68:785-95.

43. Fox KF, Cowie MR, Wood DA, et al. Coronary artery disease as the cause of incident heart failure in the population. Eur Heart J. 2001;22:228-36.

44. Arques S, Ambrosi P, Gelisse R, et al. Prevalence of angiographic coronary artery disease in patients hospitalized for acute diastolic heart failure without clinical and electrocardiographic evidence of myocardial ischemia on admission. Am J Cardiol. 2004;94:133-5.

45. Allman KC, Shaw LJ, Hachamovitch R, et al. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. J Am Coll Cardiol. 2002;39:1151-8.

46. Bax JJ, Poldermans D, Elhendy A, et al. Improvement of left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine stress echocardiography. J Am Coll Cardiol. 1999;34:163-9.

47. Rizzello V, Poldermans D, Schinkel AF, et al. Long term prognostic value of myocardial viability and ischaemia during dobutamine stress echocardiography in patients with ischaemic cardiomyopathy undergoing coronary revascularisation. Heart. 2006;92:239-44.

48. Pedone C, Bax JJ, van Domburg RT, et al. Long-term prognostic value of ejection fraction changes during dobutamine-atropine stress echocardiography. Coron Artery Dis. 2005;16:309-13.

49. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med. 2000;343:1445-53.

50. Selvanayagam JB, Kardos A, Francis JM, et al. Value of delayed-enhancement cardiovascular magnetic resonance imaging in predicting myocardial viability after surgical revascularization. Circulation. 2004;110:1535-41.

51. Jahnke C, Nagel E, Gebker R, et al. Prognostic value of cardiac magnetic resonance stress tests: adenosine stress perfusion and dobutamine stress wall motion imaging. Circulation. 2007;115:1769-76.

52. Wahl A, Paetsch I, Gollesch A, et al. Safety and feasibility of high-dose dobutamine-atropine stress cardiovascular magnetic resonance for diagnosis of myocardial ischaemia: experience in 1000 consecutive cases. Eur Heart J. 2004;25:1230-6.

53. Wagner A, Mahrholdt H, Holly TA, et al. Contrast-enhanced MRI and routine single photon emission computed tomography (SPECT) perfusion imaging for detection of subendocardial myocardial infarcts: an imaging study. Lancet. 2003;361:374-9.

54. Roes SD, Kaandorp TA, Marsan NA, et al. Agreement and disagreement between contrast-enhanced magnetic resonance imaging and nuclear imaging for assessment of myocardial viability. Eur J Nucl Med Mol Imaging. 2009;36:594-601.

55. Inaba Y, Chen JA, Bergmann SR. Quantity of viable myocardium required to improve survival with revascularization in patients with ischemic cardiomyopathy: A meta-analysis. J Nucl Cardiol. 2010;17:646-54.

56. Beanlands RS, Ruddy TD, deKemp RA, et al. Positron emission tomography and recovery following revascularization (PARR-1): the importance of scar and the development of a prediction rule for the degree of recovery of left ventricular function. J Am Coll Cardiol. 2002;40:1735-43.

57. Beanlands RS, Nichol G, Huszti E, et al. F-18-fluorodeoxyglucose positron emission tomography imaging-assisted management of patients with severe left ventricular dysfunction and suspected coronary disease: a randomized, controlled trial (PARR-2). J Am Coll Cardiol. 2007;50:2002-12.

58. Slart RH, Bax JJ, de BJ, et al. Comparison of 99mTc-sestamibi/18FDG DISA SPECT with PET for the detection of viability in patients with coronary artery disease and left ventricular dysfunction. Eur J Nucl Med Mol Imaging. 2005;32:972-9.

59. Siebelink HM, Blanksma PK, Crijns HJ, et al. No difference in cardiac event-free survival between positron emission tomography-guided and single-photon emission computed tomography-guided patient management: a prospective, randomized comparison of patients with suspicion of jeopardized myocardium. J Am Coll Cardiol. 2001;37:81-8.

60. Mendoza DD, Joshi SB, Weissman G, et al. Viability imaging by cardiac computed tomography. J Cardiovasc Comput Tomogr. 2010;4:83-91.

61. le Polain de Waroux JB, Pouleur AC, Goffinet C, et al. Combined coronary and late-enhanced multidetector-computed tomography for delineation of the etiology of left ventricular dysfunction: comparison with coronary angiography and contrast-enhanced cardiac magnetic resonance imaging. Eur Heart J. 2008;29:2544-51.

62. Gula LJ, Klein GJ, Hellkamp AS, et al. Ejection fraction assessment and survival: an analysis of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). Am Heart J. 2008;156:1196-200.

63. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002;346:1845-53.

64. Cleland J, Freemantle N, Ghio S, et al. Predicting the long-term effects of cardiac resynchronization therapy on mortality from baseline variables and the early response a report from the CARE-HF (Cardiac Resynchronization in Heart Failure) Trial. J Am Coll Cardiol. 2008;52:438-45.

65. Bax JJ, Bleeker GB, Marwick TH, et al. Left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronization therapy. J Am Coll Cardiol. 2004;44:1834-40.

66. Penicka M, Bartunek J, De BB, et al. Improvement of left ventricular function after cardiac resynchronization therapy is predicted by tissue Doppler imaging echocardiography. Circulation. 2004;109:978-83.

67. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. Circulation. 2008;117:2608-16.

68. Ypenburg C, Van Bommel RJ, Delgado V, et al. Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy. J Am Coll Cardiol. 2008;52:1402-9.

69. Sogaard P, Egeblad H, Kim WY, et al. Tissue Doppler imaging predicts improved systolic performance and reversed left ventricular remodeling during long-term cardiac resynchronization therapy. J Am Coll Cardiol. 2002;40:723-30.

70. Yu CM, Fung JW, Zhang Q, et al. Tissue Doppler imaging is superior to strain rate imaging and postsystolic shortening on the prediction of reverse remodeling in both ischemic and nonischemic heart failure after cardiac resynchronization therapy. Circulation. 2004;110:66-73.

71. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med. 2007;357:2461-71.

72. Parreira L, Santos JF, Madeira J, et al. Cardiac resynchronization therapy with sequential biventricular pacing: impact of echocardiography guided VV delay optimization on acute results. Rev Port Cardiol. 2005;24:1355-65.

73. Sawhney NS, Waggoner AD, Garhwal S, et al. Randomized prospective trial of atrioventricular delay programming for cardiac resynchronization therapy. Heart Rhythm. 2004;1:562-7.

74. Perry R, De Pasquale CG, Chew DP, et al. QRS duration alone misses cardiac dyssynchrony in a substantial proportion of patients with chronic heart failure. J Am Soc Echocardiogr. 2006;19:1257-63.

75. Yu CM, Lin H, Zhang Q, et al. High prevalence of left ventricular systolic and diastolic asynchrony in patients with congestive heart failure and normal QRS duration. Heart. 2003;89:54-60.

76. Roes SD, Borleffs CJ, van der Geest RJ, et al. Infarct tissue heterogeneity assessed with contrast-enhanced MRI predicts spontaneous ventricular arrhythmia in patients with ischemic cardiomyopathy and implantable cardioverter-defibrillator. Circ Cardiovasc Imaging. 2009;2:183-90.

77. Assomull RG, Prasad SK, Lyne J, et al. Cardiovascular magnetic resonance, fibrosis, and prognosis in dilated cardiomyopathy. J Am Coll Cardiol. 2006;48:1977-85.

78. Yokokawa M, Tada H, Koyama K, et al. Nontransmural scar detected by magnetic resonance imaging and origin of ventricular tachycardia in structural heart disease. Pacing Clin Electrophysiol. 2009;32 Suppl 1:S52-S56.

79. Bilchick KC, Dimaano V, Wu KC, et al. Cardiac magnetic resonance assessment of dyssynchrony and myocardial scar predicts function class improvement following cardiac resynchronization therapy. JACC Cardiovasc Imaging. 2008;1:561-8.

80. van RN, Jaffe CC, Krumholz HM, et al. Comparison and reproducibility of visual echocardiographic and quantitative radionuclide left ventricular ejection fractions. Am J Cardiol. 1996;77:843-50.

81. Boogers MM, Van Kriekinge SD, Henneman MM, et al. Quantitative gated SPECT-derived phase analysis on gated myocardial perfusion SPECT detects left ventricular dyssynchrony and predicts response to cardiac resynchronization therapy. J Nucl Med. 2009;50:718-25.

82. Konstam MA, Rousseau MF, Kronenberg MW, et al. Effects of the angiotensin converting enzyme inhibitor enalapril on the long-term progression of left ventricular dysfunction in patients with heart failure. SOLVD Investigators. Circulation. 1992;86:431-8.

83. Doherty NE, III, Seelos KC, Suzuki J, et al. Application of cine nuclear magnetic resonance imaging for sequential evaluation of response to angiotensin-converting enzyme inhibitor therapy in dilated cardiomyopathy. J Am Coll Cardiol. 1992;19:1294-302.

84. Kasama S, Toyama T, Sumino H, et al. Prognostic value of serial cardiac 123I-MIBG imaging in patients with stabilized chronic heart failure and reduced left ventricular ejection fraction. J Nucl Med. 2008;49:907-14.

85. Grothues F, Moon JC, Bellenger NG, et al. Interstudy reproducibility of right ventricular volumes, function, and mass with cardiovascular magnetic resonance. Am Heart J. 2004;147:218-23.

86. Grothues F, Smith GC, Moon JC, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol. 2002;90:29-34.

87. McGowan JH, Cleland JG. Reliability of reporting left ventricular systolic function by echocardiography: a systematic review of 3 methods. Am Heart J. 2003;146:388-97.