

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. <i>Circulation</i> . 2013;128(16):e240-327.	Review/Other-Dx	N/A	To assist clinicians in clinical decision making by describing a range of generally acceptable approaches to the diagnosis, management, and prevention of specific diseases or conditions.	No abstract available.	4
2. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. <i>Circulation</i> . 2016;133(4):e38-360.	Review/Other-Dx	N/A	To review the statistics of Heart Disease and Stroke.	No results stated in abstract.	4
3. Centers for Disease Control and Prevention. National Center for Health Statistics. National Health and Nutrition Examination Survey. 2017; Available at: https://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm .	Review/Other-Dx	N/A	To review the National Center for Health Statistics.	No results stated in abstract.	4

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EVIDENCE TABLE**

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4. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. <i>Circ Heart Fail.</i> 2013;6(3):606-619.	Review/Other-Dx	N/A	To update and expand on prior work and provide an in-depth look at how the changing demographics in the United States will impact the prevalence and cost of care for Heart failure (HF) for different US populations.	We estimated future costs of HF by adapting a methodology developed by the American Heart Association to project the epidemiology and future costs of HF from 2012 to 2030 without double counting the costs attributed to comorbid conditions. The model assumes that HF prevalence will remain constant by age, sex, and race/ethnicity and that rising costs and technological innovation will continue at the same rate. By 2030, >8 million people in the United States (1 in every 33) will have HF. Between 2012 and 2030, real (2010\$) total direct medical costs of HF are projected to increase from \$21 billion to \$53 billion. Total costs, including indirect costs for HF, are estimated to increase from \$31 billion in 2012 to \$70 billion in 2030. If one assumes all costs of cardiac care for HF patients are attributable to HF (no cost attribution to comorbid conditions), the 2030 projected cost estimates of treating patients with HF will be 3-fold higher (\$160 billion in direct costs).	4

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EVIDENCE TABLE**

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5. Lloyd-Jones DM, Larson MG, Leip EP, et al. Lifetime risk for developing congestive heart failure: the Framingham Heart Study. <i>Circulation</i> . 2002;106(24):3068-3072.	Observational-Dx	3757 men & 4472 women	To understand the Lifetime risk for developing congestive heart failure.	Among Framingham Heart Study subjects who were free of CHF at baseline, we determined the lifetime risk for developing overt CHF at selected index ages. We followed 3757 men and 4472 women from 1971 to 1996 for 124 262 person-years; 583 subjects developed CHF and 2002 died without prior CHF. At age 40 years, the lifetime risk for CHF was 21.0% (95% CI 18.7% to 23.2%) for men and 20.3% (95% CI 18.2% to 22.5%) for women. Remaining lifetime risk did not change with advancing index age because of rapidly increasing CHF incidence rates. At age 80 years, the lifetime risk was 20.2% (95% CI 16.1% to 24.2%) for men and 19.3% (95% CI 16.5% to 22.2%) for women. Lifetime risk for CHF doubled for subjects with blood pressure \geq 160/100 versus <140/90 mm Hg. In a secondary analysis, we only considered those who developed CHF without an antecedent myocardial infarction; at age 40 years, the lifetime risk for CHF was 11.4% (95% CI 9.6% to 13.2%) for men and 15.4% (95% CI 13.5% to 17.3%) for women.	2

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6. Merlo M, Pivetta A, Pinamonti B, et al. Long-term prognostic impact of therapeutic strategies in patients with idiopathic dilated cardiomyopathy: changing mortality over the last 30 years. <i>Eur J Heart Fail.</i> 2014;16(3):317-324.	Observational-Dx	853 IDCM patients	To analyse the long-term prognostic impact of evidence-based integrated therapeutic strategies in patients with idiopathic dilated cardiomyopathy (IDCM).	From 1978 to 2007, 853 IDCM patients (45 +/- 15 years, 72% males) were enrolled and classified as follows: Group 1, 110 patients (12.8%) enrolled during 1978-1987; Group 2, 376 patients (44.1%) enrolled during 1988-1997; Group 3, 367 patients (43.1%) enrolled during 1998-2007. ACE-inhibitors/angiotensin receptor blockers were administered in 34%, 93%, and 93% (P <0.001), and beta-blockers in 11%, 82%, and 86% (P <0.001) in Groups 1, 2, and 3, respectively; implantable cardioverter-defibrillator (ICD) were implanted in 2%, 14%, and 13% (P = 0.005); mean time to device implantation was lower in Group 3. At 8 years, heart transplant (HTx)-free survival rates were 55%, 71%, and 87% in Groups 1, 2, and 3, respectively (P <0.001). Similar progressive improvement was found for pump-failure death (DHF)/HTx, while survival free from sudden death (SD) was significantly improved only in Group 3. Multivariable models considering competing risk indicated early diagnosis (i.e. a baseline less advanced disease stage) and tailored medical therapy (HR 0.44, CI 95% 0.19-0.98) as independent protectors against DHF/HTx. Concerning SD, lower left ventricular ejection fraction emerged as a predictor, while ICD was the only therapy with a protective role (HR 0.08, CI 95% 0.01-0.61). Treatment with digitalis emerged as a predictor of both DHF/HTx and SD.	2

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7. Roger VL, Weston SA, Redfield MM, et al. Trends in heart failure incidence and survival in a community-based population. JAMA. 2004;292(3):344-350.	Review/Other-Dx	N/A	To test the hypothesis that the incidence of heart failure has declined and survival after heart failure diagnosis has improved over time but that secular trends have diverged by sex.	The incidence of heart failure was higher among men (378/100 000 persons; 95% confidence interval [CI], 361-395 for men; 289/100 000 persons; 95% CI, 277-300 for women) and did not change over time among men or women. After a mean follow-up of 4.2 years (range, 0-23.8 years), 3347 deaths occurred, including 1930 among women and 1417 among men. Survival after heart failure diagnosis was worse among men than women (relative risk, 1.33; 95% CI, 1.24-1.43) but overall improved over time (5-year age-adjusted survival, 43% in 1979-1984 vs 52% in 1996-2000, P<.001). However, men and younger persons experienced larger survival gains, contrasting with less or no improvement for women and elderly persons.	4
8. Centers for Disease Control and Prevention. National Center for Health Statistics. National Vital Statistics Reports. 2011-Mortality Multiple Cause-of-Death Public Use Record. 2017; Available at: https://www.cdc.gov/nchs/data/dvs/Record_Layout_2011.pdf .	Review/Other-Dx	N/A	To review the National Vital Statistic Reports.	No results stated in abstract.	4
9. Centers for Disease Control and Prevention. National Center for Health Statistics. National Vital Statistics Reports. 2013-Mortality Multiple Cause-of-Death Public Use Record. 2017; Available at: https://www.cdc.gov/nchs/data/dvs/Record_Layout_2013.pdf .	Review/Other-Dx	N/A	To review the reports of National Vital Statistics.	No results stated in abstract.	4

Suspected New-Onset and Known Nonacute Heart Failure
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10. Vogel-Claussen J, Elshafee ASM, Kirsch J, et al. ACR Appropriateness Criteria(R) Dyspnea-Suspected Cardiac Origin. J Am Coll Radiol. 2017;14(5S):S127-S137.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for dyspnea-suspected cardiac origin.	No results stated in abstract.	4
11. Drazner MH, Rame JE, Stevenson LW, Dries DL. Prognostic importance of elevated jugular venous pressure and a third heart sound in patients with heart failure. N Engl J Med. 2001;345(8):574-581.	Observational-Dx	2479 patients	To determine the prognostic value of elevated jugular venous pressure or a third heart sound in patients with heart failure.	Data on 2479 patients were complete and analyzed. In multivariate analyses that were adjusted for other markers of the severity of heart failure, elevated jugular venous pressure was associated with an increased risk of hospitalization for heart failure (relative risk, 1.32; 95 percent confidence interval, 1.08 to 1.62; P<0.01), death or hospitalization for heart failure (relative risk, 1.30; 95 percent confidence interval, 1.11 to 1.53; P<0.005), and death from pump failure (relative risk, 1.37; 95 percent confidence interval, 1.07 to 1.75; P<0.05). The presence of a third heart sound was associated with similarly increased risks of these outcomes.	3
12. 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. Circulation. 2009;119(14):e391-479.	Review/Other-Dx	N/A	To provide guidelines for the Diagnosis and Management of Heart Failure in Adults.	No results stated in abstract.	4

Suspected New-Onset and Known Nonacute Heart Failure
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13. Ezekowitz JA, McAlister FA, Howlett J, et al. A prospective evaluation of the established criteria for heart failure with preserved ejection fraction using the Alberta HEART cohort. ESC Heart Fail. 2018;5(1):19-26.	Observational-Dx	565 patients	To test the utility of established criteria to classify patients with heart failure with a preserved ejection fraction (HF-PEF).	For the diagnosis of HF-PEF, the positive likelihood ratios were 6.1, 6.9, and 4.8 for the Zile, European Society of Cardiology (ESC) 2007, and ESC 2016 criteria, respectively. The negative likelihood ratios were 0.58, 0.60, and 0.42 for the Zile, ESC 2007, and ESC 2016 criteria, respectively. All three criteria lacked sensitivity to detect HF-PEF (46.5%, 44.1%, and 51.8%, respectively) but were highly specific (92.4%, 93.9%, and 89%, respectively). We further evaluated the criteria to distinguish HF-PEF from other diagnoses after excluding heart failure with reduced ejection fraction; the results were similar.	1
14. Richardson P, McKenna W, Bristow M, et al. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies. Circulation. 1996;93(5):841-842.	Review/Other-Dx	N/A	To report the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies.	No results stated in abstract.	4
15. Mammen L, Woodard PK, Abbara S, et al. ACR appropriateness criteria(R) nonischemic myocardial disease with clinical manifestations (ischemic cardiomyopathy already excluded). J Thorac Imaging. 2014;29(4):W44-47.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for nonischemic myocardial disease with clinical manifestations (ischemic cardiomyopathy already excluded).	No results stated in abstract.	4

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16. Madsen EB, Gilpin E, Slutsky RA, Ahnve S, Henning H, Ross J, Jr. Usefulness of the chest x-ray for predicting abnormal left ventricular function after acute myocardial infarction. <i>Am Heart J</i> . 1984;108(6):1431-1436.	Observational-Dx	229 patients	To investigate the relationship between roentgenographic findings and left ventricular function assessed by a predischARGE left ventricular ejection fraction (EF) study in patients with acute myocardial infarction (AMI).	At discharge 134 patients (59%) had abnormal ejection fraction (less than 0.51) and 35 had pulmonary venous congestion (15%). The sensitivity of the x-ray for detecting an abnormal ejection fraction was 20% when pulmonary venous congestion was observed on the discharge x-ray film (specificity 92% and predictive value 77%), 52% if pulmonary venous congestion was present on any x-ray film during the hospitalization (specificity 74% and predictive value 73%), and 47% if the cardiothoracic ratio was abnormal (greater than or equal to 0.50) on the discharge x-ray film (specificity and predictive value 66%).	3
17. Milne EN, Pistolesi M, Miniati M, Giuntini C. The radiologic distinction of cardiogenic and noncardiogenic edema. <i>AJR Am J Roentgenol</i> . 1985;144(5):879-894.	Observational-Dx	216 chest radiographs of 61 patients	To determine, as objectively and rigorously as possible, the validity of the chest radiograph in deciding what type of pulmonary edema is present, in order to provide a rational pathophysiologic basis for the treatment of that particular type of edema.	Three principal and seven ancillary features have been identified, all of which are statistically significant and permit the cause of the edema to be determined correctly in a high percentage of cases. The three principal features are distribution of pulmonary flow, distribution of pulmonary edema, and the width of the vascular pedicle. The ancillary features are pulmonary blood volume, peribronchial cuffing, septal lines, pleural effusions, air bronchograms, lung volume, and cardiac size. Differing constellations of these features occur, each of which is characteristic of a specific type of edema. Overall accuracy of diagnosis in this study ranged from 86% to 89%. The highest accuracy was obtained in distinguishing capillary permeability edema from all other varieties (91%), and the lowest in distinguishing chronic cardiac failure from renal failure (81%).	3

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18. Souza AS, Bream PR, Elliott LP. Chest film detection of coronary artery calcification. The value of the CAC triangle. <i>Radiology</i> . 1978;129(1):7-10.	Observational-Dx	86 patients	To determine the value of the coronary artery calcifications (CAC) triangle.	Of 57 patients, 24 (42%) with CAC observed fluoroscopically had a strongly suspected or positive CAC triangle.	3
19. MacGregor JH, Chen JT, Chiles C, Kier R, Godwin JD, Ravin CE. The radiographic distinction between pericardial and myocardial calcifications. <i>AJR Am J Roentgenol</i> . 1987;148(4):675-677.	Review/Other-Dx	29 patients	To review proven cases of pericardial calcification and calcified left ventricular aneurysms in an attempt to identify distinguishing features.	Pericardial calcification was found primarily over the right-sided cardiac chambers (14 of 14 patients) and in the atrioventricular grooves (11 of 14), infrequently over the base of the left ventricle (five of 14), and rarely over the apex of the left ventricle (two of 14). When the left ventricle was involved, there was always more extensive calcification elsewhere in the pericardium. Myocardial calcification occurred predominantly in the apex of the left ventricle (13 of 15 patients), although it was rarely confined to the posterior wall of the left ventricle (two of 15).	4
20. McComb BL, Chung JH, Crabtree TD, et al. ACR Appropriateness Criteria(R) Routine Chest Radiography. <i>J Thorac Imaging</i> . 2016;31(2):W13-15.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for routine chest radiography.	No results stated in abstract.	4
21. Bhatia RS, Ivers N, Yin CX, et al. Design and methods of the Echo WISELY (Will Inappropriate Scenarios for Echocardiography Lessen Significantly) study: An investigator-blinded randomized controlled trial of education and feedback intervention to reduce inappropriate echocardiograms. <i>Am Heart J</i> . 2015;170(2):202-209.	Review/Other-Dx	N/A	To evaluate the hypothesis that an Appropriate use criteria (AUC)-based educational and feedback intervention will reduce the proportion of inappropriate echocardiograms ordered by attending physicians in the ambulatory environment.	No results stated in abstract.	4

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22. Douglas PS, Garcia MJ, Haines DE, et al. ACCF/AHA/ASA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 Appropriate Use Criteria for Echocardiography. A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance American College of Chest Physicians. J Am Soc Echocardiogr. 2011;24(3):229-267.	Review/Other-Dx	N/A	To provide guidelines for Echocardiography.	No results stated in abstract.	4
23. Giubbini R, Milan E, Bertagna F, et al. Nuclear cardiology and heart failure. Eur J Nucl Med Mol Imaging. 2009;36(12):2068-2080.	Review/Other-Dx	N/A	To review Nuclear cardiology and heart failure.	No results stated in abstract.	4

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24. Peix A, Mesquita CT, Paez D, et al. Nuclear medicine in the management of patients with heart failure: guidance from an expert panel of the International Atomic Energy Agency (IAEA). Nucl Med Commun. 2014;35(8):818-823.	Review/Other-Dx	N/A	To reinforce the information on the use of nuclear cardiology techniques for the assessment of heart failure and associated myocardial disease.	Heart failure is increasing worldwide at epidemic proportions, resulting in considerable disability, mortality, and increase in healthcare costs. Gated myocardial perfusion single photon emission computed tomography or PET imaging is the most prominent imaging modality capable of providing information on global and regional ventricular function, the presence of intraventricular synchronism, myocardial perfusion, and viability on the same test. In addition, I-mIBG scintigraphy is the only imaging technique approved by various regulatory agencies able to provide information regarding the adrenergic function of the heart. Therefore, both myocardial perfusion and adrenergic imaging are useful tools in the workup and management of heart failure patients.	4
25. Vervloet DM, J DES. Nuclear cardiac imaging for the diagnosis and management of heart failure: what can be learned from recent guidelines? Q J Nucl Med Mol Imaging. 2016:[E-pub ahead of print].	Review/Other-Dx	N/A	To provide the clinical cardiologist and nuclear medicine specialist a brief overview of the currently accepted clinical use of cardiac nuclear imaging for the diagnosis and management of patients with heart failure based on recent (2012-2015) European Society of Cardiology (ESC) guidelines.	No results stated in abstract.	4
26. Dweck MR, Williams MC, Moss AJ, Newby DE, Fayad ZA. Computed Tomography and Cardiac Magnetic Resonance in Ischemic Heart Disease. J Am Coll Cardiol. 2016;68(20):2201-2216.	Review/Other-Dx	N/A	To review the Computed Tomography and Cardiac Magnetic Resonance in Ischemic Heart Disease.	No results stated in abstract.	4

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27. Muehlberg F, Toepper A, Fritschi S, Prothmann M, Schulz-Menger J. Magnetic Resonance Imaging Applications on Infiltrative Cardiomyopathies. [Review]. Journal of Thoracic Imaging. 31(6):336-347, 2016 Nov.	Review/Other-Dx	N/A	To review the Magnetic Resonance Imaging Applications on Infiltrative Cardiomyopathies.	No results stated in abstract.	4
28. Rajiah P, Raza S, Saboo SS, Ghoshhajra B, Abbara S. Update on the Role of Cardiac Magnetic Resonance in Acquired Nonischemic Cardiomyopathies. [Review]. Journal of Thoracic Imaging. 31(6):348-366, 2016 Nov.	Review/Other-Dx	N/A	To update on the Role of Cardiac Magnetic Resonance in Acquired Nonischemic Cardiomyopathies.	No results stated in abstract.	4
29. Al-Mallah MH, Aljizeeri A, Villines TC, Srichai MB, Alsaileek A. Cardiac computed tomography in current cardiology guidelines. J Cardiovasc Comput Tomogr. 2015;9(6):514-523.	Review/Other-Dx	N/A	To provide guidelines on Cardiac computed tomography in current cardiology.	No results stated in abstract.	4
30. den Harder AM, Willeminck MJ, de Jong PA, et al. New horizons in cardiac CT. Clin Radiol. 2016;71(8):758-767.	Review/Other-Dx	N/A	To review New horizons in cardiac computed tomography (CT).	No results stated in abstract.	4

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31. Dehmer GJ, Weaver D, Roe MT, et al. A contemporary view of diagnostic cardiac catheterization and percutaneous coronary intervention in the United States: a report from the CathPCI Registry of the National Cardiovascular Data Registry, 2010 through June 2011. J Am Coll Cardiol. 2012;60(20):2017-2031.	Review/Ot her-Dx	N/A	To provide a report to the public of data from the Cath percutaneous coronary intervention (PCI) Registry of the National Cardiovascular Data Registry.	Some notable findings include, for example, that on-site cardiac surgery was not available in 83% of facilities performing fewer than 200 PCIs annually, with these facilities representing 32.6% of the facilities reporting, but performing only 12.4% of the PCIs in this data sample. Patients 65 years of age or older represented 38.7% of those undergoing PCI, with 12.3% being 80 years of age or older. Almost 80% of PCI patients were overweight (body mass index ≥ 25 kg/m ²), 80% had dyslipidemia, and 27.6% were current or recent smokers. Among patients undergoing elective PCI, 52% underwent a stress study before the procedure, with stress myocardial perfusion being used most frequently. Calcium scores and coronary computed tomography angiography were used very infrequently (<3%) before diagnostic or PCI procedures. Radial artery access was used in 8.3% of diagnostic and 6.9% of PCI procedures. Primary PCI was performed with a median door-to-balloon time of 64.5 min for nontransfer patients and 121 min for transfer patients. In-hospital risk-adjusted mortality in ST-segment elevation myocardial infarction patients was 5.2% in this sample.	4

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32. Matsumura M, Mintz GS, Kang SJ, et al. Intravascular ultrasound and near-infrared spectroscopic features of coronary lesions with intraplaque haemorrhage. <i>Eur Heart J Cardiovasc Imaging</i> . 2017;18(11):1222-1228.	Observational-Dx	101 coronary arteries; 56 autopsy hearts	To define the features of intraplaque haemorrhage as seen using grayscale intravascular ultrasound (IVUS) and near-infrared spectroscopy (NIRS).	We evaluated coronary arteries from autopsy hearts using 40MHz IVUS and NIRS and compared the imaging findings to histopathology. A total of 2324 2-mm long histological segments from 101 coronary arteries from 56 autopsy hearts were included. Intraplaque haemorrhage was found pathologically in 0.8% (18/2324) of segments. Segments with intraplaque haemorrhage had more fibroatheromas (FAs) with a greater IVUS plaque burden, a greater prevalence of IVUS echolucent zones, and a higher NIRS-lipid core burden index (LCBI) compared to segments without intraplaque haemorrhage (FAs: 72.2% vs. 18.3%, $P < 0.0001$; plaque burden: 59.7% [95% confidence interval: 55.5, 64.0] vs. 48.6% [45.8, 51.3], $P < 0.0001$; echolucent zones: 88.9% vs. 2.8%, $P < 0.0001$; NIRS-LCBI: 176 [88, 264] vs. 72 [53, 91], $P = 0.02$). The 16 IVUS superficial echolucent zones with intraplaque haemorrhage had more late FAs but shorter echolucent zone lengths (0.9 mm [0.7, 1.1] vs. 1.7 mm [1.5, 1.9], $P < 0.0001$) compared to 65 IVUS superficial echolucent zones without intraplaque haemorrhage.	2
33. Pellicano M, De Bruyne B, Toth GG, Casselman F, Wijns W, Barbato E. Fractional flow reserve to guide and to assess coronary artery bypass grafting. <i>Eur Heart J</i> . 2017;38(25):1959-1968.	Review/Other-Dx	N/A	To highlight the role of invasive functional evaluation in patients in whom coronary artery bypass graft (CABG) is indicated, and to examine the clinical evidence available in favour of fractional flow reserve (FFR) adoption in these patients, outline appropriate use, as well as point out potential pitfalls.	No results stated in abstract.	4

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34. Witteles RM, Knowles JW, Perez M, et al. Use and overuse of left ventriculography. <i>Am Heart J.</i> 2012;163(4):617-623 e611.	Review/Other-Dx	96,235 patients	To examine the “real-world” use of left ventriculography as a routine “add-on” to coronary angiography and, specifically, to examine how frequently it has been performed in patients who have had a recent assessment of left ventricular ejection fraction (LVEF) by another modality.	Of 96,235 patients who underwent coronary angiography, left ventriculography was performed in 78,705 (81.8%). Use of left ventriculography was high in all subgroups, with greatest use in younger patients, those with a diagnosis of coronary disease, and those in the Southern United States. In the population who had undergone a very recent ejection fraction assessment by another modality (within 30 days) and who had had no intervening diagnosis of new heart failure, myocardial infarction, hypotension, or shock (37,149 patients), left ventriculography was performed in 32,798 patients (88%)-a rate higher than in the overall cohort.	4
35. Botvinick EH. Current methods of pharmacologic stress testing and the potential advantages of new agents. <i>J Nucl Med Technol.</i> 2009;37(1):14-25.	Review/Other-Dx	N/A	To review the Current methods of pharmacologic stress testing and the potential advantages of new agents.	No results stated in abstract.	4
36. Roalfe AK, Mant J, Doust JA, et al. Development and initial validation of a simple clinical decision tool to predict the presence of heart failure in primary care: the MICE (Male, Infarction, Crepitations, Edema) rule. <i>Eur J Heart Fail.</i> 2012;14(9):1000-1008.	Review/Other-Dx	5 articles	To develop and provisionally validate a clinical prediction rule to optimize referral for echocardiography of people identified in primary care with suspected heart failure.	A systematic review identified studies of diagnosis of heart failure set in primary care. The individual patient data for five of these studies were obtained. Logistic regression models to predict heart failure were developed on one of the data sets and validated on the others using area under the receiver operating characteristic curve (AUROC), and goodness-of-fit calibration plots. A model based upon four simple clinical features (Male, history of myocardial Infarction, Crepitations, Edema: MICE) and natriuretic peptide had good validity when applied to other data sets, with AUROCs between 0.84 and 0.93, and reasonable calibration. The rule performed well across the data sets, with sensitivity between 81% and 96% and specificity between 57% and 74%.	4

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37. Kennedy S, Simon B, Alter HJ, Cheung P. Ability of physicians to diagnose congestive heart failure based on chest X-ray. J Emerg Med. 2011;40(1):47-52	Observational-Dx	55	To evaluate the ability of emergency physicians to recognize CHF on chest X-ray and the effect of level of training and confidence upon accuracy of interpretation.	Physicians correctly identified the CHF chest X-rays 79% of the time (sensitivity 59%, specificity 96%; positive likelihood ratio 14.6, negative likelihood ratio 0.43). Accuracy ranged from a low of 78% among first-year residents to a high of 85% among attendings, and from 73% (confidence rating of 3/5) to 91% (confidence rating of 5/5). Increasing confidence was significantly correlated with accuracy across the spectrum (p 0.001). An accuracy of 95% among radiologists suggests that a negative X-ray does not rule out CHF. High specificity (96%) and low sensitivity (59%) suggest that emergency physicians are excellent at identifying CHF on X-ray when present, but under-call it frequently. Sensitivity may be much higher in real life given clinical correlation. Both increased level of training and higher confidence significantly improved accuracy.	3
38. Shochat M, Shotan A, Trachtengerts V, et al. A novel radiological score to assess lung fluid content during evolving acute heart failure in the course of acute myocardial infarction. Acute Card Care. 2011;13(2):81-86.	Observational-Dx	624 patients	To evaluate in acute myocardial infarction (AMI) patients the ability of proposed radiological score (RS), which is the sum of selected radiological signs of congestion, to reflect correctly lung fluid content (LFC), as assessed with repeat physical examinations and lung impedance (LI) measurements.	624 acute myocardial infarction (AMI) patients without acute heart failure (AHF) at baseline were monitored (94 +/- 42 h). 476 patients (76%) with baseline RS of 0.3 +/- 0.5 did not develop AHF. Overt AHF developed in 148 patients (24%) during monitoring; baseline RS (0.6 +/- 0.8) reached 5.4 +/- 0.7, 7.0 +/- 0.8, and 9.8 +/- 0.5 at the stages of mild, moderate, and severe alveolar edema, respectively. AHF resolved with treatment. RS decreased to 1.5 +/- 1.3 (P < 0.01) and correlated with physical examination (r = 0.6, P < 0.01) and LI (r = -0.9, P < 0.01).	2

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39. Collins SP, Lindsell CJ, Yealy DM, et al. A comparison of criterion standard methods to diagnose acute heart failure. <i>Congest Heart Fail.</i> 2012;18(5):262-271.	Observational-Dx	483 patients	To compare and contrast the clinical criterion standards currently used in a cohort of emergency department (ED) patients to diagnose acute heart failure syndromes (AHFS).	Across all criterion standards, patients with AHFS were more likely to have a history of AHFS, congestion on physical examination and chest radiography, and elevated natriuretic peptide levels than those without AHFS. The standards agreed well (cardiology review vs hospital discharge diagnosis, kappa=0.74; cardiology review vs ED diagnosis, kappa=0.66; ED diagnosis vs hospital discharge diagnosis kappa=0.59). Each method had similar sensitivity but differing specificities. Different criterion standards identify different patients from among those being evaluated for AHFS.	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>40. Kelder JC, Cramer MJ, van Wijngaarden J, et al. The diagnostic value of physical examination and additional testing in primary care patients with suspected heart failure. <i>Circulation</i>. 2011;124(25):2865-2873.</p>	<p>Observational-Dx</p>	<p>721 patients</p>	<p>To determine the diagnostic value of history, physical examination, and subsequent additional testing including B-type natriuretic peptide (BNP) measurements to efficiently and accurately establish a diagnosis of new-onset heart failure in the domain of outpatients presenting with nonacute symptoms.</p>	<p>This is a cross-sectional diagnostic accuracy study with external validation. Seven hundred twenty-one consecutive patients suspected of new-onset heart failure underwent standardized diagnostic work-up including chest x-ray, spirometry, electrocardiography (ECG), N-terminal pro-B-type natriuretic peptide (NT-proBNP) measurement, and echocardiography in specially equipped outpatient diagnostic heart failure clinics. The presence of heart failure was determined by an outcome panel using the initial clinical data and 6-month follow-up data, blinded to biomarker data. Of the 721 patients, 207 (28.7%) had heart failure. The combination of 3 items from history (age, coronary artery disease, and loop diuretic use) plus 6 from physical examination (pulse rate and regularity, displaced apex beat, rales, heart murmur, and increased jugular vein pressure) showed independent diagnostic value (c-statistic 0.83). NT-proBNP was the most powerful supplementary diagnostic test, increasing the c-statistic to 0.86 and resulting in net reclassification improvement of 69% (P<0.0001). A simplified diagnostic rule was applied to 2 external validation datasets, resulting in c-statistics of 0.95 and 0.88, confirming the results.</p>	<p>3</p>

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Patel MR, White RD, Abbara S, et al. 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. J Am Coll Cardiol. 2013;61(21):2207-2231.	Review/Other-Dx	N/A	To provide guidelines on utilization of cardiovascular imaging in heart failure.	No results stated in abstract.	4
42. 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(7):1064-1071.	Observational-Dx	336 patients	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 magnetic resonance (MR). Optimal cut points for these variables were 120 ml/m ² , 150 ms, and 0.4 cm, respectively.	3

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. 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. <i>Eur Heart J</i> . 2006;27(7):839-845.	Experimental-Dx	134 patients	To determine the integrative utility of measuring plasma N-terminal prohormone of brain natriuretic peptides (NT-proBNP) levels with echocardiography in the evaluation of dyspnoeic patients.	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. Independent predictors of 1-year mortality were determined using Cox-proportional hazard analysis. Independent relationships were found between NT-proBNP levels and ejection fraction (P = 0.012), tissue Doppler early and late mitral annular diastolic velocities (P = 0.007 and 0.018), right ventricular (RV) hypokinesia (P = 0.006), and tricuspid regurgitation severity (P < 0.001) and velocity (P = 0.007). An NT-proBNP level <300 pg/mL had a negative predictive value of 91% for significant left ventricular systolic and diastolic dysfunction. Overall 1-year mortality was 20.1% and was independently predicted by NT-proBNP level [HR 8.65, 95% confidence interval (CI) 2.7-27.8, P = 0.0003], ejection fraction (HR 0.95, 95% CI 0.91-0.99, P = 0.009), RV dilation (HR 2.98, 95% CI 1.05-12.8, P = 0.04), and systolic blood pressure (HR 0.97, 95% CI 0.96-0.99, P = 0.01).	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Lim TK, Ashrafian H, Dwivedi G, Collinson PO, Senior R. 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. <i>Eur J Heart Fail.</i> 2006;8(1):38-45.	Observational-Dx	116 subjects	To assess the capacity of Left atrial volume index (LAVI) to predict left ventricular (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 137 patients, 21 were excluded (2 with significant mitral valve disease and 19 with atrial fibrillation). 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. The area under the curve of the receiver operating characteristic (ROC) curve for NTproBNP in detecting patients with LVEF $\geq 50\%$ and LAVI > 26 ml/m ² was 0.81 ($p < 0.0001$) and for patients with LAVI > 26 ml/m ² with and without LVEF $\geq 50\%$ was 0.82 ($p < 0.0001$).	2
45. Aurigemma GP, Gottdiener JS, Shemanski L, Gardin J, Kitzman D. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the cardiovascular health study. <i>J Am Coll Cardiol.</i> 2001;37(4):1042-1048.	Observational-Dx	2,671 participants	To 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. Although 96% of these participants had normal or borderline ejection fraction (EF) at baseline, only 57% had normal or borderline EF at the time of hospitalization. In multivariate modeling, fractional shortening at the endocardium (relative risk [RR] 1.85 per 10-unit decrease, confidence interval [CI] 1.27 to 2.39), fractional shortening at the midwall (RR 1.29 per five-unit decrease, 95% CI 1.11-1.51) and peak Doppler peak E (RR 1.15 for each 0.1 M/s increment; CI 1.02 to 1.21) independently predicted incident CHF. Both high and low Doppler E/A ratios were predictive of incident CHF.	3

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. 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). <i>Am J Cardiol.</i> 2001;87(9):1051-1057.	Observational-Dx	5,888 participants	To 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.	After adjustment for anthropometric and traditional cardiovascular disease (CVD) risk factors, left ventricular (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). Eccentric and concentric LV hypertrophy, respectively, conferred adjusted hazards ratios, compared with normal LV geometry, of 2.05 and 1.61 for incident CHD, and 2.95 and 3.32 for incident CHF.	2
47. Campbell SM, Fuat A, Summerton N, Lancaster N, Hobbs FR. Diagnostic triage and the role of natriuretic peptide testing and echocardiography for suspected heart failure: an appropriateness ratings evaluation by UK GPs. <i>Br J Gen Pract.</i> 2011;61(588):e427-435.	Review/Other-Dx	540 scenarios	To develop appropriateness ratings for the diagnostic application of natriuretic peptide (NP) testing or echocardiography for heart failure in general practice.	Onward referral for NP testing or echocardiography was rated as an appropriate next step in 217 (40.2%) of the 540 scenarios; in 194 (35.9%) it was rated inappropriate. The ratings also show where NP testing or echocardiography were ranked as equivalent next steps and when one test was seen as the more appropriate than the other.	4

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Martindale JL, Wakai A, Collins SP, et al. Diagnosing Acute Heart Failure in the Emergency Department: A Systematic Review and Meta-analysis. [Review]. Academic Emergency Medicine. 23(3):223-42, 2016 Mar.	Meta-analysis	57 studies	To perform a systematic review and meta-analysis of the operating characteristics of diagnostic elements available to the emergency physician for diagnosing Acute heart failure (AHF). Secondary objectives were to develop a test-treatment threshold model and to calculate interval likelihood ratios (LRs) for natriuretic peptides (NPs) by pooling patient-level results.	Based on the included studies, the prevalence of AHF ranged from 29% to 79%. Index tests with pooled positive LRs ≥ 4 were the auscultation of S3 on physical examination (4.0, 95% confidence interval [CI] = 2.7 to 5.9), pulmonary edema on both CXR (4.8, 95% CI = 3.6 to 6.4) and lung US (7.4, 95% CI = 4.2 to 12.8), and reduced ejection fraction observed on bedside echocardiogram (4.1, 95% CI = 2.4 to 7.2). Tests with low negative LRs were BNP < 100 pg/mL (0.11, 95% CI = 0.07 to 0.16), NT-proBNP < 300 pg/mL (0.09, 95% CI = 0.03 to 0.34), and B-line pattern on lung US LR (0.16, 95% CI = 0.05 to 0.51). Interval LRs of BNP concentrations at the low end of "positive" results as defined by a cutoff of 100 pg/mL were substantially lower (100 to 200 pg/mL; 0.29, 95% CI = 0.23 to 0.38) than those associated with higher BNP concentrations (1000 to 1500 pg/mL; 7.12, 95% CI = 4.53 to 11.18). The interval LR of NT-proBNP concentrations even at very high values (30,000 to 200,000 pg/mL) was 3.30 (95% CI = 2.05 to 5.31).	Good
49. Patarroyo-Aponte M, Colvin-Adams M. Evaluation of patients with heart failure. Cardiol Clin. 2014;32(1):47-62, viii.	Review/Other-Dx	N/A	To evaluate the patients with heart failure, including clinical examination and diagnostic tools.	No results stated in abstract.	4

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Gallard E, Redonnet JP, Bourcier JE, et al. Diagnostic performance of cardiopulmonary ultrasound performed by the emergency physician in the management of acute dyspnea. American Journal of Emergency Medicine. 33(3):352-8, 2015 Mar.	Observational-Dx	130 patients	To evaluate the performance of cardiopulmonary ultrasound compared with usual care for the etiologic diagnosis of acute dyspnea in the emergency department (ED).	One hundred thirty patients were analyzed. For the diagnosis of acute left-sided heart failure, cardiopulmonary ultrasound had an accuracy of 90% (95% confidence interval [CI], 84-95) vs 67% (95% CI, 57-75), P = .0001 for clinical examination, and 81% (95% CI, 72-88), P = .04 for the combination "clinical examination-NT-proBNP-x-ray". Cardiopulmonary ultrasound led to the diagnosis of pneumonia or pleural effusion with an accuracy of 86% (95% CI, 80-92) and decompensated chronic obstructive pulmonary disease or asthma with an accuracy of 95% (95% CI, 92-99). Cardiopulmonary ultrasound lasted an average of 12 +/- 3 minutes.	2

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Saito M, Negishi K, Eskandari M, et al. Association of left ventricular strain with 30-day mortality and readmission in patients with heart failure. <i>J Am Soc Echocardiogr.</i> 2015;28(6):652-666.	Observational-Dx	468 patients	To determine the association of Left ventricular (LV) strain with 30-day Heart failure (HF) readmission, independent of and incremental to clinical and basic echocardiographic parameters.	Readmission within 30 days (n = 92 patients [20%]) was associated with greater impairment of LV global longitudinal strain [GLS] (-8.6% [interquartile range, -10.9% to -5.9%] vs -11.1% [interquartile range, -14.6% to -7.7%], P < .01). The association of GLS with readmission (hazard ratio, 1.13; 95% confidence interval, 1.07-1.19; P < .01) was independent of age, male gender, systolic blood pressure, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use, and comorbidity, as well as renal function, sodium, hematocrit, LV mass, left atrial size, and mitral regurgitation. Global circumferential strain was associated with outcome but not was independent after adjustment with echocardiographic parameters. In sequential models for 30-day outcome, GLS added incremental information to clinical parameters and LV ejection fraction and significantly improved reclassification (categorical net reclassification improvement, 0.34; P = .04) when LV ejection fraction was >50%.	3

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Santas E, Garcia-Blas S, Minana G, et al. Prognostic implications of tissue Doppler imaging-derived e/ea ratio in acute heart failure patients. <i>Echocardiography</i> . 2015;32(2):213-220.	Observational-Dx	395 patients	To determine the association between early diastolic velocity ratio (E/Ea) ratio and 1-year mortality in nonselected patients with acute heart failure (AHF).	At a median follow-up of 306 days (interquartile range, 118-564), 89 deaths (22.5%) were registered. Mean age and E/Ea ratio were 72 +/- 11.5 and 20 +/- 3. Proportion of left ventricular (LV) ejection fraction >=50% was 47%. In multivariate analysis, after adjusting for well-known prognostic factors, including natriuretic peptides, E/Ea ratio was linearly associated with an increase risk of all-cause mortality (HR 1.04, 95% CI 1.03-1.05; P < 0.001, per increase in one unit of E/Ea). The threshold of risk was identified above 20. No significant interactions among the most important subgroups were found.	2
53. Moon J, Kang SM, Cho IJ, et al. Clinical and echocardiographic findings of newly diagnosed acute decompensated heart failure in elderly patients. <i>Yonsei Med J</i> . 2011;52(1):33-38.	Observational-Dx	256 patients	To investigate clinical characteristics, including echocardiographic findings and prognosis, for Elderly patients (EPs) with newly diagnosed-acute decompensated heart failure (ND-ADHF) and to compare those with non-elderly pts (NEPs).	In intergroup comparison, female gender, diabetes mellitus, previous stroke and hypertension were more common in EPs. Body mass index (22.3 +/- 4.5 vs. 24.0 +/- 4.4 kg/m(2)), estimated glomerular filtration rate (54.8 +/- 24.3 vs. 69.2 +/- 30.7 mL/min/m(2)), C-reactive protein (28.5 +/- 46.9 vs. 7.6 +/- 11.6 mg/dL), hemoglobin (12.3 +/- 2.1 vs. 13.6 +/- 2.3 g/dL) and N-terminal pro-brain natriuretic peptide level (10,538.2 +/- 10,942.3 vs. 6,771.0 +/- 8,964.7 pg/mL) were significantly different (p < 0.05 for all). Early mitral inflow velocity to early diastolic mitral annular velocity (E/E') was significantly higher in EPs than in NEPs (21.2 +/- 9.4 vs. 18.0 +/- 8.9, p < 0.05). During follow-up (44.7 +/- 14.5 months), there were no significant differences in in-hospital mortality, re-hospitalization and cardiovascular mortality between EPs and NEPs (p = NS for all).	3

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
54. From AM, Lam CS, Pitta SR, et al. Bedside assessment of cardiac hemodynamics: the impact of noninvasive testing and examiner experience. <i>Am J Med.</i> 2011;124(11):1051-1057.	Observational-Dx	116 patients	To assess bedside cardiac hemodynamics.	Two hundred fifteen observations were made by 9 examiners in 116 consecutive patients. Right and left heart pressures were accurately predicted from examination alone in 71% and 60% of observations, respectively. Examination-based accuracy was greater for staff cardiologists compared with trainees for right heart (82 vs 67%, P=.03) and left heart pressures (71% vs 55%, P=.03). Exposure to echocardiographic and brain-type natriuretic peptide (BNP) data did not enhance accuracy beyond bedside examination alone, both for left heart pressures (net reclassification improvement=-0.004; 95% confidence interval, -0.12-0.12) and right heart pressures (net reclassification improvement=0.02, 95% confidence interval, -0.09-0.13).	2
55. Rizzello V, Poldermans D, Biagini E, et al. Prognosis of patients with ischaemic cardiomyopathy after coronary revascularisation: relation to viability and improvement in left ventricular ejection fraction. <i>Heart.</i> 2009;95(15):1273-1277.	Observational-Dx	90 patients	To evaluate the prognosis of viable patients with and without improvement of left ventricular ejection fraction (LVEF) after coronary revascularisation.	After revascularisation, the mean (SD) LVEF improved from 32 (9)% to 42 (10)% in group 1, but did not change significantly in group 2 and in group 3, p<0.001 by analysis of variance (ANOVA). Heart failure symptoms improved in both groups 1 (mean (SD) New York Heart Association (NYHA) class from 3.1 (0.9) to 1.7 (0.7)) and 2 (from 3.2 (0.7) to 1.7 (0.9)), but not in group 3 (from 2.8 (1.0) to 2.7 (0.5)), p<0.001 by ANOVA. During follow-up, the cardiac event rate was low (4%) in group 1, intermediate (21%) in group 2 and high (33%) in group 3 (p = 0.01).	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Vizzardi E, D'Aloia A, Giubbini R, et al. Effect of spironolactone on left ventricular ejection fraction and volumes in patients with class I or II heart failure. <i>Am J Cardiol.</i> 2010;106(9):1292-1296.	Experimental-Dx	168 patients	To evaluate the effects of 6-month administration of spironolactone in addition to standard heart failure (HF) therapy on left ventricular (LV) systolic and diastolic functions and the functional capacity of patients with low to moderate grade HF (NYHA class I to II).	One hundred sixty-eight patients with New York Heart Association (NYHA) class I to II HF and LV ejection fraction $\leq 40\%$ were randomized to spironolactone or placebo and assessed by echocardiography, gated single-photon emission computed tomography, technetium-99m sestamibi single-photon emission computed tomographic radionuclide ventriculography, and cardiopulmonary exercise testing at baseline and after 6 months of treatment. In the spironolactone group LV ejection fraction increased from $35.2 \pm 0.7\%$ to $39.1 \pm 3.5\%$ ($p < 0.001$), with a decrease in LV end-diastolic and end-systolic volumes and myocardial mass and an improvement in LV diastolic filling pattern. Cardiopulmonary exercise testing parameters did not change.	1

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Udelson JE, Feldman AM, Greenberg B, et al. Randomized, double-blind, multicenter, placebo-controlled study evaluating the effect of aldosterone antagonism with eplerenone on ventricular remodeling in patients with mild-to-moderate heart failure and left ventricular systolic dysfunction. <i>Circ Heart Fail.</i> 2010;3(3):347-353.	Experiment al-Dx	226 patients	To evaluate the effects of aldosterone blockade, with eplerenone, on left ventricular (LV) remodeling and markers of collagen turnover in patients with LV systolic dysfunction and chronic mild-to-moderate heart failure (HF).	In a multicenter, randomized, double-blind, placebo-controlled study in patients with mild-to-moderate HF and LV systolic dysfunction, patients with New York Heart Association class II/III HF and LV ejection fraction (EF) < or =35% were randomly assigned to receive eplerenone 50 mg/d versus placebo in addition to contemporary background therapy. Quantitative radionuclide ventriculograms to assess LV volumes and ejection fraction were performed at baseline and again after 9 months of double-blind treatment and were analyzed in a central core laboratory, blinded to treatment. The primary efficacy analysis was the between-group comparison of the change in LV end-diastolic volume index. Secondary analyses examined changes in LV end-systolic volume index and ejection fraction as well as markers of collagen turnover. Of the total 226 patients enrolled, 117 were randomly assigned to receive eplerenone and 109 to receive placebo. There was high use of contemporary background therapy at baseline, with > 90% use of angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers and > 90% use of beta-blockers. Over 36 weeks of treatment, there was no apparent between-group difference in the changes in end-diastolic volume index or end-systolic volume index. There was a reduction in the collagen turnover marker procollagen type I N-terminal propeptide and plasma B-type natriuretic peptide in the eplerenone group compared with placebo (P=0.01 and P=0.04, respectively). There was no change in symptom status or quality-of-life measures.	1

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
58. 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(8):968-974.	Observational-Dx	100 patients	To 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.	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). Twenty-one patients (21%) had significant CAD. Seventy-nine (79%) had no lesions. Eighteen of the 21 patients (85%) with CAD had subendocardial/transmural LGE. In the diagnosis of CAD, LGE has a sensitivity of 85.7% (95% CI, 80-91) and specificity of 92.4% (95% CI, 87-96), respectively, with a negative predictive value of 96% (95% CI, 90-99). It has an area under the receiver operating characteristic curve of 0.906 (95% CI, 0.814-0.998).	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Steinberg BA, Zhao X, Heidenreich PA, et al. Trends in patients hospitalized with heart failure and preserved left ventricular ejection fraction: prevalence, therapies, and outcomes. <i>Circulation</i> . 2012;126(1):65-75.	Review/Other-Dx	110,621 patients	To analyze data from 275 hospitals in Get With the Guidelines-Heart Failure from January 2005 to October 2010.	Among 110,621 patients, 50% (55 083) had HF-reduced ejection fraction (EF), 14% (15 184) had HF-borderline EF, and 36% (40 354) had HF-preserved EF. From 2005 to 2010, the proportion of hospitalizations for HF-preserved EF increased from 33% to 39% (P<0.0001). In multivariable analyses, use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers at discharge decreased in all EF groups, and beta-blocker use increased. Patients with HF-preserved EF less frequently achieved blood pressure control (adjusted odds ratio, 0.44 versus HF-reduced EF; P<0.001) and were more likely discharged to skilled nursing (adjusted odds ratio, 1.16 versus HF-reduced EF; P<0.001). In-hospital mortality for HF-preserved EF decreased from 3.32% in 2005 to 2.35% in 2010 (adjusted odds ratio, 0.89 per year; P=0.01) but was stable for patients with HF-reduced EF (3.03%-2.83%; adjusted odds ratio, 0.93 per year; P=0.10).	4
60. Wachter R, Edelmann F. Diagnosis of heart failure with preserved ejection fraction. <i>Heart Fail Clin</i> . 2014;10(3):399-406.	Review/Other-Dx	N/A	To focus on the current understanding of diagnostic criteria, as presented in current guidelines and consensus recommendations, and on new insights from recent papers.	No results stated in abstract.	4

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>61. Jorge AJ, Rosa ML, Ribeiro ML, et al. Assessing strategies for heart failure with preserved ejection fraction at the outpatient clinic. <i>Arq Bras Cardiol.</i> 2014;103(3):231-237.</p>	<p>Observational-Dx</p>	<p>166 patients</p>	<p>To describe and compare two strategies derived from algorithms of the European Society of Cardiology Diastology Guidelines for the diagnosis of Heart failure with preserved ejection fraction (HFPEF).</p>	<p>In S1, patients were divided into groups based on the E/E' ratio as follows: GI, E/E' > 15 (n = 16; 9%); GII, E/E' 8 to 15 (n = 79; 48%); and GIII, E/E' < 8 (n = 71; 43%). HFPEF was confirmed in GI and excluded in GIII. In GII, tissue Doppler echocardiography (TDE) [left atrial volume index (LAVI) \geq 40 mL/m²; left ventricular mass index (LVMI) > 122 for women and > 149 g/m² for men] and ECG (atrial fibrillation) parameters were assessed, confirming HFPEF in 33 more patients, adding up to 49 (29%). In S2, patients were divided into three groups based on B-type natriuretic peptide (BNP) levels. GI (BNP > 200 pg/mL) consisted of 12 patients, HFPEF being confirmed in all of them. GII (BNP ranging from 100 to 200 pg/mL) consisted of 20 patients with LAVI > 29 mL/m², or LVMI \geq 96 g/m² for women or \geq 116 g/m² for men, or E/E' \geq 8 or atrial fibrillation on ECG, and the diagnosis of HFPEF was confirmed in 15. GIII (BNP < 100 pg/mL) consisted of 134 patients, 26 of whom had the diagnosis of HFPEF confirmed when GII parameters were used. Measuring BNP levels in S2 identified 4 more patients (8%) with HFPEF as compared with those identified in S1.</p>	<p>3</p>

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
62. Ruan W, Lim SH, Ding ZP, et al. Prevalence, Presentation, and Outcome of Heart Failure with Preserved Ejection Fraction among Patients Presenting with Undifferentiated Dyspnoea to the Emergency Room: A 10-year Analysis from a Tertiary Centre. <i>Ann Acad Med Singapore</i> . 2016;45(1):18-26.	Review/Other-Dx	N/A	To assess the local prevalence, characteristics and 10-year outcomes in a heart failure (HF) cohort from the emergency room (ER).	At different cutoffs of LVEF of $\geq 50\%$, $\geq 45\%$, $\geq 40\%$, and $> 50\%$ plus excluding LVEF 40% to 50%, HFPEF prevalence ranged from 38% to 51%. Using LVEF $\geq 50\%$ as the final cutoff point, at baseline, HFPEF (n = 35), compared to HFREF (n = 55), had lower admission NT-proBNP (1502 vs 5953 pg/mL, P < 0.001), heart rate (86 +/- 22 vs 98 +/- 22 bpm, P = 0.014), and diastolic blood pressure (DBP) (75 +/- 14 vs 84 +/- 20 mmHg, P = 0.024). On echocardiogram, compared to HFREF, HFPEF had more LV concentric remodelling (20% vs 2%, P = 0.003), less eccentric hypertrophy (11% vs 53%, P < 0.001) and less mitral regurgitation from functional mitral regurgitation (60% vs 95%, P = 0.027). At 10 years, compared to HFREF, HFPEF had similar primary endpoints of a composite of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, and rehospitalisation for congestive heart failure (CHF) (HR 0.886; 95% CI, 0.561 to 1.399; P = 0.605), all-cause mortality (HR 0.663; 95% CI, 0.400 to 1.100; P = 0.112), but lower cardiovascular mortality (HR 0.307; 95% CI, 0.111 to 0.850; P = 0.023).	4
63. Prastaro M, D'Amore C, Paolillo S, et al. Prognostic role of transthoracic echocardiography in patients affected by heart failure and reduced ejection fraction. <i>Heart Fail Rev</i> . 2015;20(3):305-316.	Review/Other-Dx	N/A	To review Prognostic role of transthoracic echocardiography in patients affected by heart failure and reduced ejection fraction.	No results stated in abstract.	4

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
64. Sanchis L, Gabrielli L, Andrea R, et al. Left atrial dysfunction relates to symptom onset in patients with heart failure and preserved left ventricular ejection fraction. <i>Eur Heart J Cardiovasc Imaging</i> . 2015;16(1):62-67.	Observational-Dx	138 elderly patients	To analyse Left atrial (LA) function in outpatients with new onset symptoms of heart failure (HF).	Results were analysed with ANOVA and Bonferroni statistical tests. Receiver operating characteristic (ROC) curves were constructed to investigate the predictive ability of LA parameters for the final diagnosis of HF. Patients were 75 +/- 9 years and 63% women. Final diagnosis was 23.2% heart failure (HF) with preserved ejection fraction (HFPEF), 45.7% HFPEF, and 31.2% non-HF. Left ventricular strain rate showed no differences between non-HF and HFPEF groups, but both groups showed differences with the HFREF group. LA strain rate (A- and S-waves) was significantly reduced in both HF groups (without differences among them) when compared with the non-HF group. LA strain rate and indexed volume showed significant accuracy for HF diagnosis in ROC curves.	2
65. Anderson KL, Jenq KY, Fields JM, Panebianco NL, Dean AJ. Diagnosing heart failure among acutely dyspneic patients with cardiac, inferior vena cava, and lung ultrasonography. <i>Am J Emerg Med</i> . 2013;31(8):1208-1214.	Observational-Dx	101 patients	To assess the accuracy of point-of-care ultrasonography (US) in making the diagnosis of Acutely decompensated heart failure (ADHF) among acutely dyspneic patients in the emergency department (ED) setting by combining all 3 modalities (cardiac, inferior vena cava (IVC), and lung US).	One hundred one participants were enrolled: 52% male, median age 62 (25%-75% interquartile, 53-91). Forty-four (44%) had a final dx of ADHF. Sensitivity and specificity (including 95% confidence interval) for the presence of ADHF were as follows: 74 (65-90) and 74 (62-85) using left ventricular ejection fraction (LVEF) less than 45%, 52 (38-67) and 86 (77-95) using the inferior vena cava for collapsibility index (IVC-CI) less than 20%, and 70 (52-80) and 75 (64-87) using B-lines at least 10. Using all 3 modalities together, the sensitivity and specificity were 36 (22-51) and 100 (95-100). As a comparison, the sensitivity and specificity of brain natriuretic peptide greater than 500 were 75 (55-89) and 83 (67-92).	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Hsiao SH, Chu KA, Wu CJ, Chiou KR. Left Atrial Expansion Index Predicts Left Ventricular Filling Pressure and Adverse Events in Acute Heart Failure With Severe Left Ventricular Dysfunction. J Card Fail. 2016;22(4):272-279.	Observational-Dx	141 patients	To assess the power of left atrial (LA) parameters for predicting left ventricular (LV) filling pressure and adverse events in acute heart failure (HF) with severe LV dysfunction, either sinus rhythm or atrial fibrillation (AF)	Echocardiography was performed in 141 patients with acute decompensated congestive HF and LV ejection fraction <35%, including 42 with permanent AF. The LA expansion index was calculated as (Volmax - Volmin) x 100%/Volmin, where Volmax was defined as maximal and Volmin as minimal LA volume. Of 141 patients, invasive LV filling pressures within 12 hours of LA expansion index measurement were available in 109. The end points were 3-year frequencies of HF hospitalization and all-cause mortality. Over a median follow-up of 3.1 years, 74 participants (52.5%) reached the end points (sinus vs AF group: 48.5% vs 61.9%, respectively; P = .047). Multivariate analysis revealed that adverse events of both groups were only independently associated with age and LA expansion index. Rates of adverse events were proportional to LA expansion index. There was a good logarithmic relationship between LA expansion index and LV filling pressure, regardless of presence or absence of AF.	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
67. Chrysohoou C, Antoniou CK, Kotrogiannis I, et al. Role of right ventricular systolic function on long-term outcome in patients with newly diagnosed systolic heart failure. <i>Circ J</i> . 2011;75(9):2176-2181.	Observational-Dx	180 patients	To evaluate the effect of this dysfunction on prognosis in patients with newly-diagnosed systolic heart failure (HF).	We enrolled 180 consecutive patients with newly diagnosed systolic HF (ischemic or dilated cardiomyopathy). Echocardiographic evaluation was performed to assess biventricular function. Pulse-wave tissue Doppler imaging (TDI) readings were obtained from the lateral tricuspid annulus and the peak systolic annular velocity (Stv) was recorded. Patients were followed for a 2-year period and events (death or HF hospitalization) were recorded. During the follow-up, 79 patients (44%) had an adverse event. An inverse relationship was observed between the height of Stv and the probability of an event (odds ratio (OR) 0.716, 95% confidence interval (CI) 0.583-0.880, P=0.001), after controlling for potential confounders. Furthermore, creatinine clearance (CrCl) was inversely associated with the outcome: a 1-unit increase in CrCl was associated with a 0.98-times lower likelihood of having an event. When the analysis was stratified by CrCl < 60 ml/min or ≥ 60 ml/min, Stv predicted adverse events in both groups (CrCl < 60 ml/min: OR 0.62, 95%CI 0.39-0.98, P = 0.04; CrCl ≥ 60 ml/min: OR 0.78, 95%CI 0.61-1.01, P=0.06).	3

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. van Riet EE, Hoes AW, Limburg A, Landman MA, van der Hoeven H, Rutten FH. Prevalence of unrecognized heart failure in older persons with shortness of breath on exertion. <i>Eur J Heart Fail.</i> 2014;16(7):772-777.	Review/Other-Dx	1527 subjects	To assess the prevalence of unrecognized heart failure in elderly patients presenting to primary care with shortness of breath on exertion.	This was a cross-sectional selective screening study. Patients aged 65 years or over presenting to primary care with shortness of breath on exertion in the previous 12 months were eligible when not known to have an established, echocardiographic confirmed diagnosis of heart failure. All participants underwent history taking, physical examination, electrocardiography, and a blood test of N-terminal pro B-type natriuretic peptide (NTproBNP). Only those with an abnormal electrocardiogram or NTproBNP level exceeding the exclusionary cut-point for non-acute onset heart failure (>15 pmol/L (approximately 125 pg/mL) underwent open-access echocardiography. An expert panel established presence or absence of heart failure according to the criteria of the European Society of Cardiology heart failure guidelines. The mean age of the 585 participants was 74.1 (SD 6.3) years, and 54.5% were female. In total, 92 (15.7%, 95% CI 12.9-19.0) participants had heart failure: 17 (2.9%, 95% CI 1.8-4.7) had heart failure with a reduced ejection fraction (\leq 45%), 70 (12.0%, 95% CI 9.5-14.9) had heart failure with preserved ejection fraction, and five (0.9%, 95% CI 0.3-2.1) had isolated right-sided heart failure.	4

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>69. Ehrman RR, Russell FM, Ansari AH, et al. Can emergency physicians diagnose and correctly classify diastolic dysfunction using bedside echocardiography? Am J Emerg Med. 2015;33(9):1178-1183.</p>	<p>Observational-Dx</p>	<p>62 patients</p>	<p>To determine if emergency physicians (EPs) can correctly perform a bedside diastology examination (DE) and correctly grade the level of diastolic function with minimal additional training in echocardiography beyond what is learned in residency</p>	<p>We enrolled 62 patients; 52% had diastolic dysfunction (DD). Using the cardiology interpretation as the criterion standard, the sensitivity and specificity of the EP-performed DE to identify clinically significant diastolic function were 92% (95% confidence interval [CI], 60-100) and 69% (95% CI, 50-83), respectively. Agreement between EPs and cardiology on grade of DD was assessed using kappa and weighted kappa: kappa = 0.44 (95% CI, 0.29-0.59) and weighted kappa = 0.52 (95% CI, 0.38-0.67). Overall, EPs rated 27% of DEs as indeterminate, compared with only 15% by cardiology. For DEs where both EPs and cardiology attempted an interpretation (indeterminates excluded) kappa = 0.45 (95% CI, 0.26 to 0.65) and weighted kappa = 0.54 (95% CI, 0.36-0.72).</p>	<p>2</p>

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
70. Shuai XX, Chen YY, Lu YX, et al. Diagnosis of heart failure with preserved ejection fraction: which parameters and diagnostic strategies are more valuable? <i>Eur J Heart Fail.</i> 2011;13(7):737-745.	Observational-Dx	236 patients	To evaluate the present main diagnostic criteria and to discover which parameters and strategies are more valuable.	Echocardiographic data and plasma N-terminal pro-brain natriuretic peptide levels were assessed in a derivation cohort (n=236) and a validation cohort (n=98). Both cohorts included normal controls, patients with hypertensive heart disease without heart failure and patients with heart failure with preserved ejection fraction (HFpEF). In the derivation cohort, the ratio of early mitral inflow velocity to tissue Doppler velocity at lateral mitral annulus (lateral E/e'≥12), left atrial volume index (LAVI≥34 mL/m ²), and the difference between duration of reversed pulmonary vein atrial systole flow and duration of mitral A wave flow (Ard-Ad>30 ms) had the greatest diagnostic value among all the single parameters. A brief strategy that consisted of either: (i) lateral E/e'≥12; or (ii) 12>lateral E/e'≥8, with either LAVI≥34 mL/m ² or Ard-Ad>30 ms, provided good diagnostic accuracy for identifying diastolic dysfunction in HFpEF, with a sensitivity of 77% and specificity of 81%. These observations were confirmed in the validation cohort	3
71. Esposito R, Sorrentino R, Galderisi M. The use of transthoracic echocardiography for the assessment of left ventricular systolic and diastolic function in patients with suspected or ascertained chronic heart failure. <i>Expert Rev Cardiovasc Ther.</i> 2016;14(1):37-50.	Review/Other-Dx	N/A	To review the use of transthoracic echocardiography for the assessment of left ventricular systolic and diastolic function in patients with suspected or ascertained chronic heart failure.	No results stated in abstract.	4

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
72. Kraigher-Krainer E, Shah AM, Gupta DK, et al. Impaired systolic function by strain imaging in heart failure with preserved ejection fraction. <i>J Am Coll Cardiol.</i> 2014;63(5):447-456.	Observational-Dx	219 patients; 50 controls	To determine the frequency and magnitude of impaired systolic deformation in heart failure with preserved ejection fraction (HFpEF).	The HFpEF patients had preserved left ventricular ejection fraction and evidence of diastolic dysfunction. Compared to both normal controls and hypertensive heart disease patients, the HFpEF patients demonstrated significantly lower longitudinal strain (LS) (-20.0 +/- 2.1 and -17.07 +/- 2.04 vs. -14.6 +/- 3.3, respectively, $p < 0.0001$ for both) and circumferential strain (CS) (-27.1 +/- 3.1 and -30.1 +/- 3.5 vs. -22.9 +/- 5.9, respectively; $p < 0.0001$ for both). In HFpEF, both LS and CS were related to LVEF (LS, $R = -0.46$; $p < 0.0001$; CS, $R = -0.51$; $p < 0.0001$) but not to standard echocardiographic measures of diastolic function (E' or E/E'). Lower LS was modestly associated with higher NT-proBNP, even after adjustment for 10 baseline covariates including LVEF, measures of diastolic function, and LV filling pressure (multivariable adjusted $p = 0.001$).	1

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>73. Morris DA, Boldt LH, Eichstadt H, Ozelik C, Haverkamp W. Myocardial systolic and diastolic performance derived by 2-dimensional speckle tracking echocardiography in heart failure with normal left ventricular ejection fraction. <i>Circ Heart Fail.</i> 2012;5(5):610-620.</p>	<p>Observational-Dx</p>	<p>450 patients</p>	<p>To investigate the myocardial systolic and diastolic performance of the left ventricle (LV) in patients with heart failure with normal LV ejection fraction (HFNEF) through novel LV myocardial indices, which assess the systolic and diastolic function of the whole myocardium of the LV.</p>	<p>LV myocardial systolic and diastolic performance were assessed as the average value of peak systolic strain and peak early-diastolic strain rate, respectively, in longitudinal, circumferential, and radial directions from all LV segments using 2-dimensional speckle-tracking echocardiography. We studied patients with HFNEF and a control group consisting of asymptomatic subjects with LV diastolic dysfunction of similar age, sex, and LV ejection fraction. A total of 322 patients were included (92 with HFNEF and 230 with asymptomatic LV diastolic dysfunction). Myocardial systolic and diastolic LV performance were significantly lower in HFNEF (20.13±6.02% and 1.14±0.27 s(-1)) than in patients with asymptomatic LV diastolic dysfunction (25.33±6.06% and 1.37±0.33 s(-1), respectively; all P<0.0001). In addition, patients with HFNEF with low systolic and diastolic LV myocardial performance had significantly higher LV filling pressures (17.1±6.6 and 17.6±6.3 versus 12.0±5.1 and 11.7±4.7, respectively; all P<0.001) and lower cardiac output (4.8±1.0 L/min and 4.9±1.1 L/min versus 5.7±1.2 L/min and 5.8±1.1 L/min, respectively; all P<0.001) than patients with normal LV myocardial performance. In relation to these findings, the symptomatic status (ie, New York Heart Association functional class) was significantly altered in those patients with low systolic and diastolic LV myocardial performance.</p>	<p>2</p>

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>74. Morris DA, Vaz Perez A, Blaschke F, Eichstadt H, Ozcelik C, Haverkamp W. Myocardial systolic and diastolic consequences of left ventricular mechanical dyssynchrony in heart failure with normal left ventricular ejection fraction. <i>Eur Heart J Cardiovasc Imaging</i>. 2012;13(7):556-567.</p>	<p>Observational-Dx</p>	<p>384 subjects</p>	<p>To test the hypothesis that left ventricular (LV) mechanical dyssynchrony deteriorates the longitudinal systolic and diastolic function of the left ventricle (LV) in patients with heart failure with a normal LV ejection fraction (HFNEF).</p>	<p>In patients with HFNEF and in a control group consisting of asymptomatic patients with LV diastolic dysfunction [LVDD], matched by age, gender, and LV ejection fraction, we assessed the global longitudinal systolic (global strain), diastolic [global early-diastolic strain rate (SRe)], and synchronous (standard deviation of time-to-peak systolic strain) function of the LV by two-dimensional speckle-tracking echocardiography using a 18-segment LV model. A total of 325 patients were included (85 with HFNEF and 240 with asymptomatic LVDD). Patients with HFNEF had a significant impairment of the longitudinal systolic and diastolic function of the LV as compared with the control group. Concerning the pathophysiological mechanisms linked to these findings, we found that HFNEF patients with asynchronous LV contractions had significantly more impaired longitudinal systolic and diastolic LV function (global strain -14.76 +/- 3.44%, global SRe 0.79 +/- 0.24 s(-1)) than patients without asynchronous LV contractions (global strain -18.57 +/- 3.10%, global SRe 1.06 +/- 0.32 s(-1); all P < 0.0001). Accordingly, in HFNEF patients with LV mechanical dyssynchrony the rates of LV longitudinal systolic and diastolic dysfunction were 64 and 70%, respectively, whereas these rates were significantly lower (19.5 and 41.3%), respectively, in patients without asynchronous LV contractions. In addition, HFNEF patients with LV mechanical dyssynchrony presented higher LV filling pressures and worse NYHA functional class than those with normal LV contractions.</p>	<p>2</p>

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
75. Morris DA, Gailani M, Vaz Perez A, et al. Right ventricular myocardial systolic and diastolic dysfunction in heart failure with normal left ventricular ejection fraction. J Am Soc Echocardiogr. 2011;24(8):886-897.	Observational-Dx	565 patients	To hypothesize that in patients with heart failure with normal left ventricular (LV) ejection fraction (HFNEF), the same fibrotic processes that affect the subendocardial layer of the LV could also alter the subendocardial fibers of the right ventricle (RV).	A total of 565 patients were included (201 with HFNEF and 364 with asymptomatic LVDD). RV longitudinal diastolic (RV global longitudinal early-diastolic strain rate [RV-SRe]) and systolic (RV global longitudinal systolic strain [RV-Strain]) function were significantly more impaired in patients with HFNEF than in patients with asymptomatic LVDD (HFNEF: RV-Strain -14.41% +/- 3.80% and RV-SRe 0.86 +/- 0.33 s(-1); asymptomatic LVDD: RV-Strain -16.90% +/- 4.28% and RV-SRe 1.02 +/- 0.34 s(-1); all P < .0001). On multiple regression analysis, LV global longitudinal systolic strain was the most important independent predictor of RV longitudinal systolic and diastolic function, in contrast with pulmonary arterial systolic pressure, which was weakly related to these functions. Furthermore, in patients with HFNEF the subendocardial function of both the LV and RV were significantly impaired in similar proportions. In that regard, in patients with HFNEF the prevalences of RV longitudinal systolic and diastolic dysfunction were 75% and 48%, whereas the rates of LV longitudinal systolic and diastolic dysfunction were 80% and 60%, respectively. In addition, patients with both systolic and diastolic longitudinal dysfunction of the RV presented worse New York Heart Association functional class.	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Morris DA, Gailani M, Vaz Perez A, et al. Left atrial systolic and diastolic dysfunction in heart failure with normal left ventricular ejection fraction. <i>J Am Soc Echocardiogr.</i> 2011;24(6):651-662.	Observational-Dx	420 patients	To hypothesize that in patients with heart failure with normal left ventricular (LV) ejection fraction (HFNEF), the same fibrotic processes that affect the subendocardial layer of the left ventricle could also alter the subendocardial fibers of the left atrium.	A total of 420 patients were included (119 with HFNEF and 301 with asymptomatic LVDD). LA longitudinal systolic (LA late diastolic strain rate) and diastolic (LA systolic strain and strain rate) function was significantly more impaired in patients with HFNEF (LA late diastolic strain rate, -1.17 ± 0.63 s ⁻¹ ; LA systolic strain, $19.9 \pm 7.3\%$; LA systolic strain rate, 1.17 ± 0.46 s ⁻¹) compared with those with asymptomatic LVDD (-1.80 ± 0.70 s ⁻¹ , $30.8 \pm 11.4\%$, and 1.67 ± 0.59 s ⁻¹), respectively) (all P values < .0001). On multiple regression analysis, LV global longitudinal systolic strain and diastolic strain rate were the most important independent predictors of LA longitudinal systolic and diastolic function, in contrast to noninvasive LV filling pressures (i.e., mitral E/e' average septal-lateral ratio), which were modestly related to LA longitudinal systolic and diastolic function. Furthermore, in patients with HFNEF, the subendocardial function of both the left atrium and the left ventricle was significantly impaired in high proportions. In that regard, in patients with HFNEF, the rate of LA longitudinal systolic and diastolic dysfunction was 65.5% and 28.5%, whereas the prevalence of LV longitudinal systolic and diastolic dysfunction was 81.5% and 58%, respectively. In addition, patients with both systolic and diastolic longitudinal dysfunction of the left atrium presented worse NYHA functional class as compared with those with normal LA longitudinal function.	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
77. Obokata M, Negishi K, Kurosawa K, et al. Incremental diagnostic value of la strain with leg lifts in heart failure with preserved ejection fraction. JACC Cardiovasc Imaging. 2013;6(7):749-758.	Observational-Dx	40 HFpEF; 46 controls	To examine left atrial (LA) functional reserve in patients with heart failure (HF) with preserved ejection fraction (HFpEF) and to determine whether LA strain has an incremental diagnostic value over clinical and conventional echocardiographic parameters.	Patients with HFpEF had an enlarged LA and reduced LA emptying fraction compared with HT controls at rest, while LA stroke volume (SV) was similar between the groups. During leg lifts, increases in LA reservoir and contractile function (i.e., global LAS and LAB) were blunted in HFpEF patients compared with HT controls, resulting in impaired LASV responses. Global LAS and LAB during leg lifts accurately differentiated HFpEF from HT controls (areas under the curve: 0.95 and 0.92, respectively). Resting global LAS had a significant incremental diagnostic value over clinical (age and sex) and conventional echocardiographic parameters (E/E' ratio, left ventricular mass index, and maximum LA volume index) (global chi-square: 49.6 vs. 30.8; p < 0.0001). The diagnostic value was further improved by adding global LAS during leg lifts (global chi-square: 72.2 vs. 49.6; p < 0.0001).	3

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>78. Meluzin J, Sitar J, Kristek J, et al. The role of exercise echocardiography in the diagnostics of heart failure with normal left ventricular ejection fraction. <i>Eur J Echocardiogr.</i> 2011;12(8):591-602.</p>	<p>Review/Other-Dx</p>	<p>98 patients; 16 controls</p>	<p>To determine the prevalence of isolated exercise-induced heart failure with normal ejection fraction (HFNEF) and to assess whether disturbances in left ventricular (LV) or right ventricular longitudinal systolic function are associated with the diagnosis of HFNEF.</p>	<p>Eighty-four patients with exertional dyspnoea and normal left ventricular ejection fraction (LV EF) and 14 healthy controls underwent spirometry, NT-proBNP plasma analysis, and exercise echocardiography. Doppler LV inflow and tissue mitral and tricuspid annular velocities were analysed at rest and immediately after the termination of exercise. Of the 30 patients with the evidence of HFNEF, 6 (20%) patients had only isolated exercise-induced HFNEF. When compared with the remaining patients, those with HFNEF had a significantly lower resting and exercise peak mitral annular systolic velocity (Sa) and the mitral annular velocity during atrial contraction, lower exercise peak mitral annular velocity at early diastole, and lower exercise peak systolic velocity of tricuspid annular motion. The multivariate logistic regression analysis including both parameters standardly defining HFNEF and the new Doppler variables potentially associated with the diagnosis of HFNEF revealed that NT-proBNP, LV mass index, left atrial volume index, and Sa significantly and independently predict the diagnosis of HFNEF.</p>	<p>4</p>

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
79. Donal E, Thebault C, Lund LH, et al. Heart failure with a preserved ejection fraction additive value of an exercise stress echocardiography. <i>Eur Heart J Cardiovasc Imaging</i> . 2012;13(8):656-665.	Observational-Dx	21 patients; 15 controls	To analyse the myocardial characteristics at rest and during a sub-maximal exercise test in patients with Heart failure preserved ejection fraction (HFPEF).	Standardized sub-maximal exercise stress echocardiography was performed in (i) 21 patients from the Karolinska Rennes Prospective Study of Heart Failure with Preserved Left Ventricular Ejection Fraction HFPEF registry, whose LVEF was $\geq 45\%$ and (ii) 15 control patients free of any manifestations of HF. During a sub-maximal exercise test, LV systolic function measured as a global four-chamber longitudinal strain was $-17 \pm 5\%$ in patients with HFPEF vs. $-22 \pm 4\%$ in controls ($P < 0.001$), LV longitudinal diastolic relaxation, expressed as e' (septal and lateral walls averaged) was 9 ± 2 cm/s in patients vs. 15 ± 4 cm/s in controls ($P < 0.001$), and RV longitudinal systolic function, expressed as RV s' , was 14 ± 3 cm/s in patients vs. 18 ± 1 cm/s in controls ($P = 0.03$). LV afterload (arterial elastance) was 2.7 ± 1 mmHg/mL and was correlated with a decrease in LV longitudinal strain ($R = 0.51$, $P < 0.01$) during exercise.	2

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>80. Bhella PS, Pacini EL, Prasad A, et al. Echocardiographic indices do not reliably track changes in left-sided filling pressure in healthy subjects or patients with heart failure with preserved ejection fraction. <i>Circ Cardiovasc Imaging</i>. 2011;4(5):482-489.</p>	<p>Observational-Dx</p>	<p>47 patients</p>	<p>To estimate changes in filling pressures associated with the titration of medical therapy in patients with heart failure.</p>	<p>Forty-seven volunteers were enrolled: 11 highly screened elderly outpatients with a clear diagnosis of heart failure with preserved ejection fraction (HFpEF), 24 healthy elderly subjects, and 12 healthy young subjects. Each patient underwent right heart catheterization with simultaneous transthoracic echo. Pulmonary capillary wedge pressure (PCWP) and key echo indices (E/e' and E/Vp) were measured at two baselines and during 4 preload altering maneuvers: lower body negative pressure -15 mm Hg; lower body negative pressure -30 mm Hg; rapid saline infusion of 10 to 15 mL/kg; and rapid saline infusion of 20 to 30 mL/kg. A random coefficient mixed model regression of PCWP versus E/e' and PCWP versus E/Vp was performed for (1) a composite of all data points and (2) a composite of all data points within each of the 3 groups. Linear regression analysis was performed for individual subjects. With this protocol, PCWP was manipulated from 0.8 to 28.8 mm Hg. For E/e', the composite random effects mixed model regression was $PCWP=0.58 \times E/e'+7.02$ ($P<0.001$), confirming the weak but significant relationship between these 2 variables. Individual subject linear regression slopes (range, -6.76 to 11.03) and $r(2)$ (0.00 to 0.94) were highly variable and often very different than those derived for the composite and group regressions. For E/Vp, the composite random coefficient mixed model regression was $PCWP=1.95 \times E/Vp+7.48$ ($P=0.005$); once again, individual subject linear regression slopes (range, -16.42 to 25.39) and $r(2)$ (range, 0.02 to 0.94) were highly variable and often very different than those derived</p>	<p>2</p>

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
				for the composite and group regressions.	
81. Sharifov OF, Schiros CG, Aban I, Denney TS, Gupta H. Diagnostic Accuracy of Tissue Doppler Index E/e' for Evaluating Left Ventricular Filling Pressure and Diastolic Dysfunction/Heart Failure With Preserved Ejection Fraction: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2016;5(1).	Meta-analysis	24 studies	To review the Diagnostic Accuracy of Tissue Doppler Index E/e' for Evaluating Left Ventricular Filling Pressure and Diastolic Dysfunction/Heart Failure With Preserved Ejection Fraction	From the PubMed, Scopus, Embase, and Cochrane databases, we identified 24 studies reporting E/e' and invasive LVFP in preserved EF ($\geq 50\%$). In random-effects models, E/e' had poor to mediocre linear correlation with LVFP. Summary sensitivity and specificity (with 95% CIs) for the American Society of Echocardiography-recommended E/e' cutoffs (lateral, mean, and septal, respectively) to identify elevated LVFP was estimated by using hierarchical summary receiver operating characteristic analysis. Summary sensitivity was 30% (9-48%), 37% (13-61%), and 24% (6-46%), and summary specificity was 92% (82-100%), 91% (80-99%), and 98% (92-100%). Positive likelihood ratio (LR+) was <5 for lateral and mean E/e'. LR+ was slightly >10 for septal E/e' obtained from 4 studies (cumulative sample size <220). For excluding elevated LVFP, summary sensitivity for E/e' (lateral, mean, and septal, respectively) was 64% (38-86%), 36% (3-74%), and 50% (14-81%), while summary specificity was 73% (54-89%), 83% (49-100%), and 89% (66-100%). Because of data set limitations, meaningful inference for identifying HFpEF by using E/e' could not be drawn. With the use of quality assessment tool for diagnostic accuracy studies (Quality Assessment of Diagnostic Accuracy Studies questionnaire), we found substantial risks of bias and/or applicability.	Inadequate

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
82. Pellicori P, Kallvikbacka-Bennett A, Khaleva O, et al. Global longitudinal strain in patients with suspected heart failure and a normal ejection fraction: does it improve diagnosis and risk stratification? <i>Int J Cardiovasc Imaging</i> . 2014;30(1):69-79.	Review/Other-Dx	N/A	To highlight the Global longitudinal strain in patients with suspected heart failure and a normal ejection fraction	No results stated in abstract.	4
83. Donal E, Lund LH, Oger E, et al. Value of exercise echocardiography in heart failure with preserved ejection fraction: a substudy from the KaRen study. <i>Eur Heart J Cardiovasc Imaging</i> . 2016;17(1):106-113.	Observational-Dx	203 patients	To describe and analyse the potential prognostic value of echocardiographic parameters recorded not only at rest but also during a submaximal exercise stress echocardiography.	Patients were prospectively recruited in a single tertiary centre following an acute HF episode with NT-pro-BNP >300 pg/mL (BNP > 100 pg/mL) and LVEF > 45% and reassessed by exercise echo-Doppler after 4-8 weeks of dedicated treatment. Image acquisitions were standardized, and analysis made at end of follow-up blinded to patients' clinical status and outcome. In total, 60 patients having standardized echocardiographic acquisitions were included in the analysis. Twenty-six patients (43%) died or were hospitalized for HF (primary outcome). The mean +/- SD workload was 45 +/- 14 watts (W). Mean +/- SD resting LVEF and LV global longitudinal strain was 57.6 +/- 9.5% and -14.5 +/- 4.2%, respectively. Mean +/- SD resting E/e' was 11.3 +/- 4.7 and 13.1 +/- 5.3 in those patients who did not and those who did experience the primary outcome, respectively (P = 0.03). Tricuspid regurgitation (TR) peak velocity during exercise were 3.3 +/- 0.5 and 3.7 +/- 0.5 m/s (P = 0.01). Exercise TR was independently associated with HF-hospitalization or death after adjustment on baseline clinical and biological characteristics.	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
84. Freed BH, Daruwalla V, Cheng JY, et al. Prognostic Utility and Clinical Significance of Cardiac Mechanics in Heart Failure With Preserved Ejection Fraction: Importance of Left Atrial Strain. <i>Circ Cardiovasc Imaging</i> . 2016;9(3):1-10.	Observational-Dx	308 patients	To (1) determine the clinical, invasive hemodynamic, and cardiopulmonary exercise testing (CPET) correlates of left atrium (LA) strain in heart failure with preserved ejection fraction (HFpEF); and (2) evaluate the prognostic utility of LA strain in HFpEF and determine its significance when compared with conventional echocardiographic and clinical factors, and indices of left ventricular (LV) and right ventricular (RV) mechanics.	We evaluated baseline LA function in 308 patients with HFpEF who were followed up longitudinally for adverse outcomes. All patients underwent speckle-tracking echocardiography for measurement of left ventricular longitudinal strain, right ventricular free wall strain, and LA booster, conduit, and reservoir strains. The clinical and prognostic significance of left ventricular, right ventricular, and LA strain measures was assessed by regression analyses. The mean age was 65±13 years, 64% were women, 26% had atrial fibrillation, and LA enlargement was present in the majority of patients (67%). Decreased LA reservoir strain was associated with increased pulmonary vascular resistance (P<0.0001) and decreased peak oxygen consumption (P=0.0001). Of the left ventricular, right ventricular, and LA strain measures, LA reservoir strain was the strongest correlate of adverse events and was independently associated with the composite outcome of cardiovascular hospitalization or death (adjusted hazard ratio per 1-SD decrease in LA strain, 1.54; 95% CI, 1.15-2.07; P=0.006).	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
85. Kato S, Saito N, Kirigaya H, et al. Prognostic significance of quantitative assessment of focal myocardial fibrosis in patients with heart failure with preserved ejection fraction. <i>Int J Cardiol.</i> 2015;191:314-319.	Experimental-Dx	111 patients	To investigate the prognostic value of myocardial focal fibrosis quantified by late gadolinium enhanced (LGE) magnetic resonance imaging (MRI) in patients with heart failure with preserved ejection fraction (HFpEF).	During a mean follow up period of 851 +/- 609 days, 10 events (2 cardiovascular death, 8 hospitalization for heart failure decompensation) were observed. Area under the receiver operating characteristics curve of LGE% for the detection of future events was 0.721 (95% CI: 0.628-0.802). Multivariate Cox proportional hazard analysis showed that LGE% is an independent predictor of future events after the adjustment with prognostic 5 factors - age, diabetes mellitus, New York Heart Association classification, history of heart failure hospitalization and left ventricular ejection fraction - which were identified in the I-PRESERVE study (Irbesartan in Heart Failure with Preserved Ejection Fraction Study) (hazard ratio=7.913, 95% CI: 1.603-39.05, P=0.012).	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
86. Hancock HC, Close H, Mason JM, et al. High prevalence of undetected heart failure in long-term care residents: findings from the Heart Failure in Care Homes (HFinCH) study. <i>Eur J Heart Fail.</i> 2013;15(2):158-165.	Review/Other-Dx	1172 residents	To ascertain heart failure prevalence and clinical management in this population.	A total of 405 residents, aged 65-100 years, in 33 UK care facilities were prospectively enrolled between April 2009 and June 2010. The presence of heart failure was determined using European Society of Cardiology guidelines, modified where necessary for immobility. Evaluation of symptoms and signs, functional capacity, and quality of life, portable on-site echocardiography, and medical record review were completed in 399 cases. The point prevalence of heart failure was 22.8% [n = 91, 95% confidence interval (CI) 18.8-27.2%]; of these, 62.7% (n = 57, 95% CI 59.6-66.5%) had heart failure with preserved ejection fraction and 37.3% had left ventricular systolic dysfunction (n = 34, 95% CI 34.8-40.5%). A total of 76% (n = 61) of previous diagnoses of heart failure were not confirmed, and up to 90% (n = 82) of study cases were new. No symptoms or signs were reliable predictors of heart failure.	4
87. Marino P. Integrating the knowledge: strength and limitations of echo techniques to diagnose and stage heart failure with preserved ejection fraction. <i>J Cardiovasc Med (Hagerstown).</i> 2014;15(2):85-91.	Review/Other-Dx	N/A	To review the strength and limitations of echo techniques to diagnose and stage heart failure with preserved ejection fraction.	No results stated in abstract.	4
88. Andersen MJ, Borlaug BA. Invasive hemodynamic characterization of heart failure with preserved ejection fraction. <i>Heart Fail Clin.</i> 2014;10(3):435-444.	Review/Other-Dx	N/A	To review the invasive hemodynamic characterization of heart failure with preserved ejection fraction.	No results stated in abstract.	4
89. Gheorghide M, Bonow RO. Chronic heart failure in the United States: a manifestation of coronary artery disease. <i>Circulation.</i> 1998;97(3):282-289.	Review/Other-Dx	N/A	To review Chronic heart failure in the United States.	No results stated in abstract.	4

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
90. 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. <i>Am J Cardiol.</i> 2005;96(4):469-473.	Experiment al-Dx	528 patients	To assess the effect of ischemia during dobutamine stress echocardiography (DSE) on cardiac mortality in patients with heart failure.	Annual rates of cardiac death were 4.8% in patients who did not have ischemia, 5.5% in those who had ischemia and underwent revascularization within 4 months, and 11.8% in those who had ischemia and were not revascularized ($p < 0.001$ vs other groups). In a multivariate analysis model, independent predictors of cardiac death were diabetes (RR 2, 95% confidence interval 1.4 to 2.9), male gender (RR 1.7, 95% confidence interval 1.2 to 3.1), low-dose wall motion score index (RR 1.4, 95% confidence interval 1.2 to 2.6), and ischemia (RR 1.9, 95% confidence interval 1.3 to 3.2). 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).	2
91. 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. <i>Clin Cardiol.</i> 2009;32(7):403-409.	Experiment al-Dx	245 patients	To assess the prognostic value of low-dose stress-induced wall motion abnormalities (SWMA) in medically treated patients with ischemic cardiomyopathy.	There were 123 cardiac deaths (52%) during follow-up of 4.1 +/- 3.3 years. Multivariate predictors of cardiac death were age ($p = 0.002$, hazard ratio [HR]: 1.03), diabetes ($p = 0.028$, HR: 1.54), New York Heart Association (NYHA) class III, IV heart failure ($p = 0.001$, HR: 1.94), the presence of peak dose SWMA ($p < 0.001$, HR: 2.59), and low-dose SWMA ($p = 0.005$, HR: 2.28). Survival of patients without ischemia was significantly better than those with peak-dose SWMA ($p < 0.0001$) and those with low-dose SWMA ($p = 0.001$). The survival of patients with low-dose SWMA was the same as those with peak-dose SWMA ($p = 0.89$).	2

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
92. Sozzi FB, Elhendy A, Rizzello V, et al. Prognostic significance of akinesis becoming dyskinesia during dobutamine stress echocardiography. <i>J Am Soc Echocardiogr.</i> 2007;20(3):257-261.	Observational-Dx	731 patients	To assess the long-term outcome of patients with Akinesis becoming dyskinesia (AKBD) during dobutamine stress echocardiography (DSE).	Dyskinesia in two or more segments at peak stress developed in 60 patients (8%). Resting wall-motion score index was 2.6 +/- 0.56 in patients with AKBD versus 2.3 +/- 0.55 in patients without AKBD (P = .0002). 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). Independent predictors of hard cardiac events were age (hazard ratio [HR] 1.03 [confidence interval {CI} = 1.01-1.04]), previous myocardial infarction (HR 1.4 [CI = 1.1-1.9]), diabetes mellitus (HR 1.8 [CI = 1.3-2.5]), resting wall-motion score index (HR 1.11 [CI = 1.01-1.04]), and AKBD (HR 1.6 [CI = 1.1-2.4]).	2
93. Gulati V, Ching G, Heller GV. The role of radionuclide imaging in heart failure. <i>J Nucl Cardiol.</i> 2013;20(6):1173-1183.	Review/Other-Dx	N/A	To assess the role of radionuclide imaging in heart failure (HF).	No results stated in abstract.	4
94. Travin MI. Cardiac radionuclide imaging to assess patients with heart failure. <i>Semin Nucl Med.</i> 2014;44(4):294-313.	Review/Other-Dx	N/A	To review Cardiac radionuclide imaging to assess patients with heart failure	No results stated in abstract.	4

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
95. Beton O, Kurmus O, Asarcikli LD, Alibazoglu B, Alibazoglu H, Yilmaz MB. The practical value of technetium-99m-MIBI SPET to differentiate between ischemic and non-ischemic heart failure presenting with exertional dyspnea. Hell J Nucl Med. 2016;19(2):147-154.	Observational-Dx	179 patients	To differentiate ischemic heart failure (HF) from non-ischemic HF in patients presenting with non-acute onset exertional dyspnea using technetium-99m methoxyisobutylisonitrile gated single photon emission tomography ((99m)Tc-MIBI gSPET) imaging.	Of the 179 patients, 127 had ischemic HF and 52 had non-ischemic HF. There was no difference between ischemic and non-ischemic groups in terms of age, gender, body mass index, any smoking history, diabetes mellitus, history of hypertension and hyperlipidemia. Global dysfunction of left ventricle was more common in non-ischemic HF group than ischemic HF group (82.7% vs 41.7% respectively, $P<0.001$). Presence of severe (3+/4+) ischemia and large perfusion defect were higher in ischemic HF group compared to non-ischemic HF group (45.7% vs 15.4%, $P<0.001$ and 23.6% vs 3.8%, $P=0.003$, respectively). Summed stress score (SSS), summed rest score and summed difference score were higher in ischemic HF group compared to non-ischemic HF group ($P<0.001$, $P<0.001$, and $P=0.021$, respectively). In multivariate analysis, absence of global dysfunction ($P<0.001$, OR=10.338, 95%CI: 3.937-27.405) and SSS ($P<0.001$, OR=1.208, 95%CI: 1.090-1.339) were the independent predictors of ischemic HF. Absence of global dysfunction had 58.3% sensitivity and 86.7% specificity for diagnosis of ischemic HF at gSPET imaging in patients presenting with newly diagnosed HF and exertional dyspnea without concomitant chest pain (AUC=0.705, 95%CI: 0.632-0.771, $P<0.001$), whereas SSS>8 had 65.4% sensitivity and 75.0% specificity (AUC=0.732, 95%CI: 0.661-0.795, $P<0.001$).	3

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
96. Chander A, Brenner M, Lautamaki R, Voicu C, Merrill J, Bengel FM. 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(10):1643-1650.	Observational-Dx	24 patients	To make use of this opportunity and compared functional parameters derived from 82Rb cardiac Positron-Emission Tomography (PET) with those from retrospectively gated contrast-enhanced computed tomography (CT) angiography, obtained during the same PET/CT session.	Inter- and intraobserver agreement was good for all methods. On CT, ejection fraction (EF) was 66% +/- 13%, end-systolic volume (ESV) was 41 +/- 29 mL, and end-diastolic volume (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.	3
97. Range FT, Paul M, Schafers KP, et al. Myocardial perfusion in nonischemic dilated cardiomyopathy with and without atrial fibrillation. J Nucl Med. 2009;50(3):390-396.	Observational-Dx	22 controls; 30 patients	To compare myocardial perfusion between patients with nonischemic dilated cardiomyopathy (DCM) with and without atrial fibrillation (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.	3

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
98. Won E, Donnino R, Srichai MB, et al. Diagnostic Accuracy of Cardiac Magnetic Resonance Imaging in the Evaluation of Newly Diagnosed Heart Failure With Reduced Left Ventricular Ejection Fraction. <i>Am J Cardiol.</i> 2015;116(7):1082-1087.	Observational-Dx	81 patients	To determine the diagnostic value of cardiac magnetic resonance (CMR) imaging with late gadolinium enhancement (LGE), cine imaging, and resting first-pass perfusion (FPP) in the evaluation for ischemic (IC) versus nonischemic (NIC) cardiomyopathy in new-onset heart failure with reduced ($\leq 40\%$) left ventricular ejection fraction (HFrEF).	Coronary angiography identified 36 patients (43%) with IC. Presence of subendocardial and/or transmural LGE alone demonstrated good discriminative power (C-statistic 0.85, 95% confidence interval 0.76 to 0.94) for the diagnosis of IC. The presence of an ischemic pattern on both LGE and cine sequences resulted in a specificity of 87% for the diagnosis of IC, whereas the absence of an ischemic pattern on both LGE and cine sequences resulted in a specificity of 94% for the diagnosis of NIC.	2
99. Assomull RG, Shakespeare C, Kalra PR, et al. Role of cardiovascular magnetic resonance as a gatekeeper to invasive coronary angiography in patients presenting with heart failure of unknown etiology. <i>Circulation.</i> 2011;124(12):1351-1360.	Observational-Dx	124 patients	To assess the diagnostic accuracy of a cardiovascular magnetic resonance (CMR) protocol incorporating late gadolinium enhancement (LGE) and magnetic resonance coronary angiography (CA) as a noninvasive gatekeeper to CA in determining the etiology of heart failure in this subset of patients.	One hundred twenty consecutive patients underwent CMR and CA. The etiology was ascribed by a consensus panel that used the results of the CMR scans. Similarly, a separate consensus group ascribed an underlying cause by using the results of CA. The diagnostic accuracy of both strategies was compared against a gold-standard panel that made a definitive judgment by reviewing all clinical data. The study was powered to show noninferiority between the 2 techniques. The sensitivity of 100%, specificity of 96%, and diagnostic accuracy of 97% for LGE-CMR were equivalent to CA (sensitivity, 93%; specificity, 96%; and diagnostic accuracy, 95%). As a gatekeeper to CA, LGE-CMR was also found to be a cheaper diagnostic strategy in a decision tree model when United Kingdom-based costs were assumed. The economic merits of this model would change, depending on the relative costs of LGE-CMR and CA in any specific healthcare system.	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>100. Hamilton-Craig C, Strugnell WE, Raffel OC, Porto I, Walters DL, Slaughter RE. CT angiography with cardiac MRI: non-invasive functional and anatomical assessment for the etiology in newly diagnosed heart failure. <i>Int J Cardiovasc Imaging</i>. 2012;28(5):1111-1122.</p>	<p>Observational-Dx</p>	<p>28 patients</p>	<p>To prospectively compare standard-of-care invasive catheter angiography (iCA) and echocardiography to a novel non-invasive strategy of both Coronary Computed Tomographic Angiography (CCTA) and Cardiovascular MRI (CMR) to determine the etiology of myocardial dysfunction.</p>	<p>426 coronary segments from 28 prospectively enrolled patients were analyzed by CCTA and quantitative iCA. The per-patient sensitivity and specificity of CCTA was 100% and 90%, respectively, negative predictive value (NPV) 100%, positive predictive value (PPV) 78%. Mean ejection fraction by CMR was 24%. Presence of ischemic-type LGE on CMR conferred a 67% sensitivity, 100% specificity, 90% NPV and 100% PPV. Combining CCTA with CMR conferred 100% specificity, 100% sensitivity, 100% PPV and 100% NPV for detection or exclusion of coronary disease. In patients with negative CCTA all invasive angiograms could have been avoided. In addition, two patients with no ischemic LGE by CMR had severe coronary disease on both CCTA and iCA, indicating global hibernation.</p>	<p>1</p>

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
101. ten Kate GJ, Caliskan K, Dedic A, et al. Computed tomography coronary imaging as a gatekeeper for invasive coronary angiography in patients with newly diagnosed heart failure of unknown aetiology. Eur J Heart Fail. 2013;15(9):1028-1034.	Observational-Dx	81 patients	To evaluate the accuracy of cardiac computed tomography (CT) in distinguishing Coronary Artery Disease (CAD) and non-CAD heart failure (HF) and its effectiveness as a gatekeeper for invasive coronary angiography (ICA).	We prospectively included 93 symptomatic patients with newly diagnosed HF of unknown aetiology (59 men; mean age 53 +/- 13) and EF <45%, and/or fractional shortening <25%, and/or end-diastolic LV diameter >60 mm (men) or >55 mm (women). In all patients, the CT calcium score (CTCS) was determined. CTCS = 0 excluded CAD HF. Additional CT coronary angiography (CTCA) was performed if CTCS >0. ICA was used as the gold standard for distinguishing between CAD and non-CAD HF in patients with >20% luminal diameter narrowing on CTCA. CAD HF was defined as >50% luminal diameter narrowing in either (i) the left main coronary artery or proximal left anterior descending coronary artery or (ii) in multiple coronary arteries. Diagnostic accuracy and follow-up data (20 +/- 16 months) were collected for all patients. CTCS = 0 ruled out CAD HF in 43 patients (46%). The CT algorithm had 100% sensitivity, 95% specificity, 67% positive predictive value, and 100% negative predictive value for detecting CAD HF. Patients with CTCS = 0 or non-CAD HF on CTCA had no coronary events during follow-up, and ICA could have been safely avoided in 76 out of 93 patients (82%).	2

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>102. Abunassar JG, Yam Y, Chen L, D'Mello N, Chow BJ. Usefulness of the Agatston score = 0 to exclude ischemic cardiomyopathy in patients with heart failure. <i>Am J Cardiol.</i> 2011;107(3):428-432.</p>	<p>Observational-Dx</p>	<p>738 patients</p>	<p>To understand the potential application of the Agatston score in patients with heart failure (HF)</p>	<p>Excluding patients with HF or LV dysfunction, 738 patients (mean age 52 ± 10 years, 43% men) had an Agatston score equal to 0. Of these, 18 (2%) had obstructive CAD (diameter stenosis =50%), 8 (1%) had diameter stenoses =70%, and none had high-risk CAD. The 74 patients with high-risk CAD without LV dysfunction had high Agatston scores (mean 895 ± 734, median 716, range 50 to 3,210). In total 153 patients with a history of HF and abnormal ejection fraction were identified. All 13 patients with ischemic cardiomyopathy had Agatston scores >0, whereas 46 of 140 patients (30.1%) with nonischemic causes had an Agatston score equal to 0. An Agatston score equal to 0 identified nonischemic causes with a specificity of 100% (confidence interval 90 to 100) and positive predictive value of 100% (confidence interval 90 to 100). Agatston score equal to 0 had incremental value to pretest probability for CAD.</p>	<p>2</p>

Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>103. Premaratne M, Shamsaei M, Chow JD, et al. Using coronary calcification to exclude an ischemic etiology for cardiomyopathy: A validation study and systematic review. <i>Int J Cardiol.</i> 2017;230:518-522.</p>	<p>Review/Other-Dx</p>	<p>754 patients</p>	<p>To determine the utility of an Agatston score equal 0 to exclude the diagnosis of ischemic cardiomyopathy</p>	<p>Eighty-two patients were enrolled in the study and underwent CAC imaging with 81.7% patients having non-ischemic cardiomyopathy. An Agatston score=0 successfully excluded an ischemic etiology for cardiomyopathy with a specificity of 100% (CI: 74.7-100%) and a positive predictive value of 100% (CI: 85.0%-100%). A systematic literature review was performed and studies were deemed suitable for inclusion if: 1) patients with CHF, cardiomyopathy or LV dysfunction were enrolled, 2) underwent CAC imaging and patients were assessed for an Agatston score=0 or the absence of CAC, and 3) the final etiologic diagnosis (ischemic or non-ischemic) was provided. Eight studies provided sufficient information to calculate operating characteristics for an Agatston score=0 and were combined with our validation cohort for a total of 754 patients. An Agatston score=0 excluded ischemic cardiomyopathy with specificity and positive predictive values of 98.4% (CI: 95.6-99.5%), and 98.3% (CI: 95.5-99.5%), respectively.</p>	<p>4</p>

**Suspected New-Onset and Known Nonacute Heart Failure
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
104. Sousa PA, Bettencourt N, Dias Ferreira N, et al. Role of cardiac multidetector computed tomography in the exclusion of ischemic etiology in heart failure patients. Rev Port Cardiol. 2014;33(10):629-636.	Observational-Dx	100 patients	To assess the value of coronary multidetector computed tomography (MDCT) angiography in the exclusion of ischemic etiology in heart failure (HF) patients and to determine whether the Agatston calcium score could be used as a gatekeeper for CTA in this context.	During this period 100 patients (mean age 57.3±10.5 years, 64% men) with HF and systolic dysfunction were referred for MDCT to exclude CAD. Median effective radiation dose was 4.8 mSv (interquartile range 5.8 mSv). Mean LVEF was 35±7.7% (range 20-48%) and median CAC score was 13 (interquartile range 212). Seven patients were in atrial fibrillation. Almost half of the patients (40%) had no CAC and none of these had significant stenosis on CTA. In an additional group of 33 patients CTA was able to confidently exclude obstructive CAD. Twenty-seven patients were classified as positive for CAD (16 due to CAC >400 and 11 with =50% stenosis) and were associated with lower LVEF (p=0.004). Of these, 21 patients subsequently underwent ICA: obstructive CAD was confirmed in nine and only six had criteria for ischemic cardiomyopathy.	3
105. Melo RM, Melo EF, Biselli B, Souza GE, Bocchi EA. Clinical usefulness of coronary angiography in patients with left ventricular dysfunction. Arq Bras Cardiol. 2012;98(5):437-441.	Review/Other-Dx	107 patients	To evaluate the prevalence of ischemic heart disease by angiographic criteria in patients with heart failure and reduced ejection fraction of unknown etiology, as well as its impact on therapy decisions.	One hundred and seven patients were included in the analysis, with 51 (47.7%) patients in Group 1 and 56 (52.3%) in Group 2. The prevalence of ischemic heart disease was 9.3% (10 patients), and all belonged to Group 1 (p = 0.0001). During follow-up, only 4 (3.7%) were referred for CABG; 3 (2.8%) patients had procedure-related complications.	4
106. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: https://www.acr.org/-/media/ACR/Files/Appropriateness-Criteria/RadiationDoseAssessmentIntro.pdf .	Review/Other-Dx	N/A	Guidance document on exposure of patients to ionizing radiation.	No results stated in abstract.	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
 - a. The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
 - b. The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
 - c. The study is an expert opinion or consensus document.
- Meta-analysis
 - a. *Good quality* – the study design, methods, analysis, and results are valid and the conclusion is supported.
 - b. *Inadequate quality* – the study design, analysis, and results lack the methodological rigor to be considered a good meta-analysis study.

Abbreviations Key

Dx = Diagnostic

Tx = Treatment