Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Brenner S, Guder G. The patient with dyspnea. Rational diagnostic evaluation. *Herz.* 2014;39(1):8-14.	Review/Other-Dx	N/A	To evaluate dyspnea in patients.	Dyspnea is the uncomfortable awareness of difficult breathing. It is a common symptom in primary and nonprimary care settings. Although multiple disorders and diseases may cause breathlessness, the majority of the conditions are of cardiac or pulmonary origin. The challenge is to establish the diagnosis timely and with minimized investigations. Frequently, information about onset, progression, and circumstances of occurrence considerably narrow the underlying etiology. In most cases, a carefully taken history and a comprehensive physical examination lead to the correct diagnosis. Nevertheless, one should be aware of concomitant conditions and not be satisfied with a diagnosis if comorbidity may still be a candidate in causing dyspnea. Otherwise, it has been observed that chronic obstructive pulmonary disease was over-diagnosed in patients with systolic HF and dyspnea. A prudential use of investigating modalities for confirmation and exclusion of a questionable diagnosis is the key for allocating the correct therapy and achieving fast symptom relief in patients with dyspnea.	4
2. Parshall MB, Schwartzstein RM, Adams L, et al. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. *Am J Respir Crit Care Med.* 2012;185(4):435-452.	Review/Other-Dx	N/A	To update the 1999 ATS Consensus Statement on dyspnea.	Progress has been made in clarifying mechanisms underlying several qualitatively and mechanistically distinct breathing sensations. Brain imaging studies have consistently shown dyspnea stimuli to be correlated with activation of cortico-limbic areas involved with interoception and nociception. Endogenous and exogenous opioids may modulate perception of dyspnea. Instruments for measuring dyspnea are often poorly characterized; a framework is proposed for more consistent identification of measurement domains.	4

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3. Wahls SA. Causes and evaluation of chronic dyspnea. *Am Fam Physician.* 2012;86(2):173-182.	Review/Other-Dx	N/A	To evaluate the causes and evaluation of chronic dyspnea.	Chronic dyspnea is shortness of breath that lasts more than 1 month. The perception of dyspnea varies based on behavioral and physiologic responses. Dyspnea that is greater than expected with the degree of exertion is a symptom of disease. Most cases of dyspnea result from asthma, HF and myocardial ischemia, chronic obstructive pulmonary disease, interstitial lung disease, pneumonia, or psychogenic disorders. The etiology of dyspnea is multifactorial in about one-third of patients. The clinical presentation alone is adequate to make a diagnosis in 66% of patients with dyspnea. Patients' descriptions of the sensation of dyspnea may be helpful, but associated symptoms and risk factors, such as smoking, chemical exposures, and medication use, should also be considered. Examination findings (eg, jugular venous distention, decreased breath sounds or wheezing, pleural rub, clubbing) may be helpful in making the diagnosis. Initial testing in patients with chronic dyspnea includes chest radiography, electrocardiography, spirometry, complete blood count, and basic metabolic panel. Measurement of brain natriuretic peptide levels may help exclude HF and D-dimer testing may help rule out pulmonary emboli. Pulmonary function studies can be used to identify emphysema and interstitial lung diseases. CT of the chest is the most appropriate imaging study for diagnosing suspected pulmonary causes of chronic dyspnea.	4

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4. Croucher B. The challenge of diagnosing dyspnea. *AACN Adv Crit Care.* 2014;25(3):284-290.	Review/Other-Dx	N/A	To discuss the differential diagnoses associated with dyspnea.	Dyspnea is a subjective and nonspecific symptom, yet very distressing for those who experience it. Acute onset dyspnea and exacerbation of chronic dyspnea from heart or lung disease significantly add to the number of emergency department visits and inpatient admissions. Although dyspnea may appear to be a simple condition to evaluate and manage, it is actually complex in description and quality. As such, dyspnea is the first symptom of many diseases. The onset of dyspnea can be due to a new acute disease, the exacerbation of an existing chronic illness, or a new disease compounding a chronic illness. Finding the cause of dyspnea is generally more difficult than it originally may appear.	4
5. Ponka D, Kirlew M. Top 10 differential diagnoses in family medicine: dyspnea. *Can Fam Physician.* 2007;53(8):1333.	Review/Other-Dx	N/A	To review the differential diagnoses of dyspnea.	No results stated in abstract.	4

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6. Poltavskaia MG, Sarkisova EA, Syrkin AL, Doletskii AA. [Chronic dyspnea in cardiological patients: prevalence and etiology]. *Klin Med (Mosk).* 2007;85(6):37-41.	Review/Other-Dx	1,414 patients	To analyze the prevalence and etiology of chronic dyspnea in patients.	Among the patients, 41.2% complained of dyspnea; the number of women with dyspnea prevailed over the number of men. Dyspnea was caused by chronic HF in 42.2% of patients, by transient myocardial ischemia in 12.3% of patients, and by paroxysmal tachyarrhythmia in 6.3% of patients. In 45.6% of the patients, mostly in women, significant non-cardial factors were revealed: obstructive or restrictive respiratory failure (20.6%), obesity (14.7%), thyroid gland dysfunction (3.9%), pulmonary arterial thromboembolism, anemia etc. A combination of 2 or more etiological factors took place in 22.6% of cases. The reason for respiratory discomfort remained unclear in 21.3% of the patients, mostly women. Symptom-limited load test with gas analysis (ergospirometry) was performed in 70 patients with dyspnea of unclear origin. According to its results, in 75% of elderly patients with essential hypertension and postinfarction cardiosclerosis, who did not have significant systolic dysfunction, restrictive diastolic dysfunction, valvular disorder, or atrial fibrillation, dyspnea was caused by hyperventilation, obesity, and respiratory pathology.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
7. Angermann C, Hoyer C, Ertl G. [Differential diagnosis of dyspnea - significance of clinic aspects, imaging and biomarkers for the diagnosis of heart failure]. *Clin Res Cardiol.* 2006;95 Suppl 4:57-70; quiz 71.	Meta-analysis	N/A	To elaborate on the specific usefulness of traditional diagnostic tools as history, symptomatology and physical signs along with chest X-ray and electrocardiogram and the more recently introduced natriuretic peptides to discriminate HF from other causes of dyspnea in the emergency setting.	According to a systematic search and meta-analysis of the respective literature, several features from history and physical examination as well as pulmonary congestion on chest X-ray, atrial fibrillation and a high level of confidence of the initial clinical judgment indicate a cardiac cause of dyspnea with high specificity, but less sensitivity. Thus, in patients presenting with one or several of these characteristic features, little further diagnostic yield is to be expected from natriuretic peptides. If, however, the suspicion of HF remains unsettled by these means, determination of biomarkers may be helpful, although it needs to be considered that moderately elevated levels have only a limited specificity in particular in elderly patients with comorbidities. As also recognized by the European Guidelines for diagnosis and treatment of chronic HF, a BNP level of <100 pg/mL has proven particularly useful for excluding HF.	M
8. 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 congestive heart failure on chest X-ray and the effect of level of training and confidence upon accuracy of interpretation.	Physicians correctly identified the congestive heart failure chest X-rays 79% of the time (sensitivity 59%, specificity 96%; positive LR 14.6, negative LR 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 congestive heart failure. High specificity (96%) and low sensitivity (59%) suggest that emergency physicians are excellent at identifying congestive heart failure 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

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
9. Karnani NG, Reisfield GM, Wilson GR. Evaluation of chronic dyspnea. *Am Fam Physician.* 2005;71(8):1529-1537.	Review/Other-Dx	N/A	To review the salient features of the history, physical examination, laboratory testing, office spirometry, and imaging in patients with dyspnea, as well as more specialized testing that is required if the cause remains unexplained after initial evaluation.	Chronic dyspnea is defined as dyspnea lasting more than one month. In approximately two thirds of patients presenting with dyspnea, the underlying cause is cardiopulmonary disease. Establishing an accurate diagnosis is essential because treatment differs depending on the underlying condition. Asthma, congestive HF, chronic obstructive pulmonary disease, pneumonia, cardiac ischemia, interstitial lung disease, and psychogenic causes account for 85% of patients with this principal symptom. The history and physical examination should guide selection of initial diagnostic tests such as electrocardiogram, chest radiograph, pulse oximetry, spirometry, complete blood count, and metabolic panel. If these are inconclusive, additional testing is indicated. Formal pulmonary function testing may be needed to establish a diagnosis of asthma, chronic obstructive pulmonary disease, or interstitial lung disease. High-resolution CT is particularly useful for diagnosing interstitial lung disease, idiopathic pulmonary fibrosis, bronchiectasis, or pulmonary embolism. Echocardiography and BNP levels help establish a diagnosis of congestive HF. If the diagnosis remains unclear, additional tests may be required. These include ventilation perfusion scans, Holter monitoring, cardiac catheterization, esophageal pH monitoring, lung biopsy, and cardiopulmonary exercise testing.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
10. Platz E, Hempel D, Pivetta E, Rivero J, Solomon SD. Echocardiographic and lung ultrasound characteristics in ambulatory patients with dyspnea or prior heart failure. *Echocardiography*. 2014;31(2):133-139.	Observational-Dx	81 patients	To investigate the utility of lung US in ambulatory subjects with dyspnea or prior HF.	Of 81 subjects, 74 (91%) (median age 66 years, 39% men, median LVEF 54%, 39% with prior HF) had adequate lung US images of all 8 zones and were included in the analysis. The number of B-lines ranged from 0–12 (median 2). Increased B-lines, analyzed by tertiles, were associated with larger LV end-diastolic (P=0.036) and end-systolic diameters (P=0.026), septal wall thickness (P=0.009), LV mass index (P=0.001), left atrial volume index (P=0.005), tricuspid regurgitation (TR) velocity (P=0.005) and estimated pulmonary artery systolic pressure (P=0.003). In a secondary analysis association between B-lines (not grouped by tertiles) and LV mass index, left atrial volume index, tricuspid regurgitation velocity and pulmonary artery systolic pressure remained stable after adjustment for age, gender, body mass index, and HF history.	2
11. Kane GC, Oh JK. Diastolic stress test for the evaluation of exertional dyspnea. *Curr Cardiol Rep.* 2012;14(3):359-365.	Review/Other-Dx	N/A	To discuss the role of the Doppler echocardiographic diastolic stress test in the evaluation of patients with cardiac dyspnea.	Recent studies have highlighted that dyspneic patients comprise a high-risk subgroup of patients referred for cardiac stress testing. Even after adjusting for the presence and degree of CAD the risk of cardiac and all-cause mortality is at least three- to fivefold higher in dyspneic patients compared to asymptomatic or those with chest pain. Stress echocardiography is uniquely positioned to characterize all potential cardiovascular etiologies of dyspnea from global and regional systolic dysfunction, myocardial ischemia to valvular heart disease, pulmonary hypertension and diastolic dysfunction. Various data point to diastolic dysfunction and associated HF as the major potential etiology for dyspnea as well as the likely cause of the heightened mortality risk. Doppler echocardiography at rest and with stress can now characterize the hemodynamics of diastolic dysfunction and close the loop on the comprehensive assessment of the patient who has exertional shortness of breath.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
12. Argulian E, Agarwal V, Bangalore S, et al. Meta-analysis of prognostic implications of dyspnea versus chest pain in patients referred for stress testing. *Am J Cardiol.* 2014;113(3):559-564.	Meta-analysis	6 studies	To evaluate the incidence of ischemia in patients with dyspnea compared with patients with chest pain referred for stress testing and assess the outcomes of such patients.	6 studies evaluated a total of 5,753 patients with dyspnea and 24,491 patients with chest pain as the clinical indication for stress testing. There was no statistically significant difference in the incidence of ischemia on stress imaging in patients with dyspnea compared with patients with chest pain (37.4% vs 30.2%, OR 1.43, 95% CI, 0.99 to 2.06, P=0.06). However, during the follow-up period, patients with dyspnea had higher all-cause mortality rates compared with patients with chest pain (annual mortality 4.9% vs 2.3%), with OR of 2.57 (95% CI, 1.75 to 3.76, P<0.001).	M
13. Min JK, Shaw LJ, Berman DS. The present state of coronary computed tomography angiography a process in evolution. *J Am Coll Cardiol.* 2010;55(10):957-965.	Review/Other-Dx	N/A	To describe the latest available published evidence supporting the potential clinical and cost efficiency of CCTA, drawing attention not only to the significance but also the limitations of such studies.	In the past 5 years since the introduction of 64-detector row CCTA, there has been an exponential growth in the quantity of scientific evidence to support the feasibility of its use in the clinical evaluation of individuals with suspected CAD. Since then, there has been considerable debate as to where CCTA precisely fits in the algorithm of evaluation of individuals with suspected CAD. Proponents of CCTA contend that the quality and scope of the available evidence to date support the replacement of conventional methods of CAD evaluation by CCTA, whereas critics assert that clinical use of CCTA is not yet adequately proven and should be restricted, if used at all. Coincident with the scientific debate underlying the clinical utility of CCTA, there has developed a perception by many that the rate of growth in cardiac imaging is disproportionately high and unsustainable. In this respect, all noninvasive imaging modalities and, in particular, more newly introduced ones, have undergone a higher level of scrutiny for demonstration of clinical and economic effectiveness.	4

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14. Nakanishi R, Rana JS, Rozanski A, et al. Relationship of dyspnea vs. typical angina to coronary artery disease severity, burden, composition and location on coronary CT angiography. *Atherosclerosis*. 2013;230(1):61-66.	Review/Other-Dx	1,443 patients	To examine the associations of coronary artery plaque severity, burden, composition and location in consecutive individuals presenting for CCTA with either dyspnea or typical angina as a primary presenting complaint.	By multivariable logistic regression, both dyspnea (OR 1.9, 95% CI, 1.1–3.3, P=0.02) and typical angina (OR 1.9, 95% CI, 1.2–3.1, P=0.01) were associated with obstructive CAD as compared to individuals without dyspnea or typical angina, while dyspnea (OR 1.8, 95% CI, 1.1–3.1, P=0.02), but not typical angina (OR 1.1, 95% CI, 0.7–1.6, P=0.76) was associated with plaque in the proximal portions of coronary arteries. Neither symptom type was associated with differences in plaque burden nor composition.	4
15. Gerber TC, Kantor B, McCollough CH. Radiation dose and safety in cardiac computed tomography. *Cardiol Clin.* 2009;27(4):665-677.	Review/Other-Dx	N/A	To review the existing data regarding biologic hazards of radiation exposure associated with medical diagnostic testing, the methodologies used to estimate radiation exposure and dose, and the measures that can be taken to effectively reduce that exposure.	The risk of causing a malignancy at the radiation dose levels used in cardiac imaging is hypothetical, not proven, and estimates of radiation dose have a wide margin of error. However, in the absence of certainty, the consensus opinions of influential expert panels advocate adopting a conservative estimate of radiation risks.	4

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16. Earls JP, Berman EL, Urban BA, et al. Prospectively gated transverse coronary CT angiography versus retrospectively gated helical technique: improved image quality and reduced radiation dose. *Radiology*. 2008;246(3):742-753.	Observational-Dx	203 patients	To retrospectively compare image quality, radiation dose, and blood vessel assessability for CCTA obtained with a prospectively gated transverse CT technique and a retrospectively gated helical CT technique.	The mean effective dose for the group with the prospectively gated transverse technique was 2.8 mSv; this represents an 83% reduction as compared with that for the group with the retrospectively gated helical technique (mean, 18.4 mSv; *P*<.001). The image quality score for each of the arteries, as well as the overall combined score, was significantly greater for images obtained with prospectively gated transverse technique than for images obtained with retrospectively gated helical technique. The combined mean image quality score was 4.791 for images obtained with prospectively gated transverse technique vs 4.514 for images obtained with retrospectively gated helical technique (proportional odds model OR, 2.8; 95% CI: 1.7, 4.8). The percentage of assessable coronary artery segments was 98.6% (1,196/1,213) for images obtained with prospectively gated transverse technique vs 97.9% (1,741/1,778) for images obtained with retrospectively gated helical technique (*P*=.83).	2
17. Husmann L, Valenta I, Gaemperli O, et al. Feasibility of low-dose coronary CT angiography: first experience with prospective ECG-gating. *Eur Heart J*. 2008;29(2):191-197.	Observational-Dx	41 consecutive patients	To determine the feasibility of prospective ECG-gating to achieve low-dose CCTA.	Mean effective radiation dose was 2.1 +/- 0.6 mSv (range, 1.1-3.0 mSv). Image quality was inversely related to heart rate (57.3 +/- 6.2, range 39-66 b.p.m.; r = 0.58, *P*<0.001), vessel attenuation (346 +/- 104, range 110-780 HU; r = 0.56, *P*<0.001), and body mass index (26.1 +/- 4.0, range 19.1-36.3 kg/m(2); r = 0.45, *P*<0.001), but not to heart rate variability (1.5 +/- 1.0, range 0.2-5.1 b.p.m.; r = 0.28, *P*=0.069). Nondiagnostic CCTA image quality was found in 5.0% of coronary segments. However, below a heart rate of 63 b.p.m. (n=28), as determined by ROC, only 1.1% of coronary segments were nondiagnostic compared with 14.8% with heart rate of >63 b.p.m. (*P*<0.001).	3

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18. Stolzmann P, Leschka S, Scheffel H, et al. Dual-source CT in step-and-shoot mode: noninvasive coronary angiography with low radiation dose. *Radiology.* 2008;249(1):71-80.	Observational-Dx	40 patients	To prospectively investigate CT image quality parameters by using different protocols and to calculate radiation dose estimates for noninvasive coronary angiography performed with dual-source CT in the step-and-shoot mode.	Mean image noise was similar with protocols A and B. Mean attenuation in the aorta and coronary arteries with protocol A (444 HU) was significantly (*P*<.001) higher than that with protocol B (358 HU). The reduced contrast material dose in protocol C yielded attenuation similar to that with protocol B. Diagnostic image quality was achieved with all protocols in 1,237 (97.9%) of 1,264 coronary segments. No significant differences in image quality between the 100- and 120-kV protocols were found. Mean heart rate had a significant effect on motion artifacts (area under ROC curve = 0.818; 95% CI: 0.723, 0.892; *P*<.001), whereas heart rate variability had a significant effect on stair-step artifacts (area under ROC curve = 0.79; 95% CI: 0.687, 0.865; *P*<.001). The mean estimated effective dose was 1.2 mSv +/- 0.2 for protocols A and C and 2.6 mSv +/- 0.5 for protocol B.	2

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19. Leipsic J, Labounty TM, Heilbron B, et al. Estimated radiation dose reduction using adaptive statistical iterative reconstruction in coronary CT angiography: the ERASIR study. *AJR Am J Roentgenol.* 2010;195(3):655-660.	Observational-Dx	574 consecutive patients	Prospectively evaluate patients undergoing CCTA at 3 centers to assess the impact of Adaptive Statistical Iterative Reconstruction (ASIR) on radiation dose and study quality for CCTA. Comparisons were performed between consecutive groups initially using filtered back projection (n = 331) and subsequently ASIR (n = 243) with regard to patient and scan characteristics, radiation dose, and diagnostic study quality.	There was no difference between groups in the use of prospective gating, tube voltage, or scan length. The examinations performed using ASIR had a lower median tube current than those obtained using filtered back projection (median [interquartile range], 450 mA [350–600] vs 650 mA [531–750], respectively; $P<0.001$). There was a 44% reduction in the median radiation dose between the filtered back projection and ASIR cohorts (4.1 mSv [2.3–5.2] vs 2.3 mSv [1.9–3.5]; $P<0.001$). After adjustment for scan settings, ASIR was associated with a 27% reduction in radiation dose compared with filtered back projection (95% CI, 21%–32%; $P<0.001$). Despite the reduced current, ASIR was not associated with a difference in adjusted signal, noise, or signal-to-noise ratio (P=not significant). No differences existed between filtered back projection and ASIR for interpretability per coronary artery (98.5% vs 99.3%, respectively; $P=0.12$) or per patient (96.1% vs 97.1%, $P=0.65$). ASIR enabled reduced tube current and lower radiation dose in comparison with filtered back projection, with preserved signal, noise, and study interpretability, in a large multicenter cohort. ASIR represents a new technique to reduce radiation dose in CCTA studies.	3
20. Achenbach S, Marwan M, Ropers D, et al. Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. *Eur Heart J.* 2010;31(3):340-346.	Observational-Dx	50 consecutive patients	To evaluate the feasibility and image quality of a new scan mode for CCTA with an effective dose of <1 mSv.	In all 50 patients, imaging was successful. Mean duration of data acquisition was 258 +/- 20 ms. Mean dose-length product was 62 +/- 5 mGy cm, the effective dose was 0.87 +/- 0.07 mSv (0.78–0.99 mSv). Of the 742 coronary artery segments, 94% had an image quality score of 1, 5.0% a score of 2, 0.9% a score of 3, and 4 segments (0.5%) were 'uninterpretable'. In nonobese patients with a low and stable heart rate, prospectively ECG-triggered high-pitch spiral CCTA provides excellent image quality at a consistent dose below 1.0 mSv.	3

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21. American College of Radiology. ACR–NASCI–SIR–SPR Practice Parameter for the Performance and Interpretation of Body Computed Tomography Angiography (CTA). Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Body_CTA.pdf.	Review/Other-Dx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	N/A	4
22. Paterson I, Mielniczuk LM, O'Meara E, So A, White JA. Imaging heart failure: current and future applications. *Can J Cardiol.* 2013;29(3):317-328.	Review/Other-Dx	N/A	To review current and future HF applications for the major noninvasive imaging modalities: TTE, SPECT, PET, CMR, and CT.	TTE is the primary imaging test used in the evaluation of patients with HF, given its widespread availability and reliability in assessing cardiac structure and function. Recent developments in myocardial strain, 3-D TTE, and echo contrast appear to offer superior diagnostic and prognostic information. SPECT imaging is a common method employed to detect ischemia and viability in patients with HF; however, PET offers higher diagnostic accuracy for both. Ongoing study of sympathetic and molecular imaging techniques may enable early disease detection, better risk stratification, and ultimately targeted treatment interventions. CMR provides high-quality information on cardiac structure and function and allows the characterization of myocardial tissue. Myocardial late gadolinium enhancement allows the determination of HF etiology and may predict patient outcomes and treatment response. Cardiac CT has become a reliable means for detecting CAD, and recent advances have enabled concurrent myocardial function, perfusion, and scar analyses.	4

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23. Greenwood JP, Motwani M, Maredia N, et al. Comparison of cardiovascular magnetic resonance and single-photon emission computed tomography in women with suspected coronary artery disease from the Clinical Evaluation of Magnetic Resonance Imaging in Coronary Heart Disease (CE-MARC) Trial. *Circulation.* 2014;129(10):1129-1138.	Observational-Dx	235 women and 393 men	To compare the sex-specific diagnostic performance of CMR and SPECT.	For CMR, the sensitivity in women and men was similar (88.7% vs 85.6%; *P*=0.57), as was the specificity (83.5% vs 82.8%; *P*=0.86). For SPECT, the sensitivity was significantly worse in women than in men (50.9% vs 70.8%; *P*=0.007), but the specificities were similar (84.1% vs 81.3%; *P*=0.48). The sensitivity in both the female and male groups was significantly higher with CMR than SPECT (*P*<0.0001 for both), but the specificity was similar (*P*=0.77 and *P*=1.00, respectively). For perfusion-only components, CMR outperformed SPECT in women (AUC, 0.90 vs 0.67; *P*<0.0001) and in men (AUC, 0.89 vs 0.74; *P*<0.0001). Diagnostic accuracy was similar in both sexes with perfusion CMR (*P*=1.00) but was significantly worse in women with SPECT (*P*<0.0001).	3
24. Schwitter J, Wacker CM, Wilke N, et al. MR-IMPACT II: Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary artery disease Trial: perfusion-cardiac magnetic resonance vs. single-photon emission computed tomography for the detection of coronary artery disease: a comparative multicentre, multivendor trial. *Eur Heart J.* 2013;34(10):775-781.	Experimental-Dx	533 patients	To compare the diagnostic performance of perfusion-CMR and SPECT for the detection of CAD using conventional X-ray coronary angiography as the reference standard.	For CMR and SPECT, the sensitivity scores were 0.67 and 0.59, respectively, with the lower confidence level for the difference of +0.02, indicating superiority of CMR over SPECT. The specificity scores for CMR and SPECT were 0.61 and 0.72, respectively (lower confidence level for the difference: -0.17), indicating inferiority of CMR vs SPECT. No severe adverse events occurred in the 515 patients.	2
25. Clausen H, Francis J, Holloway C. A pensioner with dyspnoea: cardiac magnetic resonance reveals pulmonary embolism. *BMJ Case Rep.* 2012;2012.	Review/Other-Dx	1 patient	A case report of a patient presented with acute-on-chronic dyspnoea.	Dyspnoea is a common clinical presentation with a diverse range of etiologies. This case illustrates the complexity of diagnosing dyspnoea in patients with multiple medical comorbidities. This case emphasizes the need to consider extracardiac pathology during such investigations and illustrates the utility of CMR in the assessment of cardiac disease when TTE may be technically challenging.	4

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26. Odonkor PN, Grigore AM. Patients with ischemic heart disease. *Med Clin North Am.* 2013;97(6):1033-1050.	Review/Other-Dx	N/A	To review patients with ischemic heart disease.	Patients with ischemic heart disease who are undergoing surgery are at risk for development of perioperative cardiac events, and this risk depends on the type of surgery, the presence of clinical risk factors, and the functional status of patients. Appropriate perioperative management of medications such as DAPT and b-blocker therapy has a significant impact on outcomes. Perioperative management decisions should be communicated clearly between the surgeon, cardiologist, and anesthesiologist involved in the care of the patient. Appropriate perioperative management reduces the incidence of perioperative cardiac events.	4
27. Heo R, Nakazato R, Kalra D, Min JK. Noninvasive imaging in coronary artery disease. *Semin Nucl Med.* 2014;44(5):398-409.	Review/Other-Dx	N/A	To review the strengths and limits of noninvasive cardiac imaging.	An array of high-quality imaging technologies exist to study individuals with suspected CAD, with benefits and limitations to each of them. Selection of the best test depends on the patient risk factors and the local availability and expertise of each modality. This integrated approach combining anatomical and functional imaging is critical for comprehensive evaluation of the clinically relevant aspects of CAD.	4
28. Tonino PA, Fearon WF, De Bruyne B, et al. Angiographic versus functional severity of coronary artery stenoses in the FAME study fractional flow reserve versus angiography in multivessel evaluation. *J Am Coll Cardiol.* 2010;55(25):2816-2821.	Observational-Dx	509 patients	To investigate the relationship between angiographic and functional severity of coronary artery stenoses in the FAME (Fractional Flow Reserve Versus Angiography in Multivessel Evaluation) study.	Before FFR measurement, these lesions were categorized into 50% to 70% (47% of all lesions), 71% to 90% (39% of all lesions), and 91% to 99% (15% of all lesions) diameter stenosis by visual assessment. In the category 50% to 70% stenosis, 35% were functionally significant (FFR ≤0.80) and 65% were not (FFR >0.80). In the category 71% to 90% stenosis, 80% were functionally significant and 20% were not. In the category of subtotal stenoses, 96% were functionally significant. Of all 509 patients with angiographically defined multivessel disease, only 235 (46%) had functional multivessel disease (≥2 coronary arteries with an FFR ≤0.80).	3

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29. Pakkal M, Raj V, McCann GP. Non-invasive imaging in coronary artery disease including anatomical and functional evaluation of ischaemia and viability assessment. *Br J Radiol.* 2011;84 Spec No 3:S280-295.	Review/Other-Dx	N/A	To provide an overview of all the imaging modalities in the diagnosis of CAD.	The different cardiac imaging modalities provide complementary information about various aspects of CAD. Coronary CT and MRI of the coronary arteries provide anatomical information. Functional significance of a coronary stenosis is assessed by stress CMR, radioisotope studies and stress echocardiography. Subclinical atherosclerosis is assessed by coronary calcium score and coronary CT. The NICE guideline provides a framework which incorporates anatomical and functional imaging in the setting of stable chest pain of recent onset. An integrated approach combining anatomical and functional imaging is important in guiding treatment options and in risk stratification.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
30. Berman DS, Shaw LJ, Min JK, et al. SPECT/PET myocardial perfusion imaging versus coronary CT angiography in patients with known or suspected CAD. *Q J Nucl Med Mol Imaging.* 2010;54(2):177-200.	Review/Other-Dx	N/A	To provide a synopsis of the available literature on imaging that integrates both CT and MPI in strategies for the assessment of asymptomatic patients for their atherosclerotic coronary disease burden and risk as well as symptomatic patients for diagnosis and guiding management.	Stress SPECT MPI is the most commonly utilized stress imaging technique for patients with suspected or known CAD and has a robust evidence base including the support of numerous clinical guidelines. Gated SPECT is a well-established noninvasive imaging modalities that is a core element in evaluation of patients with both acute and stable chest pain syndromes. Over the past decade, PET has become increasingly used for the same applications. By comparison, cardiac CT is a more recently developed method, providing noninvasive approaches for imaging coronary atherosclerosis and coronary artery stenosis. Noncontrast CT for imaging the extent of CAC, in clinical use since the mid-1990's, has a very extensive evidence base supporting its use in CAD prevention. While contrast-enhanced CT for noninvasive CCTA is relatively new, it has already developed an extensive base of evidence regarding diagnosing obstructive CAD and more recently evidence has emerged regarding its prognostic value. It is likely that noncontrast CT or CCTA for assessment of extent of atherosclerosis will become an increasing part of mainstream cardiovascular imaging practices as a first line test. In some patients, further ischemia testing with MPI will be required. Similarly, MPI will continue to be widely used as a first-line test, and in some patients, further anatomic definition of atherosclerosis with CT will also be appropriate.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
31. Jaarsma C, Leiner T, Bekkers SC, et al. Diagnostic performance of noninvasive myocardial perfusion imaging using single-photon emission computed tomography, cardiac magnetic resonance, and positron emission tomography imaging for the detection of obstructive coronary artery disease: a meta-analysis. *J Am Coll Cardiol.* 2012;59(19):1719-1728.	Meta-analysis	166 articles	To determine the diagnostic accuracy of the 3 most commonly used noninvasive MPI modalities, SPECT, CMR, and PET perfusion imaging for the diagnosis of obstructive CAD.	Of the 3,635 citations, 166 articles (n = 17,901) met the inclusion criteria: 114 SPECT, 37 CMR, and 15 PET articles. There were not enough publications on other perfusion techniques such as perfusion echocardiography and CT to include these modalities into the study. The patient-based analysis per imaging modality demonstrated a pooled sensitivity of 88% (95% CI: 88% to 89%), 89% (95% CI: 88% to 91%), and 84% (95% CI: 81% to 87%) for SPECT, CMR, and PET, respectively; with a pooled specificity of 61% (95% CI: 59% to 62%), 76% (95% CI: 73% to 78%), and 81% (95% CI: 74% to 87%). This resulted in a pooled diagnostic OR of 15.31 (95% CI: 12.66 to 18.52; I(2) 63.6%), 26.42 (95% CI: 17.69 to 39.47; I(2) 58.3%), and 36.47 (95% CI: 21.48 to 61.92; I(2) 0%). Most of the evaluated test and study characteristics did not affect the ranking of diagnostic performances.	M
32. Parker MW, Iskandar A, Limone B, et al. Diagnostic accuracy of cardiac positron emission tomography versus single photon emission computed tomography for coronary artery disease: a bivariate meta-analysis. *Circ Cardiovasc Imaging.* 2012;5(6):700-707.	Meta-analysis	117 studies	A bivariate meta-analysis of the published literature to compare the sensitivity and specificity of PET vs SPECT stress MPI for ≥50% stenosis of any epicardial coronary artery in patients with known or suspected CAD.	Bivariate meta-analysis demonstrated a significantly higher pooled mean sensitivity with PET (92.6% [95% CI, 88.3% to 95.5%]) compared with SPECT (88.3% [95% CI, 86.4% to 90.0%]) (*P*=0.035). No significant difference in specificity was observed between PET (81.3% [95% CI, 66.6% to 90.4%]) and SPECT (75.8% [95% CI, 72.1% to 79.1%]) (*P*=0.39). Few studies investigated coronary angiography with PET. Only 5 studies directly compared SPECT and PET.	M

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Klem I, Heitner JF, Shah DJ, et al. Improved detection of coronary artery disease by stress perfusion cardiovascular magnetic resonance with the use of delayed enhancement infarction imaging. *J Am Coll Cardiol.* 2006;47(8):1630-1638.	Observational-Dx	92 patients	To test a pre-defined visual interpretation algorithm that combines CMR data from perfusion and infarction imaging for the diagnosis of CAD.	92 patients had complete CMR examinations. Significant CAD (≥70% stenosis) was found in 37 patients (40%). The combination of perfusion and delayed enhancement-CMR had a sensitivity, specificity, and accuracy of 89%, 87%, and 88%, respectively, for CAD diagnosis, compared with 84%, 58%, and 68%, respectively, for perfusion-CMR alone. The combination had higher specificity and accuracy ($P<0.0001$), owing to incorporating the exceptionally high specificity (98%) of delayed enhancement-CMR. Receiver operating characteristic curve analysis demonstrated the combination provided better performance than cine, perfusion, or delayed enhancement-CMR alone. The accuracy was high in single-vessel and multivessel disease and independent of CAD location. Multivariable analysis including standard clinical parameters demonstrated the combination was the strongest independent CAD predictor.	2
34. Jogiya R, Kozerke S, Morton G, et al. Validation of dynamic 3-dimensional whole heart magnetic resonance myocardial perfusion imaging against fractional flow reserve for the detection of significant coronary artery disease. *J Am Coll Cardiol.* 2012;60(8):756-765.	Observational-Dx	53 patients	To determine the diagnostic accuracy of dynamic 3-D whole heart myocardial perfusion CMR against invasively determined FFR and to establish the correlation between myocardium at risk defined by using the invasive Duke Jeopardy Score (DJS) and noninvasive 3-D whole heart myocardial perfusion CMR.	FFR was measured in 64/159 coronary vessels, and 39 had an FFR <0.75. Sensitivity, specificity, and diagnostic accuracy of CMR for the detection of significant CAD were 91%, 90%, and 91%, on a patient basis and 79%, 92%, and 88%, respectively, by coronary territory. There was a strong correlation between the DJS and ischemic burden on CMR ($P<0.0001$; Pearson's r = 0.82).	2
35. Schwitter J, Wacker CM, Wilke N, et al. Superior diagnostic performance of perfusion-cardiovascular magnetic resonance versus SPECT to detect coronary artery disease: The secondary endpoints of the multicenter multivendor MR-IMPACT II (Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery Disease Trial). *J Cardiovasc Magn Reson.* 2012;14:61.	Observational-Dx	533 patients	To compare in a multicenter setting the diagnostic performance of perfusion-CMR and gated-SPECT for the detection of CAD in various populations using conventional x-ray coronary angiography as the standard of reference.	The diagnostic performance (=AUC) of CMR was superior to SPECT (P=0.0004, n = 425) and to gated-SPECT (P=0.018, n = 253). CMR performed better than SPECT in multi-vessel disease (P=0.003 vs all SPECT, P=0.04 vs gated-SPECT), in men (P=0.004, n = 313) and in women (P=0.03, n = 112) as well as in the non-infarct patients (P=0.005, n = 186 in 1–3 vessel disease and P=0.015, n = 140 in multi-vessel disease).	1

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
36. Sarwar A, Shaw LJ, Shapiro MD, et al. Diagnostic and prognostic value of absence of coronary artery calcification. *JACC Cardiovasc Imaging.* 2009;2(6):675-688.	Review/Other-Dx	49 studies	To systematically assessed the diagnostic and prognostic value of absence of CAC in asymptomatic and symptomatic individuals.	A systematic review of published articles revealed 49 studies that fulfilled our criteria for inclusion. These included 13 studies assessing the relationship of CAC with adverse cardiovascular outcomes in 64,873 asymptomatic patients. In this cohort, 146/25,903 patients without CAC (0.56%) had a cardiovascular event during a mean follow-up period of 51 months. In the 7 studies assessing the prognostic value of CAC in a symptomatic population, 1.80% of patients without CAC had a cardiovascular event. Overall, 18 studies demonstrated that the presence of any CAC had a pooled sensitivity and NPV of 98% and 93%, respectively, for detection of significant CAD on invasive coronary angiography. In 4,870 individuals undergoing myocardial perfusion and CAC testing; in the absence of CAC, only 6% demonstrated any sign of ischemia. Finally, 3 studies demonstrated that absence of CAC had a NPV of 99% for ruling out acute coronary syndrome.	4
37. Budoff MJ, McClelland RL, Nasir K, et al. Cardiovascular events with absent or minimal coronary calcification: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am Heart J.* 2009;158(4):554-561.	Review/Other-Dx	3,923 patients	To evaluate the characteristics associated with incident CHD events in the setting of minimal (score ≤10) or absent CAC (score of zero).	The final study population consisted of 3,923 MESA asymptomatic participants (mean age 58 +/- 9 years, 39% males) who had CAC scores of 0 to 10. Overall, no detectable CAC was seen in 3,415 individuals, whereas 508 had CAC scores of 1 to 10. During follow-up (median 4.1 years), there were 16 incident hard events and 28 all CHD events in individuals with absent or minimal CAC. In age-, gender-, race-, and CHD risk factor-adjusted analysis, minimal CAC (1-10) was associated with an estimated 3-fold greater risk of a hard CHD event (HR 3.23, 95% CI, 1.17–8.95) or of all CHD event (HR 3.66, 95% CI, 1.71–7.85) compared to those with CAC = 0. Former smoking (HR 3.57, 95% CI, 1.08–11.77), current smoking (HR 4.93, 95% CI, 1.20–20.30), and diabetes (HR 3.09, 95% CI, 1.07–8.93) were significant risk factors for events in those with CAC = 0.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Meijboom WB, Meijs MF, Schuijf JD, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. *J Am Coll Cardiol.* 2008;52(25):2135-2144.	Observational-Dx	360 patients	To determine the diagnostic accuracy of 64-slice CCTA to detect or rule out significant CAD.	The prevalence among patients of having at least 1 significant stenosis was 68%. In a patient-based analysis, the sensitivity for detecting patients with significant CAD was 99% (95% CI: 98% to 100%), specificity was 64% (95% CI: 55% to 73%), PPV was 86% (95% CI: 82% to 90%), and NPV was 97% (95% CI: 94% to 100%). In a segment-based analysis, the sensitivity was 88% (95% CI: 85% to 91%), specificity was 90% (95% CI: 89% to 92%), PPV was 47% (95% CI: 44% to 51%), and NPV was 99% (95% CI: 98% to 99%).	3
39. Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med.* 2008;359(22):2324-2336.	Observational-Dx	291 patients	To examine the accuracy of MDCT angiography involving 64 detectors.	The patient-based diagnostic accuracy of quantitative CT angiography for detecting or ruling out stenoses of 50% or more according to conventional angiography revealed an AUC of 0.93 (95% CI, 0.90 to 0.96), with a sensitivity of 85% (95% CI, 79 to 90), a specificity of 90% (95% CI, 83 to 94), a PPV of 91% (95% CI, 86 to 95), and a NPV of 83% (95% CI, 75 to 89). CT angiography was similar to conventional angiography in its ability to identify patients who subsequently underwent revascularization: the AUC was 0.84 (95% CI, 0.79 to 0.88) for MDCT angiography and 0.82 (95% CI, 0.77 to 0.86) for conventional angiography. A per-vessel analysis of 866 vessels yielded an AUC of 0.91 (95% CI, 0.88 to 0.93). Disease severity ascertained by CT and conventional angiography was well correlated (r=0.81; 95% CI, 0.76 to 0.84). Two patients had important reactions to contrast medium after CT angiography.	1

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
40. Gueret P, Deux JF, Bonello L, et al. Diagnostic performance of computed tomography coronary angiography (from the Prospective National Multicenter Multivendor EVASCAN Study). *Am J Cardiol.* 2013;111(4):471-478.	Observational-Dx	746 patients	To establish the diagnostic accuracy of CCTA compared to coronary angiography in a large population of symptomatic patients with clinical indications for coronary imaging.	Of 757 patients enrolled, 746 (mean age 61 +/- 12 years, 71% men) were analyzed. They underwent CCTA followed by coronary angiography 1.7 +/- 0.8 days later using a 64-detector scanner. The prevalence of significant CAD in native coronary vessels by coronary angiography was 54%. The rate of nonassessable segments by CCTA was 6%. In a patient-based analysis, sensitivity, specificity, PPV and NPV, and positive and negative LRs of CCTA were 91%, 50%, 68%, 83%, 1.82, and 0.18, respectively. The strongest predictors of false-negative results on CCTA were high estimated pretest probability of CAD (OR 1.97, $P<0.001$), male gender (OR 1.5, $P<0.002$), diabetes (OR 1.5, $P<0.0001$), and age (OR 1.2, $P<0.0001$).	1
41. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *J Am Coll Cardiol.* 2008;52(21):1724-1732.	Observational-Dx	230 patients	To evaluate the diagnostic accuracy of electrocardiographically gated 64-MDCCTA in individuals without known CAD.	On a patient-based model, the sensitivity, specificity, and PPVs and NPVs to detect ≥50% or ≥70% stenosis were 95%, 83%, 64%, and 99%, respectively, and 94%, 83%, 48%, 99%, respectively. No differences in sensitivity and specificity were noted for non-obese compared with obese subjects or for heart rates ≤65 beats/min compared with >65 beats/min, whereas calcium scores >400 reduced specificity significantly.	1

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Dodd JD, Rieber J, Pomerantsev E, et al. Quantification of nonculprit coronary lesions: comparison of cardiac 64-MDCT and invasive coronary angiography. *AJR Am J Roentgenol.* 2008;191(2):432-438.	Observational-Dx	29 patients	To evaluate the accuracy of cardiac 64-MDCT to quantify the grade of stenosis of nonculprit lesions.	Nonculprit lesions were identified in 46 analyzable coronary segments. Subgrouping lesions on the basis of reference vessel diameter resulted in strong correlations for quantifying nonculprit lesions in vessels >3 mm (R = 0.78-0.91, *P*<0.01) but poor correlations for nonculprit lesions in vessels ≤3 mm (R = 0.1-0.07). Subgrouping lesions on the basis of plaque type resulted in poor correlations for calcified plaques (R = 0.01-0.30) but moderate to strong correlations for mixed (R = 0.58-0.75, *P*<0.01) and noncalcified (R = 0.44-0.61, *P*<0.01) plaques. The best overall correlation among all CT techniques with quantitative coronary angiography was cross-sectional area (R = 0.56, *P*<0.01). Interobserver agreement (kappa values) for multiplanar reformat, MIP, coronary software diameter and area were 0.6, 0.7, 0.62, and 0.57, respectively.	2
43. Sheth T, Dodd JD, Hoffmann U, et al. Coronary stent assessability by 64 slice multi-detector computed tomography. *Catheter Cardiovasc Interv.* 2007;69(7):933-938.	Observational-Dx	44 patients	To evaluate the accessibility of contemporary stent platforms by 64-slice MDCT.	54 stents (Cypher n = 25, Vision/Minivision n = 19, Taxus Express n = 8, Liberte n = 1, Driver n = 1) in 44 patients were included in the study. The 2 independent observers classified 30/54 stents (56%) as assessable. Interobserver reproducibility was good with kappa = 0.66. Stent size was the most important determinant of assessability. Consistently assessable stents were 3.0 mm or larger (85%), whereas those under 3 mm were mostly nonassessable (26%).	2

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Mowatt G, Cook JA, Hillis GS, et al. 64-Slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. *Heart.* 2008;94(11):1386-1393.	Meta-analysis	28 studies	To assess whether 64-slice CT angiography might replace some coronary angiography for diagnosis and assessment of CAD.	40 studies were included; 28 provided sufficient data for inclusion in the meta-analyses, all using a cut off point of ≥50% stenosis to define significant CAD. In patient-based detection (n = 1,286) 64-slice CT pooled sensitivity was 99% (95% credible interval 97% to 99%), specificity 89% (95% credible interval 83% to 94%), median PPV across studies 93% (range 64%–100%) and NPV 100% (range 86%–100%). In segment-based detection (n = 14,199) 64-slice CT pooled sensitivity was 90% (95% credible interval 85% to 94%), specificity 97% (95% credible interval 95% to 98%), median PPV across studies 76% (range 44%–93%) and NPV 99% (range 95%–100%).	M
45. 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. *Circulation.* 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
46. Leone AM, Porto I, De Caterina AR, et al. Maximal hyperemia in the assessment of fractional flow reserve: intracoronary adenosine versus intracoronary sodium nitroprusside versus intravenous adenosine: the NASCI (Nitroprussiato versus Adenosina nelle Stenosi Coronariche Intermedie) study. *JACC Cardiovasc Interv.* 2012;5(4):402-408.	Observational-Dx	45 patients	To compare increasing doses of intracoronary adenosine or intracoronary sodium nitroprusside vs intravenous adenosine for FFR assessment.	Incremental doses of intracoronary adenosine and sodium nitroprusside were well tolerated and associated with fewer symptoms than intravenous adenosine infusion. Intracoronary adenosine doses (0.881 +/- 0.067, 0.871 +/- 0.068, and 0.868 +/- 0.070 with ADN60, ADN300, and ADN600, respectively) and sodium nitroprusside (0.892 +/- 0.072) induced a significant decrease of FFR compared with baseline levels (*P*<0.001). Notably, ADN600 only was associated with FFR values similar to intravenous adenosine infusion (0.867 +/- 0.072, *P*=0.28). Among the 10 patients with FFR values ≤0.80 with intravenous adenosine infusion, 5 were correctly identified also by ADN60, 6 by ADN300, 7 by ADN600, and 6 by sodium nitroprusside.	3

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Pijls NH. Fractional flow reserve to guide coronary revascularization. *Circ J.* 2013;77(3):561-569.	Review/Other-Dx	N/A	To discuss the principles of FFR measurement, its clinical applications, and the influence on patient outcome.	FFR has become an increasingly important index for decision making with respect to revascularization of coronary artery stenosis. It is the gold standard to indicate whether a particular stenosis is responsible for inducible ischemia and it is generally accepted that a stenosis with an ischemic value of FFR is responsible for angina pectoris and a worse outcome, and should be revascularized, whereas lesions with a non-ischemic FFR have a more favorable prognosis and can better be treated medically. In this review paper, the background, concept and clinical application of FFR are discussed from a practical point of view. On top of that, some in-depth considerations are given with respect to further possibilities of FFR for examining the coronary circulation, including separate assessment of coronary, myocardial, and collateral blood flows. Finally, a word of caution is given with respect to using resting pressure indexes, which seem attractive because they avoid the need for hyperemia, but negatively affect the accuracy of the measurements.	4
48. Wang R, Renker M, Schoepf UJ, et al. Diagnostic value of quantitative stenosis predictors with coronary CT angiography compared to invasive fractional flow reserve. *Eur J Radiol.* 2015;84(8):1509-1515.	Observational-Dx	32 patients	To evaluate the diagnostic performance of CCTA-derived stenosis predictors including CT-FFR for the detection of ischemia-inducing stenosis compared to invasive FFR.	The cohort included 32 patients (58+/-12 years, 66% male). Among 32 coronary lesions, 8 (25%) were considered hemodynamically significant with an FFR <0.80. Compared to invasive FFR, the per-vessel sensitivity and specificity of CCTA, CT-FFR, LL/MLD(4), CCO and TAG for detecting hemodynamically significant lesions were 100% and 54%, 100% and 91%, 85% and 92%, 66% and 88%, 37% and 58%, respectively. ROC analysis resulted in an AUC of 0.91 for CT-FFR (*P*=0.0005), 0.88 for LL/MLD(4) (*P*<0.0001), 0.85 for CCO (*P*<0.0001). TAG with an AUC of 0.67 (*P*=0.152) was unable to discriminate between vessels with or without hemodynamically significant lesions.	2

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Buckner K. Cardiac asthma. *Immunol Allergy Clin North Am.* 2013;33(1):35-44.	Review/Other-Dx	N/A	To review cardiac asthma.	Cardiac dyspnea, especially if present only with exercise, is often confused with asthma and exercise-induced bronchospasm. Cardiac dyspnea or asthma is the consequence of pulmonary edema due to pulmonary venous hypertension and not due to asthmatic bronchoconstriction. In overt, acute congestive HF, the diagnosis may be readily made by history and physical examination and pertinent laboratory and imaging data. However, in the early stages of heart disease, especially diastolic dysfunction, the diagnosis of cardiac dyspnea may be more elusive. The practicing physician must cull the history and physical examination for clues and order appropriate laboratory and imaging studies to establish the diagnosis of cardiac dyspnea. In distinguishing cardiac from pulmonary dyspnea, the most useful and informative studies include a serum BNP, echocardiogram, and if necessary, cardiopulmonary stress test.	4
50. Fonseca C, Mota T, Morais H, et al. The value of the electrocardiogram and chest X-ray for confirming or refuting a suspected diagnosis of heart failure in the community. *Eur J Heart Fail.* 2004;6(6):807-812, 821-802.	Observational-Dx	6300	To assess the value of the electrocardiogram and chest X-ray in identifying patients with chronic HF.	For the diagnosis of HF, in the Portuguese population aged over 25 years, an abnormal electrocardiogram had an estimated sensitivity of 81%, and NPV of 75%; an abnormal chest X-ray had an estimated sensitivity of 57%, and NPV of 83%. 25% of patients with chronic HF had a normal electrocardiogram or chest X-ray. Electrocardiographic and roentgenographic features are not sufficient to allow HF to be reliably predicted in the community and support the recommendation that all patients with suspected HF should undergo echocardiography.	2

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Arnold JM, Liu P, Demers C, et al. Canadian Cardiovascular Society consensus conference recommendations on heart failure 2006: diagnosis and management. *Can J Cardiol.* 2006;22(1):23-45.	Review/Other-Dx	N/A	A consensus conference was convened by the Canadian Cardiovascular Society (CCS) to review new evidence and update previous consensus conferences (2-4) to provide a set of evidence-informed recommendations that would provide clinicians, and other health care professionals involved in the management of HF patients, with clear directions and options to optimize care of individual patients.	These consensus recommendations should provide an evidence-based road map to translate knowledge into practice and allow health care practitioners to make the best clinical judgments and decisions for their individual patient. Practical tools to improve implementation are being developed by a Clinical Practice and Health Outcomes Impact Working Group of the CCS, which is also identifying potential organizational barriers to implementation and specific measurable outcome audit criteria. Because new evidence will continue to be published, these recommendations will be updated in 12 months.	4
52. Gorcsan J, 3rd, Tanaka H. Echocardiographic assessment of myocardial strain. *J Am Coll Cardiol.* 2011;58(14):1401-1413.	Review/Other-Dx	N/A	To review the physiology of myocardial strain, the technical features of strain imaging using tissue Doppler imaging and speckle tracking, their strengths and weaknesses, and the state-of-the-art present and potential future clinical applications.	Echocardiographic strain imaging, also known as deformation imaging, has provided a means to objectively quantify myocardial mechanical function. Originally introduced as a product of tissue Doppler imaging, speckle tracking is a more recent extension of strain imaging. Strain imaging has provided greater understanding of the pathophysiology of cardiac ischemia and infarction, primary diseases of the myocardium, assessment of dyssynchrony for cardiac resynchronization therapy, the effects of valvular disease on myocardial function, and the mechanics of diastolic function. Strain by 3-D speckle tracking has emerged as a further advance to provide even greater insight. Strain imaging has become established as a robust research tool and has great potential to play many roles to advance the care of the cardiovascular patient.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Dorosz JL, Lezotte DC, Weitzenkamp DA, Allen LA, Salcedo EE. Performance of 3-dimensional echocardiography in measuring left ventricular volumes and ejection fraction: a systematic review and meta-analysis. *J Am Coll Cardiol.* 2012;59(20):1799-1808.	Review/Other-Dx	23 studies	Systematic review to objectively evaluate the test performance characteristics of 3-DE in measuring LV volumes and ejection fraction.	23 studies (1,638 echocardiograms) were included. The pooled biases +/- 2 SDs for 3-DE were -19.1 +/- 34.2 ml, -10.1 +/- 29.7 ml, and - 0.6 +/- 11.8% for end-diastolic volume, end-systolic volume, and ejection fraction, respectively. 9 studies also included data from 2-D echocardiography, where the pooled biases were -48.2 +/- 55.9 ml, -27.7 +/- 45.7 ml, and 0.1 +/- 13.9% for end-diastolic volume, end-systolic volume, and ejection fraction, respectively. In this subset, the difference in bias between 3-DE and 2-D volumes was statistically significant (P=0.01 for both end-diastolic volume and end-systolic volume). The difference in variance was statistically significant (P<0.001) for all 3 measurements.	4
54. Lindenfeld J, Albert NM, Boehmer JP, et al. HFSA 2010 Comprehensive Heart Failure Practice Guideline. *J Card Fail.* 2010;16(6):e1-194.	Review/Other-Dx	N/A	The 2010 Heart Failure Society of America comprehensive practice guideline addresses the full range of evaluation, care, and management of patients with HF.	No results stated in abstract.	4
55. 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 HF and associated myocardial disease.	HF is increasing worldwide at epidemic proportions, resulting in considerable disability, mortality, and increase in healthcare costs. Gated myocardial perfusion SPECT 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 HF patients.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Salm LP, Schuijf JD, de Roos A, et al. Global and regional left ventricular function assessment with 16-detector row CT: comparison with echocardiography and cardiovascular magnetic resonance. *Eur J Echocardiogr.* 2006;7(4):308-314.	Observational-Dx	25 patients	To compare MDCT global and regional LV function assessment with echocardiography and CMR.	In 25 patients, who were referred for noninvasive angiography with 16-detector row CT, LV function assessment was also performed. A subsequent echocardiogram was performed, and in a subgroup of patients, CMR examination was completed to evaluate LV function. For global function assessment, the LVEF was calculated. Regional LV function was scored using a 17-segment model and a 4-point scoring system. MDCT agreed well with echocardiography for the assessment of LVEF (r=0.96; bias 0.54%; P<0.0001) and regional LV function (kappa=0.78). 8 patients had no contra-indications and gave informed consent for CMR examination. A fair correlation between MDCT and CMR was demonstrated in the assessment of LVEF (r=0.86; bias -1.5%; P<0.01). Regional LV function agreement between MDCT and CMR was good (kappa=0.86).	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Sugeng L, Mor-Avi V, Weinert L, et al. Quantitative assessment of left ventricular size and function: side-by-side comparison of real-time three-dimensional echocardiography and computed tomography with magnetic resonance reference. *Circulation.* 2006;114(7):654-661.	Observational-Dx	31 patients	To compare both CCT and real-time 3-DE measurements of LV size and function with the standard reference technique, CMR.	In 31 patients, real-time 3-DE data sets (Philips 7500) and long-axis CMR (Siemens, 1.5 T) and CCT (Toshiba, 16-slice MDCT) images were obtained on the same day without beta-blockers. All images were analyzed to obtain end-systolic and end-diastolic volumes and ejection fractions using the same rotational analysis to eliminate possible analysis-related differences. Intertechnique agreement was tested through linear regression and Bland-Altman analyses. Repeated measurements were performed to determine intraobserver and interobserver variability. Both CCT and real-time 3-DE measurements resulted in high correlation (r2 >0.85) compared with CMR. However, CCT significantly overestimated end-diastolic and end-systolic volumes (26 and 19 mL; $P<0.05$), resulting in a small but significant bias in ejection fraction (-2.8%). Real-time 3-DE underestimated end-diastolic and end-systolic volumes only slightly (5 and 6 mL), with no significant bias in ejection fractions (0.3%; $P=0.68$). The limits of agreement with CMR were comparable for the 2 techniques. The variability in the CCT measurements was roughly half of that in either real-time 3-DE or CMR values.	3
58. Mooij CF, de Wit CJ, Graham DA, Powell AJ, Geva T. Reproducibility of MRI measurements of right ventricular size and function in patients with normal and dilated ventricles. *J Magn Reson Imaging.* 2008;28(1):67-73.	Observational-Dx	60 patients	To determine the interobserver and intraobserver reproducibility of CMR-derived measurements of RV mass, volume, and function in patients with normal and dilated ventricles.	High ICC were found for interobserver (ICC = 0.94–0.99) and intraobserver (ICC = 0.96–0.99) comparisons of RV and LV mass, volume, and SV measurements. RV and LVEF measurements were less reproducible (ICC = 0.79–0.87). RV mass measurements were significantly less correlated than the respective LV measurements. Small but statistically significant differences in correlation were noted in RV measurements across groups.	3

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Hamlin SA, Henry TS, Little BP, Lerakis S, Stillman AE. Mapping the Future of Cardiac MR Imaging: Case-based Review of T1 and T2 Mapping Techniques. *Radiographics*. 2014;34(6):1594-1611.	Review/Other-Dx	N/A	To assess T1 and T2 myocardial mapping techniques.	CMR has grown over the past several decades into a validated, noninvasive diagnostic imaging tool with a pivotal role in cardiac morphologic and functional assessment and tissue characterization. With traditional CMR imaging sequences, assessment of various pathologic conditions ranging from ischemic and nonischemic cardiomyopathy to cardiac involvement in systemic diseases (eg, amyloidosis and sarcoidosis) is possible; however, these sequences are most useful in focal myocardial disease, and image interpretation relies on subjective qualitative analysis of signal intensity. Newer T1 and T2 myocardial mapping techniques offer a quantitative assessment of the myocardium (by using T1 and T2 relaxation times), which can be helpful in focal disease, and demonstrate special utility in the evaluation of diffuse myocardial disease (eg, edema and fibrosis). Altered T1 and T2 relaxation times in disease states can be compared with published ranges of normal relaxation times in healthy patients. In conjunction with traditional CMR imaging sequences, T1 and T2 mapping can limit the interpatient and interstudy variability that are common with qualitative analysis and may provide clinical markers for long-term follow-up.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
60. Singh RM, Singh BM, Mehta JL. Role of cardiac CTA in estimating left ventricular volumes and ejection fraction. *World J Radiol.* 2014;6(9):669-676.	Review/Other-Dx	N/A	To address the feasibility, the accuracy and the limitations of MDCT in measuring LVEF.	LVEF measurement at the time of CCTA for the study of coronary anatomy using MDCT seems reasonable given the feasibility, reproducibility, and accuracy of the data. This information can be obtained at the time of coronary imaging without the need for additional radiation or contrast exposure. Developments in hardware, software and work stations, along with the availability of automated techniques to measure LV end-systolic volume and LV end-diastolic volume have made this technique time efficient. The use of MDCT for the sole purpose of LVEF measurement is not reasonable at this time given the radiation exposure, contrast exposure and cost. Instead, this should be used as a complimentary technique to measure LVEF in patients undergoing CCTA for noninvasive coronary angiography.	4
61. Bansal D, Singh RM, Sarkar M, et al. Assessment of left ventricular function: comparison of cardiac multidetector-row computed tomography with two-dimension standard echocardiography for assessment of left ventricular function. *Int J Cardiovasc Imaging.* 2008;24(3):317-325.	Observational-Dx	52 patients	To compare global LV systolic function assessment by MDCT with 2-D standard echocardiography in a routine cardiology practice setting and to ascertain the degree of correlation between LV volumes and measurements obtained by 2-D standard echocardiography with those measured by MDCT.	On MDCT, mean LVEF in 4-chamber, 2-chamber and biplane views were 58.4 +/- 12, 59.3 +/- 12 and 59.7 +/- 12%, respectively. On 2-D standard echocardiography, mean LVEF in 4-chamber, 2-chamber and biplane views were 58 +/- 14, 57 +/- 16 and 58 +/- 13% respectively. LVEF correlated best using the biplane views (r = 0.59 and P<0.01) compared to 2-chamber (r = 0.57 and P<0.01) and 4-chamber views (r = 0.32 and P=0.02). Biplane measurement by these 2 techniques correlated well for LV volumes in both diastole (r = 0.69 and P<0.01) and systole (r = 0.73 and P<0.01), although MDCT consistently gave higher values.	3

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
62. Lessick J, Mutlak D, Rispler S, et al. Comparison of multidetector computed tomography versus echocardiography for assessing regional left ventricular function. *Am J Cardiol.* 2005;96(7):1011-1015.	Observational-Dx	39 patients	To compare semiquantitative LV segmental wall motion scoring by MDCT with echocardiography as the gold standard.	39 patients underwent MDCT angiography on a 16-slice scanner. Short- and long-axis LV slices were created at different phases of the cardiac cycle and visually evaluated using cine mode. Echocardiography was performed <48 hours after MDCT for 21 patients after acute myocardial infarctions and <1 month after MDCT for 18 patients without acute myocardial infarctions. 2 blinded observers scored the MDCT and echocardiographic examinations according to the 16-segment model, scoring each segment from 1 (normal) to 3 (akinetic). Segmental dysfunction was found in 27 patients by echocardiography and in 24 by MDCT. An identical score was given by the 2 methods in 502/616 assessable segments (82%). Using a binary analysis (normal or abnormal), there was 89% agreement (546/616 segments). MDCT had a sensitivity of 66% (103/155 segments) and a specificity of 96% (443/461 segments) compared with echocardiography as the gold standard.	2
63. Pibarot P, Larose E, Dumesnil J. Imaging of valvular heart disease. *Can J Cardiol.* 2013;29(3):337-349.	Review/Other-Dx	N/A	To review the current and emerging roles of the different imaging modalities in the diagnosis and treatment of valvular heart disease and to present the new directions for future research and clinical applications.	Imaging plays a fundamental role in the current diagnosis and treatment of valvular heart disease and in the preclinical and clinical research aiming at the development of novel pharmacologic or interventional therapies. Doppler echocardiography remains the primary imaging technique for the clinical management of valvular heart disease. However, the multifaceted and complex nature of valvular heart disease and the rapid development of transcatheter valve therapies has led to a spectacular increase in the use of multimodality imaging in the past decade.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
64. Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *Circulation.* 2006;114(5):e84-231.	Review/Other-Dx	N/A	Guidelines to develop, update, or revise practice guidelines important cardiovascular diseases and procedures.	No results stated in abstract.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
65. Zoghbi WA, Chambers JB, Dumesnil JG, et al. Recommendations for evaluation of prosthetic valves with echocardiography and doppler ultrasound: a report From the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2009;22(9):975-1014; quiz 1082-1014.	Review/Other-Dx	N/A	To provide recommendations for evaluation of prosthetic valves with echocardiography and Doppler US.	No results stated in abstract.	4
66. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012). *Eur Heart J*. 2012;33(19):2451-2496.	Review/Other-Dx	N/A	To provide guidelines on the management of valvular heart disease.	No results stated in abstract.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
67. Thavendiranathan P, Liu S, Datta S, et al. Automated quantification of mitral inflow and aortic outflow stroke volumes by three-dimensional real-time volume color-flow Doppler transthoracic echocardiography: comparison with pulsed-wave Doppler and cardiac magnetic resonance imaging. *J Am Soc Echocardiogr*. 2012;25(1):56-65.	Observational-Dx	44 patients	To compare the feasibility, accuracy, and reproducibility of automated quantification of mitral inflow and aortic SVs using real-time 3-D volume color-flow Doppler TTE, with CMR imaging as the reference method.	The mean age of the included patients was 40 +/- 16 years, and the mean LVEF was 61 +/- 9%. Automated flow measurements were feasible in all study patients. Mitral inflow SV by 2-D TTE and real-time 3-D volume color-flow Doppler TTE were 85.0 +/- 21.5 and 94.5 +/- 22.0 mL, respectively, while total SV by CMR was 95.6 +/- 22.7 mL (*P*<.001, analysis of variance). On post hoc analysis, mitral inflow SV by real-time 3-D volume color-flow Doppler TTE was not different from the CMR value (*P*=.99), while SV on 2-D TTE was underestimated (*P*=.001). The respective aortic SVs were 82.8 +/- 22.3, 94.2 +/- 22.3, and 93.4 +/- 24.6 mL (*P*<.001). On post hoc analysis, aortic SV by real-time 3-D volume color-flow Doppler TTE was not different from the CMR value (*P*=.99), while SV on 2-D TTE was underestimated (*P*=.006). The interobserver variability for SV measurements was significantly worse for 2-D TTE compared with real-time 3-D volume color-flow Doppler TTE.	2
68. Stewart SF, Herman BA, Nell DM, Retta SM. Effects of valve characteristics on the accuracy of the Bernoulli equation: a survey of data submitted to the U.S. FDA. *J Heart Valve Dis*. 2004;13(3):461-466.	Review/Other-Dx	N/A	To assess the effects of valve characteristics on the accuracy of Bernoulli equation.	K-values varied from 2.50 to 7.40 (n = 90). K was found to be dependent on valve type (*P*<0.0001), blood-mimicking fluid (*P*<0.0001) and distal pressure tap position (*P*<0.0001), but not valve size. At distal pressure tap position =30 mm, K = 3.43 +/- 0.56, 5.15 +/- 0.81, and 4.81 +/- 1.02, for bileaflet, stented and stentless valves, respectively. K averaged 10% less using the 100-mm distal pressure tap position, due to pressure recovery. Variations due to blood-mimicking fluid were likely related to the fluid density.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. Pibarot P, Dumesnil JG. Improving assessment of aortic stenosis. *J Am Coll Cardiol.* 2012;60(3):169-180.	Review/Other-Dx	N/A	To review newer approaches to improve the quantification of disease severity taking into account the interrelation between the different valvular, arterial, and ventricular variables that may be responsible for the appearance of symptoms and/or poorer prognosis in patients with aortic stenosis.	"Degenerative" or calcific aortic stenosis is a complex, multifaceted, systemic disease that is not solely limited to the aortic valve but also includes reduced arterial compliance as well as alterations of LV geometry and function. This particular nature of the disease underscores the need for a more comprehensive evaluation of disease severity going beyond the standard parameters routinely used to assess stenosis severity (i.e., peak jet velocity, pressure gradients, valve effective orifice area) or left ventricle function (i.e., LVEF).	4
70. Lancellotti P, Tribouilloy C, Hagendorff A, et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 1: aortic and pulmonary regurgitation (native valve disease). *Eur J Echocardiogr.* 2010;11(3):223-244.	Review/Other-Dx	N/A	To provide recommendations on a basic quantification of valvular regurgitation but provide elements on the assessment of ventricular performance, cardiac chambers size, and anatomy of valve.	Valvular regurgitation represents an important cause of cardiovascular morbidity and mortality. Echocardiography has become the primary noninvasive imaging method for the evaluation of valvular regurgitation. The echocardiographic assessment of valvular regurgitation should integrate quantification of the regurgitation, assessment of the valve anatomy, and function as well as the consequences of valvular disease on cardiac chambers. In clinical practice, the management of patients with valvular regurgitation thus largely integrates the results of echocardiography. It is crucial to provide standards that aim at establishing a baseline list of measurements to be performed when assessing regurgitation.	4
71. Lancellotti P, Moura L, Pierard LA, et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). *Eur J Echocardiogr.* 2010;11(4):307-332.	Review/Other-Dx	N/A	To provide standards for the assessment of mitral and tricuspid regurgitation.	Mitral and tricuspid are increasingly prevalent. Doppler echocardiography not only detects the presence of regurgitation but also permits to understand mechanisms of regurgitation, quantification of its severity and repercussions.	4
72. Cawley PJ, Maki JH, Otto CM. Cardiovascular magnetic resonance imaging for valvular heart disease: technique and validation. *Circulation.* 2009;119(3):468-478.	Review/Other-Dx	N/A	To summarize the general principles of CMR and validate CMR as a tool for evaluation of valvular heart disease.	No results stated in abstract.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
73. American College of Radiology. ACR Appropriateness Criteria®: Imaging for Transcatheter Aortic Valve Replacement. Available at: https://acsearch.acr.org/docs/3082594/Narrative/.	Review/Other-Dx	N/A	To evaluate the appropriateness of preprocedural imaging for transcatheter aortic valve replacement	No abstract available.	4
74. Al-Najafi S, Sanchez F, Lerakis S. The Crucial Role of Cardiac Imaging in Transcatheter Aortic Valve Replacement (TAVR): Pre- and Post-procedural Assessment. *Curr Treat Options Cardiovasc Med.* 2016;18(12):70.	Review/Other-Dx	N/A	To discuss the importance of cardiac imaging in transcatheter aortic valve replacement by exploring the current practices, guidelines, and recommendations with the supporting data.	We believe that the key for a successful transcatheter aortic valve replacement is careful preprocedural planning and early detection of any possible post-implantation complications. To achieve this, multimodality imaging is cornerstone. Throughout the stages of patient-evaluation, echocardiography and CT play complementary roles. MRI, on the other hand, has emerged as a useful tool in quantifying post-implantation paravalvular regurgitation.	4
75. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). *J Am Coll Cardiol.* 2006;48(5):e247-346.	Review/Other-Dx	N/A	Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death.	No results stated in abstract.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the Task Force Criteria. *Eur Heart J.* 2010;31(7):806-814.	Review/Other-Dx	N/A	To review the clinical diagnosis of ARVD/D.	Revision of the diagnostic criteria provides guidance on the role of emerging diagnostic modalities and advances in the genetics of ARVD/D. The criteria have been modified to incorporate new knowledge and technology to improve diagnostic sensitivity, but with the important requisite of maintaining diagnostic specificity. The approach of classifying structural, histological, electrocardiographic, arrhythmic, and genetic features of the disease as major and minor criteria has been maintained. In this modification of the Task Force criteria, quantitative criteria are proposed and abnormalities are defined on the basis of comparison with normal subject data.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
77. Nowalany-Kozielska E. [Imaging studies in arrhythmias]. *Przegl Lek.* 2014;71(3):150-154.	Review/Other-Dx	N/A	To review imaging studies in arrhythmias.	Imaging studies play a very important role in the diagnosis of cardiac arrhythmias. They are able to answer many questions relating to the diagnosis and treatment of patients. Not all types of arrhythmias require you to perform imaging studies. Diagnosis require above all: ventricular tachycardia and supraventricular tachycardia, ventricular extrasystoles requiring treatment, atrialfibrillation, individuals who are at genetically diseases leading to severe arrhythmia, patients before ablation procedures and cardioversion, arrhythmias in athletes and people performing specific professions (eg pilots). The primary noninvasive imaging technique for the diagnosis of arrhythmias is the ECHO, also safe in pregnant women. Other imaging studies should be performed in case of inability to obtain sufficient diagnostic information in ECHO, because of the cost, availability and worse side effects (class of recommendation IIaB by AHA/ACC/ESC). Among these studies is the study of MRI "gold standard" for assessing the anatomy and function of the heart, allows the assessment of myocardial structure and can significantly supplement the information obtained in the study of ECHO, is also safe in pregnant women.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
78. White JA, Fine NM, Gula L, et al. Utility of cardiovascular magnetic resonance in identifying substrate for malignant ventricular arrhythmias. *Circ Cardiovasc Imaging*. 2012;5(1):12-20.	Observational-Dx	82 patients	To evaluate the diagnostic yield of CMR-based imaging vs non-CMR-based imaging in patients with resuscitated sudden cardiac death or sustained monomorphic ventricular tachycardia.	82 patients with resuscitated sudden cardiac death or sustained monomorphic ventricular tachycardia underwent routine non-CMR imaging, followed by a CMR protocol with comprehensive tissue characterization. Clinical reports of non-CMR imaging studies were blindly adjudicated and used to assign each patient to 1 of 7 diagnostic categories. CMR imaging was blindly interpreted using a standardized algorithm used to assign a patient diagnosis category in a similar fashion. The diagnostic yield of CMR-based and non-CMR-based imaging, as well as the impact of the former on diagnosis reclassification, was established. Relevant myocardial disease was identified in 51% of patients using non-CMR-based imaging and in 74% using CMR-based imaging (P=0.002). 41 patients (50%) were reassigned to a new or alternate diagnosis using CMR-based imaging, including 15 (18%) with unsuspected acute myocardial injury. 20 patients (24%) had no abnormality by non-CMR imaging but showed clinically relevant myocardial disease by CMR imaging.	2
79. Scott PA, Rosengarten JA, Curzen NP, Morgan JM. Late gadolinium enhancement cardiac magnetic resonance imaging for the prediction of ventricular tachyarrhythmic events: a meta-analysis. *Eur J Heart Fail*. 2013;15(9):1019-1027.	Meta-analysis	11 studies	To perform a meta-analysis to better gauge the predictive accuracy of late gadolinium enhancement-CMR for sudden cardiac death risk stratification.	11 studies comprising 1,105 patients were identified. During a mean/median follow-up of 8.5–41 months 207 patients had ventricular arrhythmic events. Ventricular arrhythmic events were more common in patients with a greater extent of LV scar: relative risk 4.33 [95% CI, 2.98–6.29], positive LR 1.98 (95% CI, 1.66–2.37), and negative LR 0.33 (95% CI, 0.24–0.46).	M

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
80. Bomma C, Dalal D, Tandri H, et al. Evolving role of multidetector computed tomography in evaluation of arrhythmogenic right ventricular dysplasia/cardiomyopathy. *Am J Cardiol.* 2007;100(1):99-105.	Observational-Dx	31 patients	To report one center's experience with MDCT in the evaluation of patients suspected to have ARVD/C.	31 patients (19 men; mean age 41 +/- 12 years) referred for evaluation of known or suspected ARVD/C had a complete reevaluation including contrast-enhanced cardiac MDCT at the center. Two patients underwent both CMR and MDCT. 17/31 patients met Task Force criteria for ARVD/C and were confirmed to have ARVD/C. MDCT images were analyzed for qualitative and quantitative characteristic findings of ARVD/C. Increased RV trabeculation (P<0.001), RV intramyocardial fat (P<0.001), and scalloping (P<0.001) were significantly associated with the final diagnosis of ARVD/C. RV volumes, RV inlet dimensions, and RV outflow tract surface area were increased in patients with ARVD/C compared with patients who did not meet the criteria. RV and LV functional analysis was performed in 2 patients.	3
81. Cochet H, Denis A, Komatsu Y, et al. Automated Quantification of Right Ventricular Fat at Contrast-enhanced Cardiac Multidetector CT in Arrhythmogenic Right Ventricular Cardiomyopathy. *Radiology.* 2015;275(3):683-691.	Experimental-Dx	108	To evaluate an automated method for the quantification of fat in the RV free wall on MDCT images and assess its diagnostic value in ARVC.	Fat extent was 16.5% +/- 6.1 in ARVC and 4.6% +/- 2.7 in non-ARVC (P<.0001). No significant difference was observed between control and ischemic groups (P=.23). A fat extent threshold of 8.5% of RV free wall was used to diagnose ARVC with 94% sensitivity (95% CI: 82%, 98%) and 92% specificity (95% CI: 83%, 96%). This diagnostic performance was higher than the one for RV volume (mean AUC curve, 0.96 +/- 0.02 vs 0.88 +/- 0.04; P=.009). In patients with ARVC, fat correlated to RV volume (R = 0.63, P<.0001), RV function (R = -0.67, P=.001), epsilon waves (R = 0.39, P=.02), inverted T waves in V1-V3 (R = 0.38, P=.02), and presence of PKP2 mutations (R = 0.59, P=.02). Fat distribution differed between patients with ARVC and those without, with posterolateral RV wall being the most ARVC-specific area.	1

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
82. Nakajima T, Kimura F, Kajimoto K, Kasanuki H, Hagiwara N. Utility of ECG-gated MDCT to differentiate patients with ARVC/D from patients with ventricular tachyarrhythmias. *J Cardiovasc Comput Tomogr.* 2013;7(4):223-233.	Observational-Dx	77	To propose a comprehensive system for scoring characteristic CT findings to diagnose ARVC/D and discuss its utility.	For overall (definite and borderline) and definite ARVC/D diagnosis, sensitivities were 77.8% and 87.0%, specificities were 96.0% and 94.4%, PPVs were 91.3% and 87.0%, NPVs were 88.9% and 94.4%, and accuracies were 89.6% and 92.2%, respectively.	3
83. Alter P, Figiel JH, Rupp TP, Bachmann GF, Maisch B, Rominger MB. MR, CT, and PET imaging in pericardial disease. *Heart Fail Rev.* 2013;18(3):289-306.	Review/Other-Dx	N/A	To evaluate MR, CT, and PET imaging in pericardial disease.	CT imaging can assess pericardial calcification. MR and CT imaging allow a comprehensive delineation of the pericardium. Superior to echocardiography, both methods provide a larger field of view and depiction of the complete chest including abnormalities of the surrounding mediastinum and lungs. PET provides unique information on the in vivo metabolism of 18-fluorodeoxyglucose that can be superimposed on CT findings and is useful for identifying inflammatory processes or masses.	4
84. Verhaert D, Gabriel RS, Johnston D, Lytle BW, Desai MY, Klein AL. The role of multimodality imaging in the management of pericardial disease. *Circ Cardiovasc Imaging.* 2010;3(3):333-343.	Review/Other-Dx	N/A	To discuss the potential role of different imaging modalities in the diagnosis and management of pericardial disorders, with a specific focus on what constitutes a rational multimodality imaging approach.	Clinicians increasingly rely on cardiac imaging in the diagnostic workup of patients with pericardial disease. Continuous advances in cardiac CT and CMR technology allow for an excellent visualization and characterization of pericardial pathology, making these tomographic techniques complimentary to echocardiography. An integrated multimodality imaging strategy is sometimes needed to answer specific clinical questions, but the rational use of such an approach also requires good knowledge of the strengths and limitations of each technique. Given the paucity of evidence-based guidelines, more clinical studies are needed to better define the role of cardiac imaging in the management of patients with pericardial disease.	4

Dyspnea Suspected Cardiac Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
85. Yared K, Baggish AL, Picard MH, Hoffmann U, Hung J. Multimodality imaging of pericardial diseases. *JACC Cardiovasc Imaging.* 2010;3(6):650-660.	Review/Other-Dx	N/A	To review the imaging modalities most useful in the assessment of patients with pericardial disease, with an emphasis on the complementary value of multimodality cardiac imaging.	The pericardium can be affected by a wide variety of primary processes and systemic diseases. Echocardiography remains the initial diagnostic imaging modality of choice due to its availability and affordability. It performs particularly well in the diagnosis of pericardial effusions, tamponade, and constrictive pericarditis. On the other hand, both cardiac CT and CMR are becoming more widely available and provide novel and complementary information with respect to the morphologic and functional features of the diseased pericardium. Although they should not replace echocardiography as first-line imaging, they should be used when findings on TTE are difficult to interpret or conflict with clinical findings.	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.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

3-DE = Three-dimensional echocardiography

ARVC/D = Arrhythmogenic right ventricular cardiomyopathy/dysplasia

ARVD/C = Arrhythmogenic right ventricular dysplasia/cardiomyopathy

AUC = Area under the receiver operating characteristic curve

BNP = Brain-type natriuretic peptide

CAC = Coronary artery calcification

CAD = Coronary artery disease

CCTA = Coronary computed tomography angiography

CI = Confidence interval

CMR = Cardiac magnetic resonance

CT = Computed tomography

FFR = Fractional flow reserve

HF = Heart failure

HR = Hazard ratio

ICC = Intraclass correlation coefficients

LR = Likelihood ratio

LV = Left ventricular

LVEF = Left ventricular ejection fraction

MDCT = Multidetector computed tomography

MPI = Myocardial perfusion imaging

MRI = Magnetic resonance imaging

NPV = Negative predictive value

OR = Odds ratio

PET = Positron emission tomography

PPV = Positive predictive value

ROC = Receiver-operator characteristic

RV = Right ventricular

SPECT = Single-photon-emission computed tomography

SV = Stroke volume

TTE = Transthoracic echocardiography

US = Ultrasound