Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. 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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2. 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
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. Michelson E, Hollrah S. Evaluation of the patient with shortness of breath: an evidence based approach. Emerg Med Clin North Am. 1999; 17(1):221-237, x.	Review/Other-Dx	N/A	Evidence-based medicine approach to the evaluation of patients with shortness of breath.	Evaluation of patients includes a thorough history and physical examination, and chest radiograph. Further researched needed.	4
5. Vogel-Claussen J, Elshafee ASM, Kirsch J, et al. ACR Appropriateness Criteria(R) Dyspnea-Suspected Cardiac Origin. J Am Coll Radiol. 2017;14(5S):S127-S137.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for dyspnea-suspected cardiac origin.	No results stated in abstract.	4
6. Expert Panel on Thoracic Imaging:, Sirajuddin A, Donnelly EF, et al. ACR Appropriateness Criteria Suspected Pulmonary Hypertension. [Review]. Journal of the American College of Radiology. 14(5S):S350-S361, 2017 May.	Review/Other-Dx	N/A	To provide guidelines on Suspected Pulmonary Hypertension.	No results stated in abstract.	4
7. Pratter MR, Abouzgheib W, Akers S, Kass J, Bartter T. An algorithmic approach to chronic dyspnea. Respir Med. 2011;105(7):1014-1021.	Observational-Dx	123 patients	To prospectively evaluate an algorithmic approach to the cause(s) of chronic dyspnea.	Cause(s) was(were) diagnosed in 122/123 patients (99%); 97 patients had one diagnosis and 25 two diagnoses. Fifty-three percent of diagnoses were respiratory and 47% were non-respiratory. Following therapy, dyspnea improved in 63% of patients.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
8. Klein JS, Gamsu G, Webb WR, Golden JA, Muller NL. High-resolution CT diagnosis of emphysema in symptomatic patients with normal chest radiographs and isolated low diffusing capacity. Radiology. 1992; 182(3):817-821.	Review/Other-Dx	470 HRCT studies	To determine the prevalence of "nonobstructive" (impairment of gas transfer) emphysema in a select population of smokers with dyspnea, a retrospective study of patients with emphysema evident at HRCT was undertaken.	In 47 cases, centrilobular emphysema was the dominant parenchymal abnormality. Concomitant chest radiographs were available in 41 of these cases; 16 of the 41 lacked radiographic findings of emphysema. Among these 16 patients, pulmonary function testing revealed 10 to have normal flow rates (ratio of FEV in 1 second to FVC and FEV in 1 second greater than 80% predicted) and impaired gas transfer (single-breath carbon monoxide diffusing capacity <80% predicted). With the exclusion of one patient with congestive heart failure from the group of 10, the severity of emphysema at HRCT correlated inversely with single-breath carbon monoxide diffusing capacity (r = -.643). Results indicate that HRCT allows detection of emphysema in symptomatic patients when chest radiographs and pulmonary function tests are nondiagnostic.	4
9. Zompatori M, Bna C, Poletti V, et al. Diagnostic imaging of diffuse infiltrative disease of the lung. Respiration. 2004; 71(1):4-19.	Review/Other-Dx	N/A	Review the role of chest radiography and HRCT in the diagnosis and assessment of diffuse infiltrative lung disease.	The initial diagnostic approach to imaging of diffuse lung disease is the chest radiograph. However, because of chest radiography's limitations in sensitivity, specificity and diagnostic accuracy, HRCT is required especially for symptomatic patients with normal or nonspecific chest radiographic findings. HRCT is considered the best imaging tool for diffuse lung disease.	4
10. Capitanio S, Nordin AJ, Noraini AR, Rossetti C. PET/CT in nononcological lung diseases: current applications and future perspectives. Eur Respir Rev. 2016;25(141):247-258.	Review/Other-Dx	N/A	To review the Positron emission tomography (PET) combined with computed tomography (CT) diagnostic modalities in nononcological lung diseases.	No results stated in abstract.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
11. Pratter MR, Curley FJ, Dubois J, Irwin RS. Cause and evaluation of chronic dyspnea in a pulmonary disease clinic. Arch Intern Med. 1989; 149(10):2277-2282.	Observational-Dx	85 patients	Prospectively study patients with chronic dyspnea to determine whether findings based on objective testing (including chest radiograph) were superior to clinical impression alone.	Objective testing was more accurate than clinical impression alone (cause of dyspnea identified in 100% vs 66%). Chest radiograph most useful for identification of interstitial lung disease.	3
12. Grenier P, Chevret S, Beigelman C, Brauner MW, Chastang C, Valeyre D. Chronic diffuse infiltrative lung disease: determination of the diagnostic value of clinical data, chest radiography, and CT and Bayesian analysis. Radiology. 1994; 191(2):383-390.	Observational-Dx	Training set 208 retrospective observations Test set – 100 consecutive patients	To evaluate the value of clinical, chest radiography, and CT findings in classifying chronic diffuse infiltrative lung disease.	The frequency of correct diagnosis in test group (100 cases) was 27% with clinical data, which increased to 53% (P<.0001) with radiographic findings and 61% when clinical, radiographic and CT findings were combined (P=.07). CT provides supplementary information to radiographic findings and can help determine the specific diagnosis in patients with chronic diffuse infiltrative lung disease.	2
13. Oelsner EC, Lima JA, Kawut SM, et al. Noninvasive tests for the diagnostic evaluation of dyspnea among outpatients: the Multi-Ethnic Study of Atherosclerosis lung study. Am J Med. 2015;128(2):171-180 e175.	Observational-Dx	1969 participants	To assess which diagnostic tests were associated with dyspnea among participants without diagnosed cardiac or pulmonary disease from a large panel of tests that were performed in a multiethnic, population-based cohort.	Among 1969 participants without known cardiopulmonary disease, 9% had dyspnea. The forced expiratory volume in 1 second (FEV1) (P < .001), NT-proBNP (P = .004), and percent emphysema on CT (P = .004) provided independent information on the probability of self-reported dyspnea. Associations with the FEV1 were stronger among smokers and participants with other recent respiratory symptoms or seasonal allergies; associations with NT-proBNP were present only among participants with coexisting symptoms of lower-extremity edema. Only the FEV1 provided a significant improvement in the receiver operating curve.	3
14. Cleverley JR, Muller NL. Advances in radiologic assessment of chronic obstructive pulmonary disease. Clin Chest Med. 2000;21(4):653-663.	Review/Other-Dx	N/A	To review the advances in radiologic assessment of chronic obstructive pulmonary disease.	No results stated in abstract.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Wallace GM, Winter JH, Winter JE, Taylor A, Taylor TW, Cameron RC. Chest X-rays in COPD screening: are they worthwhile? Respir Med. 2009; 103(12):1862-1865.	Review/Other-Dx	546 consecutive chest X-ray reports	Retrospective study to determine clinical utility of chest x-rays in COPD screening.	Considerable benign and malignant pathology is detected by chest X-ray performed at initial COPD assessment. Clinical management is changed in the majority with a potentially treatable abnormality. This evidence suggests that the National Institute for Health and Clinical Excellence (NICE) guideline to perform chest X-ray at initial COPD evaluation should be elevated from a grade D to grade C recommendation.	4
16. Lynch DA, Austin JH, Hogg JC, et al. CT-Definable Subtypes of Chronic Obstructive Pulmonary Disease: A Statement of the Fleischner Society. Radiology. 2015;277(1):192-205.	Review/Other-Dx	N/A	To describe and define the phenotypic abnormalities that can be identified on visual and quantitative evaluation of computed tomographic (CT) images in subjects with chronic obstructive pulmonary disease (COPD), with the goal of contributing to a personalized approach to the treatment of patients with COPD.	No results stated in abstract.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
17. Regan EA, Lynch DA, Curran-Everett D, et al. Clinical and Radiologic Disease in Smokers With Normal Spirometry. JAMA Intern Med. 2015;175(9):1539-1549.	Observational-Dx	10192 smokers; 108 non-smokers	To identify clinical and radiologic evidence of smoking-related disease in a cohort of current and former smokers who did not meet spirometric criteria for chronic obstructive pulmonary disease (COPD), for whom we adopted the discarded label of Global Initiative for Obstructive Lung Disease (GOLD) 0.	One or more respiratory-related impairments were found in 54.1% (2375 of 4388) of the GOLD 0 group. The GOLD 0 group had worse quality of life (mean [SD] St George's Respiratory Questionnaire total score, 17.0 [18.0] vs 3.8 [6.8] for the never smokers; P < .001) and a lower 6-minute walk distance, and 42.3% (127 of 300) of the GOLD 0 group had computed tomography (CT) evidence of emphysema or airway thickening. The forced expiratory volume in the first second of expiration [FEV1] percent predicted distribution and mean for the GOLD 0 group were lower but still within the normal range for the population. Current smoking was associated with more respiratory symptoms, but former smokers had greater emphysema and gas trapping. Advancing age was associated with smoking cessation and with more CT findings of disease. Individuals with respiratory impairments were more likely to use respiratory medications, and the use of these medications was associated with worse disease.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
18. Kim SS, Seo JB, Lee HY, et al. Chronic obstructive pulmonary disease: lobe-based visual assessment of volumetric CT by Using standard images--comparison with quantitative CT and pulmonary function test in the COPDGene study. Radiology. 2013;266(2):626-635.	Observational-Dx	200 participants	To provide a new detailed visual assessment scheme of computed tomography (CT) for chronic obstructive pulmonary disease (COPD) by using standard reference images and to compare this visual assessment method with quantitative CT and several physiologic parameters.	The type of emphysema, determined by four readers, showed good agreement (kappa = 0.63). The extent of the emphysema in each lobe showed good agreement (mean weighted kappa = 0.70) and correlated with findings at quantitative CT (r = 0.75), forced expiratory volume in 1 second (FEV(1)) (r = -0.68), FEV(1)/forced vital capacity (FVC) ratio (r = -0.74) (P < .001). Agreement for airway wall thickening was fair (mean kappa = 0.41), and the number of lobes with thickened bronchial walls correlated with FEV(1) (r = -0.60) and FEV(1)/FVC ratio (r = -0.60) (P < .001).	2
19. Boes JL, Hoff BA, Bule M, et al. Parametric response mapping monitors temporal changes on lung CT scans in the subpopulations and intermediate outcome measures in COPD Study (SPIROMICS). Acad Radiol. 2015;22(2):186-194.	Observational-Dx	89 subjects	To demonstrate the utility of parametric response mapping (PRM), a computed tomography (CT)-based biomarker, for monitoring regional disease progression in chronic obstructive pulmonary disease (COPD) patients, linking expiratory- and inspiratory-based CT metrics over time.	PRM metrics varied by approximately 6.5% of total lung volume for normal parenchyma (PRM(Normal)) and functional small airways disease (PRM(fSAD)) and 1% for emphysema (PRM(Emph)) when testing 30-day repeatability. Over a 1-year interval, only PRM(Emph) in severe COPD subjects produced significant change (19%-21%). However, 11 of 76 subjects showed changes in PRM(fSAD) greater than variations observed from analysis of 30-day data. Mathematical model simulations agreed with experimental PRM results, suggesting fSAD is a transitional phase from normal parenchyma to emphysema.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. Gu S, Leader J, Zheng B, et al. Direct assessment of lung function in COPD using CT densitometric measures. Physiol Meas. 2014;35(5):833-845.	Observational-Dx	600 subjects	To investigate whether lung function in patients with chronic obstructive pulmonary disease (COPD) can be directly predicted using computed tomography (CT) densitometric measures and assess the underlying prediction errors as compared with the traditional spirometry-based measures.	The averaged percentage errors in prediction of forced expiratory volume in one second (FEV1), FEV1/forced vital capacity (FVC)%, total lung capacity (TLC), residual volume (RV)/TLC% and lung diffusion capacity by single breath carbon monoxide (DLCO)% predicted were 33%, 17%, 9%, 18% and 23%, respectively. When classifying the exams in terms of disease severity grades using the CT measures, 37% of the subjects were correctly classified with no error and 83% of the exams were either correctly classified or classified into immediate neighboring categories. The linear weighted kappa and quadratic weighted kappa were 0.54 (moderate agreement) and 0.72 (substantial agreement), respectively.	3
21. Lee YK, Oh YM, Lee JH, et al. Quantitative assessment of emphysema, air trapping, and airway thickening on computed tomography. Lung. 2008; 186(3):157-165.	Observational-Dx	34 patients	To evaluate the correlation between the parameters measured on volumetric CT, including the extent of emphysema, air trapping, and airway thickening, and clinical parameters. In-house software was used to measure CT parameters, including volume fraction of emphysema (V(950)), mean lung density, CT air trapping index, segmental bronchial wall area, lumen area, and wall area percent.	CT parameters were correlated with the pulmonary function test results, BMI, the modified Medical Research Council Dyspnea scale (MMRC scale), the six-minute-walk distance, and the BODE index. V(950) correlated to the BMI, FEV1, six-minute-walk distance, and the BODE index. The CT air trapping index correlated with the physiologic air trapping index (VC-FVC) (R=0.345, P=0.045) and the MMRC scale (R=0.532, P=0.001). There was a positive correlation between the wall area percent and the BMI (R=0.563, P<0.001). Mean lung density showed the strongest correlation with the BODE index (R= -0.756, P<0.001). Study concludes that the severity of emphysema and air trapping measured on CT correlated with the pulmonary function test parameters six-minute-walk distance and BMI.	3

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22. Wang G, Wang L, Ma Z, Zhang C, Deng K. Quantitative emphysema assessment of pulmonary function impairment by computed tomography in chronic obstructive pulmonary disease. J Comput Assist Tomogr. 2015;39(2):171-175.	Observational-Dx	46 patients	To determine the capability of quantitative emphysema by computed tomography (CT) to assess pulmonary function impairment in a population of current smokers with and without airflow limitation.	Quantitative CT measurements of emphysema were moderately, negatively correlated to airflow limitation (forced expiratory volume in 1 second [FEV1] and ratio of FEV1 to forced vital capacity) (r = -0.68 to -0.52, P < 0.001). Except for right middle and lower lobes, all the quantitative CT measurements showed moderate, negative correlations with diffusing capacity (DLCO) (r = -0.63 to -0.54, P </= 0.001) and weak to moderate correlations with residual volume to total lung capacity(RV) (RV/TLC) (r = 0.36-0.41, P < 0.01). As compared with control samples, the low attenuation volume (%LAVs) of whole lung, right lung, left lung, and each lobe was increased in patients with GOLD stages 2, 3, and 4 disease (P < 0.05), and the % LAV of whole lung, right lung and right upper lobe was increased in patients with GOLD stage 1 (P < 0.05).	3
23. Yahaba M, Kawata N, Iesato K, et al. The effects of emphysema on airway disease: correlations between multi-detector CT and pulmonary function tests in smokers. Eur J Radiol. 2014;83(6):1022-1028.	Observational-Dx	124 subjects	To determine whether emphysematous changes alter the relationships between airflow limitation and airway dimensions as measured by inspiratory and expiratory multi-detector computed tomography (MDCT).	In patients without emphysema, airway luminal area (Ai) and wall area percentage (WA%) from both the inspiratory and expiratory scans were significantly correlated with forced expiratory volume in 1 second (FEV1). No correlation was detected in patients with emphysema. In addition, emphysematous Chronic obstructive pulmonary disease (COPD) patients with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 1 or 2 disease had significantly lower changes in B8 Ai than non-emphysematous patients.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
24. Lee JS, Lee SM, Seo JB, et al. Clinical utility of computed tomographic lung volumes in patients with chronic obstructive pulmonary disease. Respiration. 2014;87(3):196-203.	Observational-Dx	75 patients	To evaluate the clinical utility of the computed tomography (CT) expiratory-to-inspiratory lung volume ratio (CT Vratio) by assessing the relationship with clinically relevant outcomes.	The CT Vratio correlated significantly with Body Mass Index (BMI) ($r = -0.528$, $p < 0.001$). The CT Vratio was also significantly associated with Medical Research Council (MMRC) dyspnea ($r = 0.387$, $p = 0.001$), 6-min walk distance (6MWD) ($r = -0.459$, $p < 0.001$), and St. George's Respiratory Questionnaire (SGRQ) ($r = 0.369$, $p = 0.001$) scores. Finally, the CT Vratio had significant correlations with the BMI, airflow obstruction, dyspnea, and exercise capacity index (BODE) and airflow obstruction (ADO) multidimensional chronic obstructive pulmonary disease (COPD) severity indices ($r = 0.605$, $p < 0.001$; $r = 0.411$, $p < 0.001$).	2

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25. Martinez CH, Chen YH, Westgate PM, et al. Relationship between quantitative CT metrics and health status and BODE in chronic obstructive pulmonary disease. Thorax. 2012;67(5):399-406.	Observational-Dx	1200 patients	To identify chronic obstructive pulmonary disease (COPD) phenotypes is increasingly appreciated.	In separate models predicting St George's Respiratory Questionnaire (SGRQ) score, a 1 unit standard deviation (SD) increase in each airway measure predicted higher SGRQ scores (for wall thickness (WT), 1.90 points higher, p=0.002; for wall area percentage (WA%0, 1.52 points higher, p=0.02; for pi10, 2.83 points higher p<0.001). The comparable increase in SGRQ for a 1 unit SD increase in emphysema percentage in these models was relatively weaker, significant only in the pi10 model (for emphysema percentage, 1.45 points higher, p=0.01). In separate models predicting Body-Mass Index, Airflow Obstruction, Dyspnea and Exercise Capacity Index (BODE), a 1 unit SD increase in each airway measure predicted higher BODE scores (for WT, 1.07-fold increase, p<0.001; for WA%, 1.20-fold increase, p<0.001; for pi10, 1.16-fold increase, p<0.001). In these models, emphysema more strongly influenced BODE (range 1.24-1.26-fold increase, p<0.001).	3

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26. Nambu A, Zach J, Schroeder J, et al. Quantitative computed tomography measurements to evaluate airway disease in chronic obstructive pulmonary disease: Relationship to physiological measurements, clinical index and visual assessment of airway disease. Eur J Radiol. 2016;85(11):2144-2151.	Observational-Dx	188 subjects	To correlate currently available quantitative computed tomography (CT) measurements for airway disease with physiological indices and the body-mass index, airflow obstruction, dyspnea, and exercise capacity (BODE) index in patients with chronic obstructive pulmonary disease (COPD).	Quantitative CT measurements had significant correlations with physiological indices. Among them, expiratory to inspiratory ratio of mean lung density (E/I-ratio MLD) had the strongest correlations with FEF25-75% (r=-0.648, <0.001) and specific airway conductance (sGaw) (r=-0.624, <0.001) while in the subjects with mild emphysema subsegmental WA% and segmental airway wall area percent (WA%) had the strongest correlation with forced expiratory flow (FEF)25-75% (r=-0.669, <0.001) and sGaw (r=-0.638, <0.001), respectively. The multiple variable analyses showed that RVC-856 to -950 was an independent predictor of the body-mass index, airflow obstruction, dyspnea, and exercise capacity index (BODE) index showing the highest R2 (0.468) as an independent variable among the Quantitative CT (QCT) measurements.	3
27. Han MK, Bartholmai B, Liu LX, et al. Clinical significance of radiologic characterizations in COPD. COPD. 2009; 6(6):459-467.	Observational-Dx	156 patients	To describe a comprehensive, correlative study in patients who underwent extensive clinical, physiological and radiological evaluation prior to surgical resection. The authors assessed the relationship between HRCT defined emphysema severity and airway abnormalities and clinically relevant outcomes including health status as measured by SF12 and St. George's Respiratory Questionnaire (SGRQ), self-reported exacerbation frequency and BODE.	HRCT provides unique COPD phenotyping information. Radiographic quantification of emphysema and bronchial thickness are independently associated with SGRQ and physical component score of the SF-12. Bronchial thickness but not emphysema is associated with exacerbation frequency, whereas emphysema is a stronger predictor of BODE and its systemic components modified MMRC, 6-min walk test, and BMI.	3

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28. Van Tho N, Ogawa E, Trang le TH, et al. A mixed phenotype of airway wall thickening and emphysema is associated with dyspnea and hospitalization for chronic obstructive pulmonary disease. Ann Am Thorac Soc. 2015;12(7):988-996.	Observational-Dx	240 patients	To propose a method of phenotyping chronic obstructive pulmonary disease (COPD) based on quantitative computed tomography (CT) and to compare clinically relevant outcomes between patients with COPD with the mixed phenotype and those with other CT-based phenotypes.	Of 240 patients with COPD, 52 (21.7%) were classified as CT-normal phenotype, 39 (16.3%) as airway-dominant phenotype, 103 (42.9%) as emphysema-dominant phenotype, and 46 (19.2%) as mixed phenotype. Patients with COPD with the mixed phenotype were associated with more severe dyspnea than those with each of the remaining CT-based phenotypes ($P < 0.01$ for all comparisons). The number of hospitalizations for COPD exacerbations during the preceding year was 2.0 to 3.6 times higher in patients with the mixed phenotype than in those with each of the remaining CT-based phenotypes ($P < 0.05$ for all comparisons). Findings persisted after adjustment for age, pack-years of smoking, smoking status, body mass index, and forced expiratory volume (FEV1).	3
29. Zulueta JJ, Wisnivesky JP, Henschke CI, et al. Emphysema scores predict death from COPD and lung cancer. Chest. 2012;141(5):1216-1223.	Observational-Dx	9,047 subjects	To assess the usefulness of emphysema scores in predicting death from Chronic Obstructive Pulmonary Disease (COPD) and lung cancer.	Median age was 65 years, 4,433 (49%) were men, and 4,133 (46%) were currently smoking or had quit within 5 years. Emphysema was identified in 2,637 (29%) and was a significant predictor of death from COPD (HR, 9.3; 95% CI, 4.3-20.2; $P < .0001$) and from lung cancer (HR, 1.7; 95% CI, 1.1-2.5; $P = .013$), even when adjusted for age and smoking history.	2
30. Camiciottoli G, Bartolucci M, Maluccio NM, et al. Spirometrically gated high-resolution CT findings in COPD: lung attenuation vs lung function and dyspnea severity. Chest. 2006; 129(3):558-564.	Observational-Dx	51 patients	To examine the relationship between HRCT lung attenuation measurements acquired under spirometric control of inspiratory and expiratory lung volume and pulmonary dysfunction as well as dyspnea severity in patients with COPD.	Inspiratory measurements assess the extent of emphysematous tissue loss. Expiratory measurements reflect airflow limitation and lung hyperinflation and correlate better with dyspnea perception. Both modalities should be utilized in HRCT.	3

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31. Capaldi DP, Zha N, Guo F, et al. Pulmonary Imaging Biomarkers of Gas Trapping and Emphysema in COPD: (3)He MR Imaging and CT Parametric Response Maps. Radiology. 2016;279(2):597-608.	Experimental-Dx	58 participants	To directly compare magnetic resonance (MR) imaging and computed tomography (CT) parametric response map (PRM) measurements of gas trapping and emphysema in ex-smokers both with and without chronic obstructive pulmonary disease (COPD).	Ventilation defect percent (VDP), apparent diffusion coefficient (ADC), and parametric response map (PRM) gas trapping and emphysema (ANOVA, P < .001) measurements were significantly different in healthy ex-smokers than they were in ex-smokers with COPD. In all ex-smokers, VDP was correlated with PRM gas trapping (r = 0.58, P < .001) and with PRM emphysema (r = 0.68, P < .001). VDP was also significantly correlated with PRM in ex-smokers with COPD (gas trapping: r = 0.47 and P = .03; emphysema: r = 0.62 and P < .001) but not in healthy ex-smokers. In a multivariate model that predicted PRM gas trapping, the forced expiratory volume in 1 second normalized to the forced vital capacity (standardized coefficients [betaS] = -0.69, P = .001) and airway wall area percent (betaS = -0.22, P = .02) were significant predictors. PRM emphysema was predicted by the diffusing capacity for carbon monoxide (betaS = -0.29, P = .03) and VDP (betaS = 0.41, P = .001). Helium 3 ADC values were significantly elevated in PRM gas-trapping regions (P < .001). The spatial relationship for ventilation defects was significantly greater with PRM gas trapping than with PRM emphysema in patients with mild (for gas trapping, spatial overlap coefficient (SOC)= 36% +/- 28; for emphysema, SOC = 1% +/- 2; P = .001) and moderate (for gas trapping, SOC = 34% +/- 28; for emphysema, SOC = 7% +/- 15; P = .006) COPD. For severe COPD, the spatial relationship for ventilation defects with PRM emphysema (SOC = 64% +/- 30) was significantly greater than that for PRM gas trapping (SOC = 36% +/- 18; P = .01).	3

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32. Ohno Y, Koyama H, Yoshikawa T, et al. Comparison of capability of dynamic O(2)-enhanced MRI and quantitative thin-section MDCT to assess COPD in smokers. Eur J Radiol. 2012;81(5):1068-1075.	Observational-Dx	186 patients	To directly and prospectively compare the capability of dynamic Oxygen-enhanced Magnetic Resonance Imaging (MRI) and quantitatively assessed thin-section multi dimensional computed tomography (MDCT) to assess smokers' Chronic obstructive pulmonary disease (COPD) in a large prospective cohort.	All indexes had significant correlations with functional parameters ($p<0.0001$). All indexes except computed tomography-based functional lung volume (CT-based FLV) in all groups had significant differences each other ($p<0.05$).	2
33. Zhang WJ, Hubbard Cristinacce PL, Bondesson E, et al. MR Quantitative Equilibrium Signal Mapping: A Reliable Alternative to CT in the Assessment of Emphysema in Patients with Chronic Obstructive Pulmonary Disease. Radiology. 2015;275(2):579-588.	Observational-Dx	24 patients; 12 healthy subjects	To compare magnetic resonance (MR) quantitative equilibrium signal (qS0) mapping with quantitative computed tomography (CT) in the estimation of emphysema in patients with chronic obstructive pulmonary disease (COPD).	Whole-lung mean qS0 and 15th percentile of qS0 were significantly lower, whereas relative lung area with a qS0 value below 0.20 (RA0.20) and standard deviation of qS0 were significantly higher in patients with COPD than in healthy control subjects ($P = .014$, $P = .002$, $P = .005$, and $P < .001$, respectively). Whole-lung mean qS0, the 15th percentile of qS0, and RA0.20 strongly correlated with RA-950 ($r = -0.78$, $r = -0.81$, and $r = 0.86$, respectively; $P < .001$) and PA15 ($r = 0.78$, $r = 0.79$, and $r = -0.71$, respectively; $P < .001$) and moderately correlated with the ratio of forced expiratory volume in 1 second (FEV1) to forced vital capacity ($r = 0.63$, $r = 0.67$, and $r = -0.60$, respectively; $P < .001$) and percentage predicted FEV1 ($r = 0.54$, $r = 0.62$, and $r = -0.56$, respectively; P </= .001). Good reproducibility of qS0 readouts was found in both groups (ICC range, 0.89-0.98).	3

Chronic Dyspnea-Noncardiovascular Origin
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
34. Ciccarese F, Poerio A, Stagni S, et al. Saber-sheath trachea as a marker of severe airflow obstruction in chronic obstructive pulmonary disease. Radiol Med. 2014;119(2):90-96.	Observational-Dx	71 patients	To investigate the correlation between saber-sheath trachea and clinical-radiological findings in a group of patients with chronic obstructive pulmonary disease (COPD) of varying severity.	Saber-sheath trachea was found in 18/71 (25.4 %) patients, with a greater prevalence in patients with lower Tiffenau Index ($p = 0.02$), Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages III-IV and visual severity score 3 (severe) on chest computed tomography (CT). Saber-sheath trachea was not found to be related to other radiological signs of COPD. The sensitivity, specificity and accuracy values of radiography were 72.2, 97.0 and 88.5 %, with perfect concordance between the radiographic and CT tracheal index ($p < 0.00001$).	2
35. Stevic R, Milenkovic B, Stojsic J, Pesut D, Ercegovac M, Jovanovic D. Clinical and radiological manifestations of primary tracheobronchial tumours: a single centre experience. Ann Acad Med Singapore. 2012;41(5):205-211.	Review/Other-Dx	10,955 patients	To analyse clinical, radiological and histological characteristics of the patients with tracheobronchial tumours diagnosed for a period of 7 years.	Among these 65 patients (36 men and 29 women) with a mean age of 48.8 years (range, 15 to 75), 50 had malignant tumours while 15 had benign ones. The most common symptoms were cough, chest pain and haemoptysis. Cough was a more frequent symptom in patients with benign tumours ($P <0.0014$). Only 2 patients were asymptomatic. Tumours were predominantly localised in the large airways (46 in large bronchi and 2 in trachea). The most common radiological manifestation of malignant tumours was tumour mass (46%) followed by atelectasis. One third benign tumour caused atelectasis, while tumour mass and consolidation were found in 3 patients each. Computerised tomography revealed endoluminal tumour mass in 29.2% of the cases, which was more frequently found in benign than malignant tumours (47% vs 24%, respectively). On bronchoscopy, tumours were visible in 73% and 70% benign and malignant cases respectively.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
36. Heidinger BH, Occhipinti M, Eisenberg RL, Bankier AA. Imaging of Large Airways Disorders. AJR Am J Roentgenol. 2015;205(1):41-56.	Review/Other-Dx	N/A	To review the advanced imaging techniques of large airways disorders.	No results stated in abstract.	4
37. Sun M, Ernst A, Boiselle PM. MDCT of the central airways: comparison with bronchoscopy in the evaluation of complications of endotracheal and tracheostomy tubes. J Thorac Imaging. 2007;22(2):136-142.	Observational-Dx	174 patients	To evaluate the accuracy of multidetector row computed tomography (MDCT) compared with bronchoscopy in the assessment of airway complications related to endotracheal and tracheostomy tubes.	The study population was comprised of 32 patients (range: 26 to 88 y, mean 55.6) with a total of 47 airway complications: tracheal stenosis (n=25), tracheomalacia (n=8), tracheal granulation tissue (n=8), tracheal cartilage fracture (n=4), tracheal perforation (n=1), and tracheostomy tube disruption (n=1). Computed tomography (CT) accurately diagnosed 42 of 47 airway complications (sensitivity 89.4%, specificity 95.2%, positive predictive value 85.7%, negative predictive value 96.5%). False negative findings at CT occurred in 5 (11.1%) of 47 cases. Contributing technical factors were identified in 3 (60.0%) of 5 false-negative cases, including the presence of tracheostomy tube during imaging and patient inability to complete the CT protocol.	3
38. Lee KS, Sun MR, Ernst A, Feller-Kopman D, Majid A, Boiselle PM. Comparison of Dynamic Expiratory CT With Bronchoscopy for Diagnosing Airway Malacia: A Pilot Evaluation. Chest. 2007; 131(3):758-764.	Observational-Dx	29 patients	Retrospective study to assess the accuracy of dynamic expiratory CT for detecting airway malacia using bronchoscopy as the diagnostic “gold standard.”	CT correctly diagnosed malacia in 28/29 patients (97%). The most common presenting symptoms were dyspnea in 20 patients (69%), severe or persistent cough in 16 patients (55%), and recurrent infection in 7 patients (24%). The estimated radiation dose (expressed as dose-length product) for the dual-phase study is 508 mGy-cm, which is comparable to a routine chest CT. Dynamic expiratory CT is a highly sensitive method for detecting airway malacia and has the potential to serve as an effective, noninvasive test for diagnosing this condition.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. O'Donnell CR, Bankier AA, O'Donnell DH, Loring SH, Boiselle PM. Static end-expiratory and dynamic forced expiratory tracheal collapse in COPD. Clin Radiol. 2014;69(4):357-362.	Observational-Dx	100 patients	To determine the range of tracheal collapse at end-expiration among chronic obstructive pulmonary disease (COPD) patients and to compare the extent of tracheal collapse between static end-expiratory and dynamic forced-expiratory multidetector-row computed tomography (MDCT).	Mean percentage expiratory collapse among COPD patients was 17 +/- 18% at end-expiration compared to 62 +/- 16% during forced expiration. Over the observed range of end-expiratory tracheal collapse (approximately 10-50%), the positive predictive value of end-expiratory collapse to predict excessive (>/=80%) forced expiratory tracheal collapse was <0.3.	3
40. Ferretti GR, Jankowski A, Perrin MA, et al. Multi-detector CT evaluation in patients suspected of tracheobronchomalacia: comparison of end-expiratory with dynamic expiratory volumetric acquisitions. Eur J Radiol. 2008;68(2):340-346.	Observational-Dx	70 patients	To compare dynamic expiratory imaging and end-expiratory imaging using multi-detector Computed Tomography (MDCT) of the central airways in patients suspected of tracheobronchomalacia (TBM).	In the entire population, the mean percentage of airway collapse was significantly greater with dynamic expiratory imaging than with the end-expiratory imaging at three different levels: lower thoracic trachea (26% vs. 16.6%, p<0.009), right (25.2% vs. 14%, p<0.01) and left main (24.7% vs. 13.3%, p<0.01) bronchus. Whatever the threshold value for defining TBM, dynamic expiratory imaging always resulted in diagnosing TBM in more patients than end-expiratory imaging.	3
41. Boiselle PM, O'Donnell CR, Loring SH, Bankier AA. Reproducibility of forced expiratory tracheal collapse: assessment with MDCT in healthy volunteers. Acad Radiol. 2010;17(9):1186-1189.	Observational-Dx	51 healthy controls	To assess the reproducibility of multidetector-row computed tomography (MDCT)-measured forced expiratory tracheal collapse in healthy volunteers.	Mean end-inspiratory cross-sectional area (CSA) was 255.3 +/- 56 mm(2) at year 1 (Yr1) and 255.1 +/- 52 mm(2) at Yr2; mean dynamic expiratory CSA was 125.6 +/- 60 mm(2) at Yr1 and 132.1 +/- 58 mm(2) at Yr2; and mean % expiratory reduction was 51.7 +/- 18% at Yr1 and 48.7 +/- 19% at Yr2. Mean differences between Yr1 and Yr2 values were 0.2 mm(2) for end-inspiratory CSA, 6.5 mm(2) for dynamic expiratory CSA, and 3.0% for percentage expiratory reduction. There was excellent correlation between the Yr1 and Yr2 measures of end-inspiratory CSA (r(2) = 0.97, P < .001), dynamic expiratory CSA (r(2) = 0.89, P < .001), and % expiratory reduction (r(2) = 0.86, P < .001).	3

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Klink T, Holle J, Laudien M, et al. Magnetic resonance imaging in patients with granulomatosis with polyangiitis (Wegener's) and subglottic stenosis. MAGMA 2013;26:281-90.	Observational-Dx	18 patients	To evaluate the ability of MRI to detect subglottic stenosis and to differentiate between active and inactive subglottic inflammation in patients with granulomatosis with polyangiitis (GPA).	MRI confirmed SGS in all GPA patients with significant narrowing of the airway lumen and thickening of subglottic wall. Assessing the subglottic inflammatory activity, MRI showed a sensitivity of 87.5 % and a specificity of 60.0 %. Interrater agreement was ? = 0.769. Of the different MR technical approaches tested, edema imaging was most sensitive and specific. DWI led to significant differences in the apparent diffusion coefficient between active and inactive subglottic inflammation. No significant differences were found with DCE imaging.	1
43. Ciet P, Boiselle PM, Heidinger B, et al. Cine MRI of Tracheal Dynamics in Healthy Volunteers and Patients With Tracheobronchomalacia. AJR Am J Roentgenol 2017;209:757-61.	Observational-Dx	12 patients	To assess cine MRI airway dynamics during various breathing conditions and compare cine MRI and MDCT measurements in healthy volunteers and patients with suspected TBM.	No results was stated	2
44. Liszewski MC, Ciet P, Sodhi KS, Lee EY. Updates on MRI Evaluation of Pediatric Large Airways. AJR Am J Roentgenol 2017;208:971-81.	Review/Other-Dx	N/A	To present a practical approach to imaging of common congenital and acquired diseases of the pediatric large airways with MRI and to describe the imaging findings.	No results stated.	4
45. Puderbach M, Eichinger M, Gahr J, et al. Proton MRI appearance of cystic fibrosis: comparison to CT. Eur Radiol 2007;17:716-24.	Observational-Dx	N/A	To review the comparison between proton MRI appearance of cystic fibrosis with CT	No results stated	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Or DY, Karmakar MK, Lam GC, Hui JW, Li JW, Chen PP. Multiplanar 3D ultrasound imaging to assess the anatomy of the upper airway and measure the subglottic and tracheal diameters in adults. Br J Radiol. 2013;86(1030):20130253.	Observational-Dx	11 healthy volunteers	To evaluate the feasibility of using three-dimensional (3D) ultrasound to assess the anatomy of the airway.	The airway anatomy was clearly delineated in the multiplanar 3D ultrasound images. It was also possible to identify the cricothyroid junction, and a simple method to measure the anteroposterior (AP) diameter of the subglottic space using this landmark is described. We were also able to accurately measure the transverse diameter of the upper trachea, but the transverse diameter of the subglottic space was overestimated using ultrasound. There was a strong correlation for the AP diameter measurement ($r=0.94$, $p<0.05$) and moderate correlation for the transverse diameter measurement ($r=0.82$, $p=0.002$) of the subglottic space, and a strong correlation for the transverse diameter measurement ($r=0.91$, $p<0.05$) of the upper trachea, in the ultrasound and MR images.	2
47. Epler GR, McLoud TC, Gaensler EA, Mikus JP, Carrington CB. Normal chest roentgenograms in chronic diffuse infiltrative lung disease. N Engl J Med. 1978;298(17):934-939.	Review/Other-Dx	458 patients	To determine the prevalence of normal roentgenograms in chronic diffuse infiltrative lung diseases.	The vital capacity was reduced in 57 per cent, and the single-breath diffusing capacity in 71 per cent. In half, histological changes and functional impairment were moderately severe.	4
48. Walsh SL, Hansell DM. High-resolution CT of interstitial lung disease: a continuous evolution. Semin Respir Crit Care Med. 2014;35(1):129-144.	Review/Other-Dx	N/A	To review the high resolution computed tomography of interstitial lung disease.	No results stated in abstract.	4

Chronic Dyspnea-Noncardiovascular Origin
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Grydeland TB, Dirksen A, Coxson HO, et al. Quantitative computed tomography measures of emphysema and airway wall thickness are related to respiratory symptoms. Am J Respir Crit Care Med. 2010; 181(4):353-359.	Observational-Dx	463 subjects with COPD and 488 subjects without COPD	To describe the independent relationship between respiratory symptoms of COPD and quantitative HRCT measures of emphysema (percent low-attenuation areas less than –950 Hounsfield units) and airway wall thickness at an internal perimeter of 10 mm. Also assessed whether these relationships varied between subjects with and without COPD, and between sexes.	Median (25th percentile, 75th percentile) percent low-attenuation areas less than -950 Hounsfield units was 7.0 (2.2, 17.8) in subjects with COPD and 0.5 (0.2, 1.3) in subjects without COPD. Mean (standard deviation) standardized airway wall thickness at an internal perimeter of 10 mm was 4.94 (0.33) mm in subjects with COPD and 4.77 (0.29) in subjects without COPD. Both percent low-attenuation areas and airway wall thickness at an internal perimeter of 10 mm were independently and significantly related to the level of dyspnea among subjects with COPD, even after adjustments for percent predicted FEV in 1 second. Airway wall thickness at an internal perimeter of 10 mm was significantly related to cough and wheezing in subjects with COPD, and to wheezing in subjects without COPD. Odds ratios (95% CI) for increased dyspnea in subjects with COPD and in subjects without COPD were 1.9 (1.5-2.3) and 1.9 (0.6-6.6) per 10% increase in percent low-attenuation areas, and 1.07 (1.01-1.14) and 1.11 (0.99-1.24) per 0.1-mm increase in airway wall thickness at an internal perimeter of 10 mm, respectively. Quantitative CT assessment of the lung parenchyma and airways may be used to explain the presence of respiratory symptoms beyond the information offered by spirometry.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Muller NL, Mawson JB, Mathieson JR, Abboud R, Ostrow DN, Champion P. Sarcoidosis: correlation of extent of disease at CT with clinical, functional, and radiographic findings. Radiology. 1989; 171(3):613-618.	Observational-Dx	27 consecutive patients	To compare the efficacy of CT with that of chest radiography in estimating disease severity as assessed by means of clinical and pulmonary function data. CT scans and radiographs were each read twice by two independent observers.	The severity of parenchymal changes on the CT scan and on the radiograph was significantly correlated with the severity of dyspnea (r = .61 and .58, respectively; P<.001), diffusing capacity (r = -.62 and -.52, P<.01), and VC (r = -.49 and -.51, P<.01). Patients with predominantly irregular opacities had more severe dyspnea and lower lung volumes than patients with predominantly nodular opacities (P<.05).	2
51. Papiris SA, Daniil ZD, Malagari K, et al. The Medical Research Council dyspnea scale in the estimation of disease severity in idiopathic pulmonary fibrosis. Respir Med. 2005; 99(6):755-761.	Observational-Dx	26 patients	To evaluate the association of Medical Research Council (MRC) chronic dyspnea scale with lung function indices and HRCT scores such as the total interstitial disease score and the fibrosis score.	There is good correlation between fibrosis score on HRCT and level of dyspnea in patients with IPF. Observations suggest MRC dyspnea scale could offer useful information about the estimation of severity in patients with IPF.	2
52. Staples CA, Muller NL, Vedal S, Abboud R, Ostrow D, Miller RR. Usual interstitial pneumonia: correlation of CT with clinical, functional, and radiologic findings. Radiology. 1987; 162(2):377-381.	Observational-Dx	23 patients	Review clinical data, pulmonary function tests, chest radiographs, and CT scans of patients with UIP to assess the efficacy of CT compared with the chest radiograph in estimating disease severity. CT scans and chest radiographs were each read twice by two independent observers.	There was good intraobserver and interobserver agreement for both CT and radiograph scores (all r =.71). CT scans gave a better estimate of disease extent and showed more extensive honeycombing than did the radiograph. A significant correlation was found between the extent of disease as assessed with CT and the severity of dyspnea (r = .62, P<.001), as well as between CT and impairment in gas exchange as assessed by the diffusing capacity (r = .64, P<.001). There was poor correlation between disease severity as assessed with chest radiography and the clinical and functional variables (all r = to .39).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Terriff BA, Kwan SY, Chan-Yeung MM, Muller NL. Fibrosing alveolitis: chest radiography and CT as predictors of clinical and functional impairment at follow-up in 26 patients. Radiology. 1992; 184(2):445-449.	Observational-Dx	26 patients	To quantitate severity and extent of disease as depicted on the chest radiograph by scoring six lung zones independently; to compare the usefulness of radiographic and CT findings to enable estimation of clinical and functional impairment; to evaluate the change in the pattern of disease over time; and to determine if the changes in findings on serial chest radiographs and CT scans correlated with the interval change in the clinical and functional impairment.	The standard profusion score showed no significant correlation with clinical or functional parameters (P>.05). However, the average profusion score of the six lung zones correlated with severity of dyspnea and with static lung volumes (P<.01). Extent of irregular linear opacities on CT scans correlated with severity of dyspnea and impairment in gas transfer (carbon monoxide-diffusing capacity) (P<.01). The profusion of ground-glass opacities on the radiograph showed no significant correlations (P>.05). The profusion and extent of ground-glass opacities on CT scans correlated with severity of dyspnea, impairment in gas transfer, and reduction in static lung volumes (P<.01). Ground-glass opacities on CT scans preceded and predicted the development of irregular linear opacities on follow-up CT scans and correlated with an increase in the average profusion score of the chest radiograph (P<.01).	3
54. Chung JH, Chawla A, Peljto AL, et al. CT scan findings of probable usual interstitial pneumonitis have a high predictive value for histologic usual interstitial pneumonitis. Chest. 2015;147(2):450-459.	Observational-Dx	201 patients	To determine the predictive effect of probable usual interstitial pneumonitis (UIP) on computed tomography (CT) scan on histology and the effect of the promoter polymorphism in mucin gene (MUC5B) (rs35705950) on histologic and CT scan UIP diagnosis.	The proportion of CT scan diagnoses were as follows: inconsistent with (69 of 201, 34.3%), indeterminate (72 of 201, 35.8%), probable (34 of 201, 16.9%), and definite (26 of 201, 12.9%) UIP. Subjects with probable UIP on CT scan were more likely to have histologic probable/definite UIP than subjects with indeterminate UIP on CT scan (82.4% [28 of 34] vs 54.2% [39 of 72]; P = .01). CT scan and microscopic honeycombing were not associated with each other (P = .76). The minor (T) allele of the MUC5B polymorphism was associated with concordant CT scan and histologic UIP diagnosis (P = .03)	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Elicker B, Pereira CA, Webb R, Leslie KO. High-resolution computed tomography patterns of diffuse interstitial lung disease with clinical and pathological correlation. J Bras Pneumol. 2008;34(9):715-744.	Review/Other-Dx	N/A	To present the key High-resolution computed tomography (HRCT) patterns in diffuse interstitial lung disease (DILD), providing the clinical context and histopathological correlations for each.	No results stated in abstract.	4
56. Sundaram B, Gross BH, Martinez FJ, et al. Accuracy of high-resolution CT in the diagnosis of diffuse lung disease: effect of predominance and distribution of findings. AJR Am J Roentgenol. 2008; 191(4):1032-1039.	Observational-Dx	100 patients 3 reviewers	Retrospective, blinded review to determine whether the predominant findings on HRCT influence the accuracy of diagnosis of diffuse lung disease.	The predominant findings of honeycombing and bronchovascular thickening are associated with more than 90% accuracy in the first choice diagnosis of diffuse lung disease. The finding of lung cysts has 80%-89% accuracy. Ground glass opacification is less reliable but the accuracy is improved when combined with honeycombing or lower lung distribution.	4
57. Verrastro CG, Antunes VB, Jasinowodolinski D, D'Ippolito G, Meirelles GS. High-Resolution Computed Tomography in the Diagnosis of Diffuse Parenchymal Lung Diseases: Is it Possible to Improve Radiologist's Performance?. J Comput Assist Tomogr. 40(2):248-55, 2016 Mar-Apr.	Observational-Dx	82 patients	To assess the concordance between high-resolution computed tomography (HRCT) diagnostic hypotheses (DH) and final diagnosis in patients with diffuse lung disease and to evaluate whether clinical data or the radiologist's degree of certainty influence concordance.	Concordances of HRCT DH and final diagnosis were 48% and 76%, respectively, considering first or any of the DH without access to clinical data. Accessing clinical data improved concordance especially for hypersensitivity pneumonitis. Diagnostic hypotheses formulated with high degree of confidence were correct in 69% of cases.	2
58. Flaherty KR, King TE, Jr., Raghu G, et al. Idiopathic interstitial pneumonia: what is the effect of a multidisciplinary approach to diagnosis? Am J Respir Crit Care Med. 2004;170(8):904-910.	Observational-Dx	58 patients	To establish a diagnosis of idiopathic interstitial pneumonia.	In general, as more information was provided the confidence level for a given diagnosis improved, and the diagnoses rendered with a high level of confidence were more likely congruent with the final pathologic consensus diagnosis. The final consensus pathologist diagnosis was idiopathic pulmonary fibrosis in 30 cases. Clinicians identified 75% and radiologists identified 48% of these cases before presentation of the histopathologic information.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Thomeer M, Demedts M, Behr J, et al. Multidisciplinary interobserver agreement in the diagnosis of idiopathic pulmonary fibrosis. Eur Respir J. 2008;31(3):585-591.	Observational-Dx	36 local investigators; 179 HRCT; 82 open or thoracoscopic lung biopsy (OLB/TLB) TLB,	To evaluate the accuracy of the diagnosis of idiopathic pulmonary fibrosis (IPF) by respiratory physicians in six European countries, and to calculate the interobserver agreement between high-resolution computed tomography (HRCT) reviewers and histology reviewers in IPF diagnosis.	The diagnosis of usual interstitial pneumonia (UIP) was confirmed by the expert panels in 87.2% of cases. A total of 179 thoracic high-resolution computed tomography scans were independently reviewed, and an interobserver agreement of 0.40 was found. Open or thoracoscopic lung biopsy was performed in 97 patients, 82 of whom could be reviewed by the expert committee. The weighted kappa between histology readers was 0.30.	1
60. Watadani T, Sakai F, Johkoh T, et al. Interobserver variability in the CT assessment of honeycombing in the lungs. Radiology. 2013;266(3):936-944.	Observational-Dx	80 chest CT	To quantify observer agreement and analyze causes of disagreement in identifying honeycombing at chest computed tomography (CT).	Agreement of scores of honeycombing presence by 43 observers with the reference standard was moderate (Cohen weighted kappa values: 0.40-0.58). There were no significant differences in kappa values among groups defined by either subspecialty or geographic region (Tukey-Kramer test, P = .38 to >.99). In 29% of cases, there was disagreement on identification of honeycombing. These cases included honeycombing mixed with traction bronchiectasis, large cysts, and superimposed pulmonary emphysema.	3
61. Hozumi H, Nakamura Y, Johkoh T, et al. Nonspecific interstitial pneumonia: prognostic significance of high-resolution computed tomography in 59 patients. J Comput Assist Tomogr. 2011;35(5):583-589.	Observational-Dx	59 patients	To retrospectively analyze the prognostic implications of high-resolution computed tomography (HRCT) findings for patients with biopsy-proven nonspecific interstitial pneumonia (NSIP).	The 5-year survival rate was 83% and the 10-year survival rate was 66%. Univariate analysis revealed that the extent of areas with ground-glass attenuation without traction bronchi-bronchiolectasis and that of airs-pace consolidation were associated with favorable outcome, whereas that of intralobular reticular opacities was associated with worse prognosis. Multivariate analysis showed that the extent of air-space consolidation was an independent factor of favorable outcome.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
62. Hwang JH, Misumi S, Curran-Everett D, Brown KK, Sahin H, Lynch DA. Longitudinal follow-up of fibrosing interstitial pneumonia: relationship between physiologic testing, computed tomography changes, and survival rate. J Thorac Imaging. 2011;26(3):209-217.	Observational-Dx	72 patients	To evaluate the prognostic implications of computed tomography (CT) and physiologic variables at baseline and on sequential evaluation in patients with fibrosing interstitial pneumonia.	On follow-up CT, the extent of mixed ground-glass and reticular opacities (P<0.001), pure reticular opacity (P=0.04), honeycombing (P=0.02), and overall extent of disease (P<0.001) was increased in the idiopathic group, whereas these variables remained unchanged in the collagen vascular disease group. Patients with idiopathic disease had a shorter rate of survival than those with collagen vascular disease (P=0.03). In model 1, the extent of honeycombing on baseline CT was the only independent predictor of mortality (P=0.02). In model 2, progression in honeycombing was the only predictor of mortality (P=0.005). In model 3, baseline extent of honeycombing and progression of honeycombing were the only independent predictors of mortality (P=0.001 and 0.002, respectively). Neither baseline nor serial change physiologic variables, nor the presence of collagen vascular disease, was predictive of rate of survival.	2
63. Ohno Y, Nishio M, Koyama H, et al. Pulmonary MR imaging with ultra-short TEs: utility for disease severity assessment of connective tissue disease patients. Eur J Radiol. 2013;82(8):1359-1365.	Observational-Dx	18 patients	To evaluate the utility of pulmonary magnetic resonance (MR) imaging with ultra-short echo times (UTEs) at a 3.0 T MR system for pulmonary functional loss and disease severity assessments of connective tissue disease (CTD) patients with interstitial lung disease (ILD).	Mean T2 values for normal and CTD subjects were significantly different (p=0.0019) and showed significant correlations with percentage of vital capacity (%VC), diffusion capacity of the lung (%DLCO), serum KL-6 and CT-based disease severity of CTD patients (p<0.05).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
64. Ohno Y, Nishio M, Koyama H, et al. Oxygen-enhanced MRI for patients with connective tissue diseases: comparison with thin-section CT of capability for pulmonary functional and disease severity assessment. Eur J Radiol. 2014;83(2):391-397.	Observational-Dx	53 patients	To prospectively and directly compare oxygen-enhanced magnetic resonance imaging ((O2-enhanced) MRI) with thin-section computed tomography (CT) for pulmonary functional loss and disease severity assessment in connective tissue disease (CTD) patients with interstitial lung disease (ILD).	Mean relative enhancement ratio (MRER)and CT-assessed disease severity showed significant differences between CTD patients with (MRER: 0.15 +/- 0.08, CT-assessed disease severity: 13.0 +/- 7.4%) and without ILD (MRER: 0.25 +/- 0.06, p=0.0011; CT-assessed disease severity: 1.6 +/- 1.6%, p<0.0001). MRER and CT-assessed disease severity correlated significantly with pulmonary functional parameters and serum KL-6 in all subjects (0.61 </= r </= 0.79, p<0.05).	2
65. Yi CA, Lee KS, Han J, Chung MP, Chung MJ, Shin KM. 3-T MRI for differentiating inflammation- and fibrosis-predominant lesions of usual and nonspecific interstitial pneumonia: comparison study with pathologic correlation. AJR Am J Roentgenol. 2008; 190(4):878-885.	Observational-Dx	26 patients	To evaluate the utility of 3T MRI of the lung for differentiating inflammation- and fibrosis-predominant lesions in the usual and nonspecific types of interstitial pneumonia.	Inflammation-predominant specimens were obtained from 31% (17/54) of the biopsy sites. Inflammation-predominant biopsy sites had an early enhancement pattern (82%, 14/17 sites, P<0.001) on dynamic studies and high signal intensity (53%, 9/17 sites, P=0.001) on T2-weighted triple-inversion black blood fast-spin echo images. Multiphase dynamic enhancement studies with a turbo field-echo sequence and T2-weighted triple-inversion black blood fast-spin echo images on 3-T MRI appear to be useful for differentiating inflammation- and fibrosis-predominant lesions.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Kato S, Sekine A, Kusakawa Y, et al. Prognostic value of cardiovascular magnetic resonance derived right ventricular function in patients with interstitial lung disease. J Cardiovasc Magn Reson. 2015;17:10.	Observational-Dx	76 patients	To determine the prognostic significance of Cardiovascular magnetic resonance (CMR) derived right ventricular (RV) ejection fraction (RVEF) in interstitial lung disease (ILD) patients.	The median RVEF was 59.2% in controls (n = 24), 53.8% in ILD patients without PH (n = 42) and 43.1% in ILD patients with Pulmonary hypertension (PH) (n = 13) ($p < 0.001$ by one-way ANOVA). During a mean follow-up of 386 days, 18 patients with right ventricular systolic dysfunction (RVSD) had 11 severe events (3 deaths, 3 right heart failure, 3 exacerbation of dyspnea requiring oxygen, 2 pneumonia requiring hospitalization). In contrast, only 2 exacerbation of dyspnea requiring oxygen were observed in 58 patients without right ventricular systolic dysfunction (RVSD). Multivariate Cox regression analysis showed that RVEF independently predicted future events, after adjusting for age, sex and RV fractional area change (RVFAC) by echocardiography (hazard ratio: 0.889, 95% confidence interval: 0.809-0.976, $p = 0.014$).	2
67. Keijsers RG, Grutters JC, Thomeer M, et al. Imaging the inflammatory activity of sarcoidosis: sensitivity and inter observer agreement of (67)Ga imaging and (18)F-FDG PET. Q J Nucl Med Mol Imaging. 2011;55(1):66-71.	Observational-Dx	34 patients	To investigate sensitivity of 67Ga imaging and Fluorodeoxyglucose F18 Positron Emission Tomography Computed Tomography(FDG-PET/CT (PET)) for sarcoidosis activity and their inter observer variability.	Overall sensitivity to detect active sarcoidosis was 88% for (67)Ga imaging and 97% for (18)F-FDG PET. Although these results were not significantly different, 18F-FDG PET detected more lesions in the mediastinum ($P<0.05$), hila ($P<0.05$), lymph nodes ($P<0.001$) and extra pulmonary regions in general ($P<0.001$). Inter observer agreement was poor to moderate for (67)Ga imaging (kappa 0.19-0.59) and good to very good for (18)F-FDG PET (kappa 0.65-1.00).	2
68. Mostard RL, van Kroonenburgh MJ, Drent M. The role of the PET scan in the management of sarcoidosis. Curr Opin Pulm Med. 2013;19(5):538-544.	Review/Other-Dx	N/A	To review the knowledge and understanding about the appropriate use of Positron-Emission Tomography (PET) scan in the management of sarcoidosis patients.	No results stated in abstract.	4

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. Groves AM, Win T, Screaton NJ, et al. Idiopathic pulmonary fibrosis and diffuse parenchymal lung disease: implications from initial experience with 18F-FDG PET/CT. J Nucl Med. 2009; 50(4):538-545.	Observational-Dx	36 consecutive patients	To evaluate integrated FDG-PET/CT in patients with IPF and diffuse parenchymal lung disease.	Raised pulmonary FDG metabolism in 36/36 patients was observed. The parenchymal pattern on HRCT at the site of maximal FDG metabolism was predominantly ground-glass (7/36), reticulation/honeycombing (26/36), and mixed (3/36). The mean SUVmax in patients with ground-glass and mixed patterns was 2.0 +/- 0.4, and in reticulation/honeycombing it was 3.0 +/- 1.0 (Mann-Whitney U test, P=0.007). The mean SUVmax in patients with IPF was 2.9 +/- 1.1, and in other diffuse parenchymal lung disease it was 2.7 +/- 0.9 (Mann-Whitney U test, P=0.862). The mean mediastinal lymph node SUVmax (2.7 +/- 1.3) correlated with pulmonary SUVmax (r = 0.63, P<0.001). Pulmonary FDG uptake correlated with the global health score (r = 0.50, P=0.004), forced VC (r = 0.41, P=0.014), and transfer factor (r = 0.37, P=0.042). Increased pulmonary FDG metabolism in all patients with IPF and other forms of diffuse parenchymal lung disease was observed. Pulmonary FDG uptake predicts measurements of health and lung physiology in these patients. FDG metabolism was higher when the site of maximal uptake corresponded to areas of reticulation/honeycomb on HRCT than to those with ground-glass patterns.	3

Chronic Dyspnea-Noncardiovascular Origin
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
70. Jacquelin V, Mekinian A, Brillet PY, et al. FDG-PET/CT in the prediction of pulmonary function improvement in nonspecific interstitial pneumonia. A Pilot Study. Eur J Radiol. 2016;85(12):2200-2205.	Observational-Dx	18 patients	To analyse the characteristics of nonspecific interstitial pneumonia (NSIP) using Fluorodeoxyglucose F18 Positron Emission Tomography Computed Tomography(FDG-PET/CT (PET)) and to evaluate its ability to predict the therapeutic response.	All patients had an increased pulmonary FDG uptake (median SUVmax=3.1 [2-7.6]), with a median extent of 19% [6-67]. Consolidations, ground-glass opacities, honeycombing and reticulations showed uptake in 90%, 89%, 85% and 76%, respectively. FDG uptake extent was associated with improvement of pulmonary function under treatment (increase in forced vital capacity>10%, p=0.03), whereas SUVmax and high resolution CT scan (HRCT) fibrosis score were not (p>0.5). For FDG uptake extent, Receiver Operating Characteristic (ROC) analysis showed an area under the curve at 0.85+/-0.11 and sensitivity/specificity was 88%/80% for a threshold fixed at 21%.	2

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Nobashi T, Kubo T, Nakamoto Y, et al. 18F-FDG Uptake in Less Affected Lung Field Provides Prognostic Stratification in Patients with Interstitial Lung Disease. J Nucl Med. 2016;57(12):1899-1904.	Observational-Dx	90 patients	To evaluate the clinical significance of Fluorodeoxyglucose F18 Positron Emission Tomography Computed Tomography (18F-FDG PET/CT) in patients with interstitial lung disease (ILD), by investigating the relationships between 18F-FDG PET/CT parameters and clinical indicators and by evaluating the prognostic implications of 18F-FDG PET/CT	SUVmean, SUVTF, and CTmean were significantly higher in ILD patients than in healthy controls, except for CTmean in patients with a nonusual interstitial pneumonia pattern. SUVmean and CTmean were significantly correlated with %FVC, %DLco, KL-6, and SP-D; SUVTF was significantly correlated with %DLco, Krebs von den Lungen-6 (KL-6), surfactant protein D (SP-D), and lactate dehydrogenase (LDH); and SUVmax was weakly correlated with KL-6 and C-reactive protein (CRP). Univariate analysis showed that SUVmean, SUVTF, sex, forced vital capacity (%FVC), diffusion capacity of the lungs for carbon monoxide (%DLco), KL-6, and ILD-sex-agephysiology (GAP) index were significantly prognostic of lung transplantation-free survival; and multivariate analysis showed that SUVmean and ILD-GAP index were independently prognostic of lung transplantation-free survival. A higher SUVmean indicated a poorer prognosis, especially in patients with moderate risk based on ILD-GAP index.	3
72. Barskova T, Gargani L, Guiducci S, et al. Lung ultrasound for the screening of interstitial lung disease in very early systemic sclerosis. Ann Rheum Dis. 2013;72(3):390-395.	Observational-Dx	58 patients	To evaluate whether lung ultrasound (LUS) is reliable in the screening of interstitial lung disease (ILD) in patients with systemic sclerosis (SSc).	At high resolution Computed Tomography (HRCT), ILD was detected in 88% of the SSc population and in 41% of the very early SSc population. A significant difference in the number of B-lines was found in patients with and without ILD on HRCT (57+/-53 vs 9+/-9; $p<0.0001$), with a concordance rate of 83%. All discordant cases were false positive at LUS, providing a sensitivity and negative predictive value of 100% in both SSc and very early SSc.	2

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
73. Hasan AA, Makhlouf HA. B-lines: Transthoracic chest ultrasound signs useful in assessment of interstitial lung diseases. Ann Thorac Med. 2014;9(2):99-103.	Observational-Dx	61 patients	To evaluate the value of sonographic B-lines (previously called "comet tail artifacts"), which are long, vertical, well-defined, hyperechoic, dynamic lines originating from the pleural line in assessment of interstitial lung diseases (ILD) and compare them with the findings of chest high-resolution computed tomography (HRCT) and pulmonary function tests (PFTs).	All patients had diffuse bilateral B-lines. The distance between each of the two adjacent B lines correlated with the severity of the disease on chest HRCT where B3 (the distance was 3 mm) correlated with ground glass opacity and B7 (the distance was 7 mm) correlated with extensive fibrosis and honey combing. Also, the distance between B-lines inversely correlated with forced vital capacity (FVC) ($r = -0.848$, $P < 0.001$), total lung capacity (TLC) ($r = -0.664$, $P < 0.001$), diffusion capacity for carbon monoxide (DLCO) ($r = -0.817$, $P < 0.001$) and partial arterial oxygen pressure (PaO2) ($r = -0.902$, $P < 0.001$).	3
74. Sener Cömert S, Çaglayan B, Dogan C, et al. Ultrasound in the assessment of interstitial lung diseases: Correlation with high-resolution computed tomography and lung functions. European Respiratory Journal. 2015;46(suppl 59):PA3841.	Observational-Dx	34 patients; 21 controls	To evaluate the value of comet tail artifacts(B-lines) in assessment of interstitial lung diseases(ILD) and investigate the correlation between B-lines and high-resolution computed tomography(HRCT) findings,pulmonary function tests(PFTs), and diffusion capacity(DLCO).	34 patients with a diagnosis of ILD and 21 controls were included with a mean age of 59.2±14.2 years.There is a significant differance in B-line scores between ILD patients and control group(p<0.0001).Also the number of comet lines correlated with severity of the disease on HRCT and DLCO.A significant correlation was found between US B-line score and HRCT findings(p=0.001) and DLCO(p<0.000)	3

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
75. Gigante A, Rossi Fanelli F, Lucci S, et al. Lung ultrasound in systemic sclerosis: correlation with high-resolution computed tomography, pulmonary function tests and clinical variables of disease. Internal & Emergency Medicine. 11(2):213-7, 2016 Mar.	Observational-Dx	39 patients	To evaluate if there is a correlation between lung ultrasound (LUS), chest high-resolution computed tomography (HRCT), pulmonary function tests findings and clinical variables of the disease.	A positive correlation exists between the number of B-lines and the HRCT score ($r = 0.81$, $p < 0.0001$), conversely a negative correlation exists between the number of B-lines and diffusing capacity of the lung for carbon monoxide (DLCO) ($r = -0.63$, $p < 0.0001$). The number of B-lines increases along with the progression of the capillaroscopic damage. A statistically significant difference in the number of B-lines was found between patients with and without digital ulcers [42 (3-84) vs 16 (4-55)]. We found that the number of B-lines increased with the progression of both HRCT score and digital vascular damage.	3
76. Blackmore CC, Black WC, Dallas RV, Crow HC. Pleural fluid volume estimation: a chest radiograph prediction rule. Acad Radiol. 1996;3(2):103-109.	Observational-Dx	16 patients	To estimate pleural effusion volume on the basis of posteroanterior and lateral chest radiographs.	For the test and validation sets, the weighted accuracies of the prediction rule were 86% and 85%, respectively. The respective weighted interobserver agreements were 97% and 88%. Pleural effusions became visible as a meniscus on the lateral chest radiograph at a volume of approximately 50 ml; at a volume of 200 ml, the meniscus could be identified on the posteroanterior radiograph. At a volume of about 500 ml, the meniscus obscured the hemidiaphragm.	3
77. Kuhlman JE, Singha NK. Complex disease of the pleural space: radiographic and CT evaluation. Radiographics. 1997;17(1):63-79.	Review/Other-Dx	N/A	To review Complex disease of the pleural space.	No results stated in abstract.	4

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
78. Hallifax RJ, Haris M, Corcoran JP, et al. Role of CT in assessing pleural malignancy prior to thoracoscopy. Thorax. 2015;70(2):192-193.	Review/Other-Dx	370 patients	To assess the sensitivity and specificity of computed tomography (CT) in detecting pleural malignancy prior to definitive histology obtained via thoracoscopy in a large cohort of patients with suspected malignant pleural disease.	211 (57%) of 370 patients included in the analysis had malignant disease: CT scans were reported as 'malignant' in 144, giving a sensitivity of 68% (95% CI 62% to 75%). Of the 159 patients with benign disease, 124 had CT scans reported as benign: specificity 78% (72% to 84%). The positive predictive value of a malignant CT report was 80% (75% to 86%), with a negative predictive value of 65% (58% to 72%). A significant proportion of patients being investigated for malignant disease will have malignancy despite a negative CT report.	4
79. Tsujimoto N, Saraya T, Light RW, et al. A Simple Method for Differentiating Complicated Parapneumonic Effusion/Empyema from Parapneumonic Effusion Using the Split Pleura Sign and the Amount of Pleural Effusion on Thoracic CT. PLoS One. 2015;10(6):e0130141.	Observational-Dx	83 patients	To develop a simple method to distinguish complicated parapneumonic effusion (CPPE)/empyema from parapneumonic effusion (PPE) using computed tomography (CT) focusing on the split pleura sign, fluid attenuation values (HU: Hounsfield units), and amount of fluid collection measured on thoracic CT prior to diagnostic thoracentesis.	On univariate analysis, the split pleura sign (odds ratio (OR), 12.1; p<0.001), total amount of pleural effusion (>/=30 mm) (OR, 6.13; p<0.001), HU value>/=10 (OR, 5.94; p=0.001), and the presence of septum (OR, 6.43; p=0.018), atelectasis (OR, 6.83; p=0.002), or air (OR, 9.90; p=0.002) in pleural fluid were significantly higher in the CPPE/empyema group than in the PPE group. On multivariate analysis, only the split pleura sign (hazard ratio (HR), 6.70; 95% confidence interval (CI), 1.91-23.5; p=0.003) and total amount of pleural effusion (>/=30 mm) on thoracic CT (HR, 7.48; 95%CI, 1.76-31.8; p=0.006) were risk factors for empyema. Sensitivity, specificity, positive predictive value, and negative predictive value of the presence of both split pleura sign and total amount of pleural effusion (>/=30 mm) on thoracic CT for CPPE/empyema were 79.4%, 80.9%, 75%, and 84.4%, respectively, with an area under the curve of 0.801 on receiver operating characteristic curve analysis.	2

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
80. McLoud TC, Flower CD. Imaging the pleura: sonography, CT, and MR imaging. AJR Am J Roentgenol. 1991;156(6):1145-1153.	Review/Other-Dx	N/A	To evaluate the pleura and the pleural space.	No results stated in abstract.	4
81. Inan N, Sarisoy HT, Cam I, Sakci Z, Arslan A. Diffusion-weighted Magnetic Resonance Imaging in the Differential Diagnosis of Benign and Metastatic Malignant Pleural Thickening. J Thorac Imaging. 2016;31(1):37-42.	Observational-Dx	42 patients	To investigate the value of diffusion-weighted (DW) imaging in the differential diagnosis of benign and metastatic malignant pleural thickening.	Quantitatively, differences in signal intensities on DW trace images with b factors of 650 and 1000 mm/s were not statistically significant. The apparent diffusion coefficient (ADC)1 and ADC2 of the metastatic malignant thickening were significantly lower than those of benign ones [mean ADC1 was 1.37+/-0.65x10 mm/s for metastatic malignant thickening and 2.11+/-0.69x10 mm/s for benign thickening (P=0.045); ADC2 was 1.06+/-0.56x10 mm/s for metastatic malignant thickening and 1.56+/-0.71x10 mm/s for benign thickening (P=0.038)]. However, because of the ADC overlap between malignant and benign disease, a sufficiently discriminative cutoff value could not be defined by the receiver operating characteristic curve analysis.	2
82. Rinaldi P, Parapatt GK, Giuliani M, et al. Chest and breast MRI: the added value of a fast imaging for a new diagnostic approach in the planning of augmentation surgery in patients with thoracic asymmetries. Eur Rev Med Pharmacol Sci. 2015;19(13):2359-2367.	Observational-Dx	13 patients	To evaluate breast and chest wall asymmetry, and considers the feasibility of preoperative measurements which are useful for performing an objective preoperative evaluation.	All patients showed some degree of left-right side asymmetry on specific thoracic, breast and implant measurements. Magnetic Resonance Imaging (MRI) provided detailed and objective data.	3

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
83. Svigals PZ, Chopra A, Ravenel JG, Nietert PJ, Huggins JT. The accuracy of pleural ultrasonography in diagnosing complicated parapneumonic pleural effusions. Thorax. 72(1):94-95, 2017 01.	Observational-Dx	66 patients	To determine radiographic complexity in predicting a complicated parapneumonic effusion (CPPE) defined by pleural fluid analysis.	Pleural ultrasound had a sensitivity of 69.2% (95% CI 48.2% to 85.7%) and specificity of 90.0% (95% CI 76.3% to 97.2%). Chest computed tomography (CT) had a sensitivity of 76.9% (95% CI 56.3% to 91.0%) and specificity of 65.0% (95% CI 48.3% to 79.4%). Chest radiograph (CXR) had a sensitivity of 61.5% (95% CI 40.6% to 79.8%) and specificity of 60.0% (95% CI 43.3% to 75.1%).	3
84. Tsai T-H, Jerng J-S, Yang P-C. Clinical Applications of Transthoracic Ultrasound in Chest Medicine. Journal of Medical Ultrasound. 2008;16(1):7-25.	Review/Other-Dx	N/A	To present the general techniques and wide applications of transthoracic ultrasound (US) and US-guided invasive procedures in the diagnosis and management of various chest diseases.	No results stated in abstract.	4
85. Verhey PT, Gosselin MV, Primack SL, Kraemer AC. Differentiating diaphragmatic paralysis and eventration. Acad Radiol. 2007;14(4):420-425.	Observational-Dx	32 patients	To qualitatively and quantitatively measure the utility of chest radiography in determining the presence or absence of diaphragmatic paralysis in patients with an elevated diaphragm.	Of 32 patients with elevated diaphragm on chest radiograph, 17 had diaphragmatic paralysis confirmed with fluoroscopic sniff test. Our results indicate that the radius of curvature or shape of the diaphragm on lateral chest radiograph is the most important factor for detection of the presence or absence of diaphragmatic paralysis. HH/APD > 0.28 suggests against paralysis.	2
86. Nason LK, Walker CM, McNeeley MF, Burivong W, Fligner CL, Godwin JD. Imaging of the diaphragm: anatomy and function. Radiographics. 2012;32(2):E51-70.	Review/Other-Dx	N/A	To review the Imaging of the diaphragm: anatomy and function	No results stated in abstract.	4

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
87. Saltiel RV, Grams ST, Pedrini A, Paulin E. High reliability of measure of diaphragmatic mobility by radiographic method in healthy individuals. Braz J Phys Ther. 2013;17(2):128-136.	Observational-Dx	42 patients	To analyze the reliability of radiographic measurement as a method for assessing the mobility of the left and right hemidiaphragms.	In the analysis of intra-observer reproducibility in radiographic evaluations of the left and right hemidiaphragms, ICC[2,1] indicated a "very high correlation" for both observer A (ICC[2,1] = 0.99, p <0.001 and ICC[2,1] = 0.97, p <0.001, respectively) and observer B (ICC[2,1] = 0.99, p <0.001 and ICC[2,1] = 0.99 p <0.001, respectively). In the analysis of interobserver reproducibility, the ICC[2,1] indicated a "very high correlation" for the 1st and 2nd radiographic evaluations of the right hemidiaphragm (ICC[2,1] = 0.98 and ICC[2,1] = 0,99, respectively, p <0.001) and left hemidiaphragm (ICC[2,1] = 0.98 and ICC[2,1] = 0.99, respectively, p <0.001).	2
88. Kiryu S, Loring SH, Mori Y, Rofsky NM, Hatabu H, Takahashi M. Quantitative analysis of the velocity and synchronicity of diaphragmatic motion: dynamic MRI in different postures. Magn Reson Imaging. 2006;24(10):1325-1332.	Observational-Dx	8 healthy men	To assess the relationship between right and left hemidiaphragmatic motions during breathing in normal subjects and to investigate alterations in lung motion with changes in posture, using dynamic magnetic resonance (MR) imaging.	Excursion was greater in the right hemidiaphragm in most postures, except the left lateral decubitus. In supine and prone postures, both hemidiaphragms moved synchronously in both inspiratory and expiratory phases. In both lateral decubitus postures, the hemidiaphragms moved asynchronously with different velocities in the expiratory phase but with the same velocities in the inspiratory phase.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
89. Mogalle K, Perez-Rovira A, Ciet P, et al. Quantification of Diaphragm Mechanics in Pompe Disease Using Dynamic 3D MRI. PLoS One. 2016;11(7):e0158912.	Observational-Dx	10 Pompe patients; 6 controls	To investigate the suitability of dynamic magnetic resonance (MR) imaging in combination with state-of-the-art image analysis methods to assess respiratory muscle weakness.	Results in 16 3D+t MRI scans (10 Pompe patients and 6 controls) of a slow expiratory maneuver show that kinematic analysis from dynamic 3D images reveals important additional information about diaphragm mechanics and respiratory muscle involvement when compared to conventional pulmonary function tests. Pompe patients with severely reduced pulmonary function showed severe diaphragm weakness presented by minimal motion of the diaphragm. In patients with moderately reduced pulmonary function, cranial displacement of posterior diaphragm parts was reduced and the diaphragm dome was oriented more horizontally at full inspiration compared to healthy controls.	3
90. Noh DK, Lee JJ, You JH. Diaphragm breathing movement measurement using ultrasound and radiographic imaging: a concurrent validity. Biomed Mater Eng. 2014;24(1):947-952.	Observational-Dx	14 patients	To validate the accuracy of ultrasound imaging measurements of diaphragm movements by concurrently comparing these measurements to the gold standard of radiographic imaging measurements.	Pearson correlation analysis showed strong correlations, ranging from r=0.78 to r=0.83, between ultrasound and radiographic imaging measurements of the diaphragm during inhalation, exhalation, and excursion. These findings suggest that ultrasound imaging measurement is useful to accurately evaluate diaphragm movements during tidal breathing.	3
91. Sarwal A, Walker FO, Cartwright MS. Neuromuscular ultrasound for evaluation of the diaphragm. Muscle Nerve. 2013;47(3):319-329.	Review/Other-Dx	N/A	To review different techniques for assessing the diaphragm using neuromuscular ultrasound and the application of these techniques to enhance diagnosis and prognosis by neuromuscular clinicians.	No results stated in abstract.	4

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
92. Boon AJ, Sekiguchi H, Harper CJ, et al. Sensitivity and specificity of diagnostic ultrasound in the diagnosis of phrenic neuropathy. Neurology. 83(14):1264-70, 2014 Sep 30.	Observational-Dx	82 patients	To determine the sensitivity and specificity of B-mode ultrasound in the diagnosis of neuromuscular diaphragmatic dysfunction, including phrenic neuropathy.	Of 82 patients recruited over a 2-year period, 66 were enrolled in the study. Sixteen patients were excluded because of inconclusive or insufficient reference testing. One hemidiaphragm could not be adequately visualized; therefore, hemidiaphragm assessment was conducted in a total of 131 hemidiaphragms in 66 patients. Of the 82 abnormal hemidiaphragms, 76 had abnormal sonographic findings (atrophy or decreased contractility). Of the 49 normal hemidiaphragms, none had a false-positive ultrasound. Diaphragmatic ultrasound was 93% sensitive and 100% specific for the diagnosis of neuromuscular diaphragmatic dysfunction.	2
93. Fantini R, Mandrioli J, Zona S, et al. Ultrasound assessment of diaphragmatic function in patients with amyotrophic lateral sclerosis. Respirology. 2016;21(5):932-938.	Observational-Dx	41 patients	To assess whether diaphragmatic thickness measured by ultrasound (US) correlates with lung function impairment in Amyotrophic Lateral Sclerosis (ALS) patients. The secondary aim was then to compare US diaphragm thickness index (DeltaTdi) with a new parameter (DeltaTmax index).	DeltaTdiTLC ($p < 0.001$) and DeltaTmax ($p = 0.007$), but not DeltaTdiVt, differed between patients and controls. Significant correlation ($p < 0.05$) was found between DeltaTdiTLC, DeltaTmax and forced vital capacity (FVC). The ROC curve analysis for comparison of individual testing showed better accuracy with Deltatmax than with DeltatdiTLC for FVC (AUC 0.76 and 0.27) and sniff nasal inspiratory pressure (SNIP) (AUC 0.71 and 0.25).	2

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
94. Hiwatani Y, Sakata M, Miwa H. Ultrasonography of the diaphragm in amyotrophic lateral sclerosis: clinical significance in assessment of respiratory functions. Amyotroph Lateral Scler Frontotemporal Degener. 2013;14(2):127-131.	Observational-Dx	36 patients	To evaluate diaphragm thicknesses during respiration by ultrasonography, and compare with conventional measurements of respiratory functions in patients with amyotrophic lateral sclerosis (ALS).	The diaphragm was clearly identifiable by ultrasonography. Maximal diaphragm thickness during the maximal inspiratory effort (DTmax) , minimum diaphragm thickness at the end expiratory position (DTmin) and the thickening ratio (TR) were all significantly decreased in ALS patients with %VC (vital capacity) < 80, compared with those in either ALS patients with %VC >/= 80 or healthy controls. DTmax, DTmin and the TR were all significantly correlated with %VC. In addition, significant inverse correlations were found between all three parameters and pCO(2). The inter-observer reliability of measurements of diaphragm thickness was high.	3
95. O'Gorman CM, O'Brien T G, Boon AJ. Utility Of diaphragm ultrasound in myopathy. Muscle Nerve. 2017;55(3):427-429.	Observational-Dx	19 cases	To evaluate ultrasound (US) of diaphragm thickness and contractility is an effective tool in neurogenic diaphragm dysfunction.	There were 19 eligible cases, of which 14 (73.7%) had abnormal US findings. Mean diaphragm thickness was 0.12 cm (SD 0.10), and the mean thickening ratio was 1.29 (SD 0.35). In all cases with abnormal US evaluation, the thickening ratio was abnormal. There were no cases with abnormal thickness alone.	3
96. Baria MR, Shahgholi L, Sorenson EJ, et al. B-mode ultrasound assessment of diaphragm structure and function in patients with COPD. Chest. 2014;146(3):680-685.	Observational-Dx	50 COPD patients; 150 control subjects	To determine the diaphragm muscle thickness and thickening ratio in patients with chronic obstructive pulmonary disease(COPD)compared with normal control subjects.	There was no significant difference in diaphragm thickness or thickening ratio between sides within groups (control subjects or patients with COPD) or between groups, with the exception of the subgroup with severe air trapping (residual volume > 200%), in which the only difference was that the thickening ratio was higher on the left (P = .0045).	3

Chronic Dyspnea-Noncardiovascular Origin
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
97. Carrie C, Bonnardel E, Vally R, Revel P, Marthan R. Vital Capacity Impairment due to Neuromuscular Disease and its Correlation with Diaphragmatic Ultrasound: A Preliminary Study. Ultrasound Med Biol. 2016;42(1):143-149.	Observational-Dx	47 patients	To evaluate the correlation between diaphragmatic excursion measured by a right sub-costal ultrasound approach and forced vital capacity in patients with amyotrophic lateral sclerosis (ALS) or myotonic dystrophy (MD).	There was a significant correlation between EDEmax values and forced vital capacity (FVC) values (r = 0.68 [0.46-0.90], p < 0.0001) and between EDEmax values and percentage of predicted FVC values (r = 0.75 [0.55-0.95], p < 0.0001). At a threshold of EDEmax < 5.5 cm, the sensitivity and specificity of ultrasonic diaphragmatic excursion in predicting FVC </= 50% of theoretical values were 100% [66%-100%] and 69% [52%-84%] respectively, without any significant difference between males and females. There was no statistical correlation between maximal inspiratory pressure and Esniff.	2
98. Noda Y, Sekiguchi K, Kohara N, Kanda F, Toda T. Ultrasonographic diaphragm thickness correlates with compound muscle action potential amplitude and forced vital capacity. Muscle Nerve. 2016;53(4):522-527.	Observational-Dx	36 patients; 10 controls	To determine the utility of ultrasonography (USG) for evaluating diaphragm dysfunction in patients with neuromuscular disorders such as motor neuron disease, myopathy, and other disorders of varying etiology.	Diaphragm thickness was significantly correlated with forced vital capacity (FVC) (r = 0.74) and compound muscle action potentials (CMAP) amplitude (r = 0.53).	3
99. Pinto S, Alves P, Pimentel B, Swash M, de Carvalho M. Ultrasound for assessment of diaphragm in ALS. Clin Neurophysiol. 2016;127(1):892-897.	Observational-Dx	42 patients	To evaluate the correlation between diaphragm thickness assessed by ultrasound (US) with respiratory function tests and the diaphragm motor responses, in patients with amyotrophic lateral sclerosis (ALS).	The mean age at disease onset was 58.4 +/- 11.1 years and with a mean disease duration of 17.8 +/- 13.6 months. Ultrasound studies of diaphragm thickness in full inspiration correlated with diaphragm compound muscle action potential (CMAP) in the whole population and in spinal-onset patients; and were similar in the two groups. Multiple linear modelling showed that forced vital capacity (FVC), SNIP and maximal voluntary ventilation (MVV) were dependent on the change of thickness (p=0.001, 0.001 and 0.020, respectively) and that maximal inspiratory (MIP) and maximal expiratory (MEP) were related to diaphragm CMAP p=0.003 and p=0.025, respectively).	2

Chronic Dyspnea-Noncardiovascular Origin
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
100. Santana PV, Prina E, Albuquerque AL, Carvalho CR, Caruso P. Identifying decreased diaphragmatic mobility and diaphragm thickening in interstitial lung disease: the utility of ultrasound imaging. J Bras Pneumol. 2016;42(2):88-94.	Observational-Dx	40 ILD patients; 16 healthy volunteers	To investigate the applicability of ultrasound imaging of the diaphragm in interstitial lung disease (ILD).	Between the ILD patients (n = 40) and the controls (n = 16), mean diaphragmatic mobility was comparable during quiet breathing, although it was significantly lower in the patients during deep breathing (4.5 +/- 1.7 cm vs. 7.6 +/- 1.4 cm; p < 0.01). The patients showed greater diaphragm thickness at functional residual capacity (FRC) (p = 0.05), although, due to lower diaphragm thickness at total lung capacity (TLC), they also showed a lower thickening fraction (TF) (p < 0.01). The forced vital capacity (FVC) as a percentage of the predicted value (FVC%) correlated with diaphragmatic mobility (r = 0.73; p < 0.01), and an FVC% cut-off value of < 60% presented high sensitivity (92%) and specificity (81%) for indentifying decreased diaphragmatic mobility.	3
101. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: https://www.acr.org/-/media/ACR/Files/Appropriateness-Criteria/RadiationDoseAssessmentIntro.pdf.	Review/Other-Dx	N/A	Guidance document on exposure of patients to ionizing radiation.	No results stated in abstract.	4

Evidence Table Key

Study Quality Category Definitions

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

Abbreviations Key

Dx = Diagnostic

Tx = Treatment