Assessment of breathlessness: a pulmonologist's perspective – short of breath, but not short of answers

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Breathlessness is a complex symptom requiring a systematic approach. We propose a tiered system of history and static tests followed by dynamic investigation if the diagnosis remains unclear. https://bit.ly/4hj7NEt

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Abstract
Breathlessness, or dyspnoea, is a complex symptom influenced by respiratory, cardiovascular and neural mechanisms, necessitating a systematic and tiered approach for accurate diagnosis and effective management. This review presents a structured, three-tier diagnostic framework, comprising history-taking, static testing (such as pulmonary function tests and thoracic imaging), and dynamic testing (*e.g.*, 6-minute walk test and cardiopulmonary exercise testing) for comprehensive assessment. Each tier is designed to progressively investigate and characterise underlying conditions. This framework is specifically tailored for use in an outpatient general respiratory clinic setting, where clinicians evaluate chronic or unexplained dyspnoea in non-acute patients. Literature and guidelines support this approach, highlighting the importance of combining clinical examination, imaging, laboratory testing and dynamic assessments to capture both static and exertional components of dyspnoea. Emphasising a patient-centred approach, this framework aims to improve diagnostic accuracy and guide targeted therapeutic interventions.

Educational aims
The aim of this narrative review is to provide a comprehensive framework for healthcare professionals, particularly pulmonologists, in the assessment and management of dyspnoea. The text seeks to enhance the accuracy of diagnosis and the effectiveness of treatment plans for patients experiencing breathlessness by outlining a systematic approach that includes detailed history-taking, physical examination and the use of various diagnostic tools. The step-by-step exploration of different tiers of investigation equips physicians with the knowledge and skills to identify the underlying causes of dyspnoea and to tailor interventions accordingly. Furthermore, the text emphasises the importance of integrating multiple diagnostic modalities – ranging from pulmonary function tests to advanced imaging and dynamic assessments – to capture the multifaceted nature of dyspnoea. It aims to educate physicians on the significance of selecting appropriate diagnostic tools based on the patient's unique presentation, thus ensuring a more targeted and patient-centred approach to care. By combining theoretical knowledge with practical guidelines, the text aspires to elevate the standard of care provided to patients with dyspnoea, ultimately improving their clinical outcomes.

Introduction
Dyspnoea, or breathlessness, is a complex symptom with multiple potential causes, making thorough assessment essential for accurate diagnosis and effective management. This framework provides clinicians with a structured approach, emphasising the importance of detailed history-taking, physical examination and diagnostic tests. A three-tier system for assessing dyspnoea is proposed (figure 1) with investigations sequenced as follows:

- Tier 1: history
- Tier 2: static tests
- Tier 3: dynamic tests

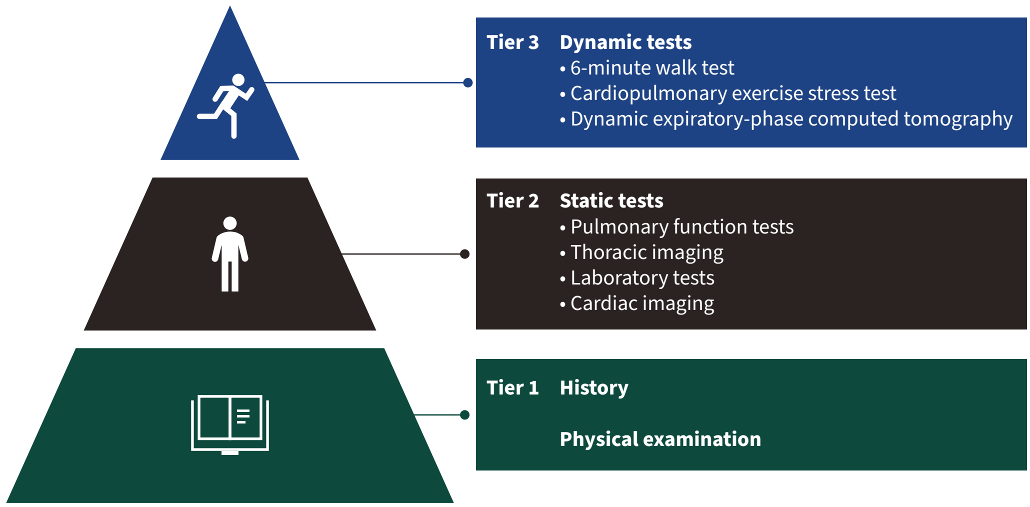

FIGURE 1 Proposed three-tier system for assessing dyspnoea.

This review focuses on the assessment of dyspnoea in an outpatient general respiratory clinic setting, where clinicians encounter patients with chronic or unexplained breathlessness requiring systematic evaluation. Dyspnoea is challenging to define precisely, with multiple definitions, acknowledging its subjective nature. The most widely accepted definition is the 1999 American Thoracic Society (ATS) consensus statement: "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity" [1]. Breathlessness arises from complex interactions among the respiratory, cardiovascular and nervous systems, as well as peripheral receptors [2]. Key mechanisms include chemoreceptor and mechanoreceptor stimulation, which respond to changes in blood gases and mechanical lung changes [3–5]. Cortical factors, such as anxiety, and respiratory muscle dysfunction further contribute to the perception of breathlessness [6]. Given the complex aetiology of breathlessness, it is unsurprising that not all experiences of dyspnoea are the same; different underlying causes can lead to distinct perceptions [7]. Evaluating a patient referred for breathlessness requires a structured approach, with a thorough medical history forming the foundation for further assessment.

Tier 1: history

History taking is paramount in the assessment of dyspnoea, as it allows for a thorough understanding of the patient's symptoms and their relationship to potential underlying causes. By exploring the onset, progression and associated factors, physicians can form a more accurate clinical picture. Some key components of a comprehensive respiratory history are highlighted below.

Onset and duration

Understanding the timeline of symptom development is crucial for diagnosing respiratory conditions. Acute dyspnoea, arising within minutes to hours, may indicate life-threatening issues such as pulmonary embolism, pneumothorax or an asthma exacerbation. In contrast, chronic dyspnoea developing over months or years often points to an underlying chronic disease. The age at onset can also help differentiate between different conditions. Additionally, variations in dyspnoea severity, whether day-to-day, within a single day, or worsening at night, can provide important insights, particularly in conditions like asthma. When assessing breathlessness, noting the symptom onset and any coinciding medical or stressful life events can offer valuable context for diagnosis and management.

Description

Different descriptions of breathlessness can point to specific underlying conditions.

Breathlessness, much like pain, is a multidimensional symptom; what "shortness of breath" means to you may differ from your patient's experience. Probing further to clarify what the patient feels, such as for example chest tightness, air hunger, a sense of increased work of breathing or an inability to take a full breath can prove helpful. Chest tightness can signal bronchoconstriction [7], while terms like "air hunger" or "gasping" may relate to dynamic hyperinflation [8, 9] or restrictive lung disease [10]. An unsatisfying breath, frequent yawning, or excessive sighing may suggest an underlying breathing pattern disorder, particularly if further testing is normal [11]. Understanding the patient's experience is crucial in delivering patient-centred care. In a recent study evaluating the sensitivity and specificity of 15 different descriptors of dyspnoea, it was shown that "My chest feels tight" had an 88% specificity for asthma, while "My breathing is shallow" had 84% specificity for interstitial lung disease (ILD) [12]. When probing for a more nuanced description of how the patient perceives breathlessness, it is important to consider any linguistic or cultural differences as these may affect how a symptom is presented [13]. Medical jargon and lay language often overlap in terms like "wheezy" and "chesty", commonly used by both patients and physicians during consultations. It is crucial not to assume that a patient's interpretation of these terms matches your own.

Triggers and relievers
Identifying factors that exacerbate or alleviate dyspnoea is critical in diagnosis. Orthopnoea, breathlessness when lying flat, is a classic sign of heart failure. Relief with bronchodilators may suggest obstructive airway disease. However, the time between bronchodilator use and symptom relief can be telling – immediate relief might indicate the cessation of activity rather than the medication's effectiveness, while delayed relief after hours could simply reflect the passage of time. Immediate reactions to strong smells, such as perfume or bleach, have been linked with asthma, but these triggers should prompt consideration of a laryngeal origin to the patient's symptoms [14].

Associated symptoms
The presence of other symptoms such as chest pain, cough, haemoptysis, fever or weight loss can narrow down possible diagnoses. A productive cough with purulent sputum may suggest a respiratory infection or a COPD exacerbation, while haemoptysis could indicate a pulmonary embolism or lung cancer. Other associated symptoms may include wheezing, palpitations or pre-syncope, which could suggest cardiac origins.

Impact on daily life
Evaluating how breathlessness impacts daily activities, work and sleep provides critical insights into the severity of the condition and its effect on a patient's quality of life. This can also help prioritise the urgency of medical interventions. Symptom burden can be measured with tools like the modified Medical Research Council (mMRC) scale, which is useful for tracking patient progress [15]. It is important to consider the patient's baseline activity levels, as athletic individuals may notice a reduction in exercise tolerance but still score well on scores like the mMRC and patients who lead a sedentary life may underreport symptoms due to a lack of overall activity during their daily life.

However, obtaining a detailed history of breathlessness – including its effect on daily activities, functional limitations and coping mechanisms – is essential to capturing its full impact beyond structured scales. Understanding how patients subjectively experience and manage breathlessness allows for tailored interventions; for instance, the approach for a patient struggling with dyspnoea during basic self-care activities like dressing, washing and toileting will differ significantly from that for someone who experiences breathlessness only during strenuous exertion, such as fast hill walking.

Medical, social and family history
A detailed medical history, including previous diagnoses, medication use, smoking history and exposure to environmental toxins, is essential in diagnosing dyspnoea. For example, a prospective observational study, evaluating an algorithmic approach to chronic dyspnoea in 123 patients, demonstrated that a history of smoking has a negative predictive value of up to 100% for COPD, and although it had a low positive predictive value of 40%, they did find that no patient with <10-pack-year history had COPD [16].

By the time patients are referred to a respiratory specialist, many will already have trialled inhaled therapy. It is crucial to assess inhaler technique, adherence and response to treatment. Bronchodilator responsiveness can also provide important information, with significant reversibility suggesting asthma, while minimal response may indicate fixed airflow obstruction due to COPD or an alternative cause of dyspnoea. Furthermore, evaluating strategies used during acute breathlessness episodes, such as short-acting bronchodilators or non-invasive ventilation, provides valuable insights into disease severity and management needs.

A family history of respiratory or cardiac disease may offer important diagnostic clues. Additionally, involving caregivers in discussions about breathlessness management can enhance patient support, improve adherence to care plans and reduce anxiety during acute episodes [17].

Psychosocial factors

Psychological factors such as anxiety, depression and panic disorders can significantly affect the perception of breathlessness [18]. Understanding the patient's mental health and stress levels at the time of assessment and during symptom onset is crucial for a holistic approach to treatment. Furthermore, severe dyspnoea episodes, particularly those associated with acute respiratory distress and mechanical ventilation, have been shown to activate brain regions involved in post-traumatic stress disorder development, contributing to long-term psychological distress, including intrusive symptoms and avoidance behaviours [19].

Dyspnoea assessment tools

Dyspnoea assessment tools can be used as an adjunct to history taking to help evaluate the severity of dyspnoea. In the 2012 updated ATS consensus statement on dyspnoea, they categorised dyspnoea assessment tools into three primary domains [20].

The first domain is the "sensory–perceptual experience", which assesses the sensation of breathing from the perspective of the patient. This can be evaluated using single-item intensity ratings, like the Borg scale, where patients score their perceived exertion from 1–10 with descriptors ranging from very light activity to maximum effort activity or a similar visual analogue scale, as well as through descriptors of particular sensations or groups of related sensations.

The second domain is "affective distress", focusing on how distressing the act of breathing is perceived to be. This includes immediate feelings of panic and helplessness, and addressing these emotional responses may prevent further exacerbation of their symptoms.

The third domain, "symptom impact", assesses how dyspnoea impacts a person's functional ability, activities of daily living, or overall health. This allows for targeted and realistic goals in programmes such as pulmonary rehabilitation or can help identify occupational therapy targets to allow for a better quality of life.

The number and diversity of dyspnoea-assessment tools makes it challenging to comprehensively compare their effectiveness. However, a systematic review by Bausewein *et al*. [21] of 35 dyspnoea-assessment tools failed to identify a single scale that could "accurately reflect the far-reaching effects of breathlessness". They advised combining multiple dyspnoea assessment tools to cover all domains.

The tool selected by a physician during a review should be based on a careful assessment of how well the questionnaire content aligns with the specific domains of dyspnoea that are most relevant to the patient's experience. To monitor progression of symptoms and to guide further investigations, the domain assessed and the individual item scores should be accurately recorded. Furthermore, the time frame of assessment is also important to record as this can influence accuracy, this can be at the present moment of the review (such an asthma exacerbation), the recent past (such as a recently resolved COPD exacerbation), or short-term recall of a specific event (such as how breathing felt during a period of strenuous activity).

Physical examination

Physical examination in patients with dyspnoea helps differentiate amongst causes, evaluate severity, and guides management.

Inspection is the first step, where clinicians observe the patient's appearance, breathing pattern and effort. Signs such as accessory muscle use may suggest respiratory or cardiac causes; for example, patients with severe COPD often adopt a "tripod" posture and pursed-lip breathing, which improves diaphragm function and respiratory mechanics. Examining extremities may reveal clues like tar staining, cyanosis or clubbing. Volume status can be assessed through peripheral oedema and jugular venous distension, while signs of neuromuscular disorders (*e.g.*, muscle wasting) or chest wall deformities (*e.g.*, scoliosis) may indicate restrictive lung disease. Body mass index is also relevant, as deconditioning is a common contributor to dyspnoea.

Palpation and percussion provide further diagnostic information. Palpation can detect chest wall deformity or tenderness, which may indicate rib fracture, while percussion may reveal dullness, suggestive of pleural effusion or lobar pneumonia, or hyperresonance, indicative of pneumothorax.

Auscultation delivers direct insights into respiratory and cardiovascular function. Abnormal lung sounds like wheezes, crackles or stridor signal specific pathologies. Wheezes reflect airflow through narrowed, smaller airways, while rhonchi suggest larger airway obstruction. Crackles are caused by the sudden opening of small airways and are categorised as coarse (often seen in pneumonia or bronchiectasis) or fine (indicative of pulmonary oedema or fibrosis). Stridor, a high-pitched sound on inspiration, is often a sign of upper airway obstruction. Cardiac auscultation may reveal murmurs or abnormal sounds, such as gallops or rubs, indicating potential valvular disease or heart failure.

Finally, vital signs – respiratory rate, heart rate, blood pressure and oxygen saturation – are essential for assessing dyspnoea severity. Tachycardia or tachypnoea may be compensatory responses to hypoxaemia.

Tier 1 conclusion

Several studies over the past decades have highlighted the importance of history and physical examination in diagnosing a cause for dyspnoea. Notably, PRATTER *et al*. [22], in a prospective study of 85 patients with dyspnoea, found that in 66% of cases a diagnosis could be determined based on these clinical methods alone. These findings underscore the necessity for physicians to prioritise thorough history taking and physical examination during initial consultations to avoid unnecessary tests and delays in diagnosis.

Tier 2: static tests

Pulmonary function tests

Pulmonary function tests (PFTs) are essential in evaluating dyspnoea, providing critical information on lung function parameters like airflow, lung volumes and diffusion capacity. These measurements help distinguish between obstructive and restrictive lung diseases. Key spirometry metrics include forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC). The FEV_1 to FVC ratio is fundamental in diagnosing obstructive diseases such as COPD and asthma, where this ratio is typically reduced. Historically, asthma was thought to frequently show significant improvement after bronchodilator use, a hallmark of its reversibility. In contrast, COPD generally presents with persistent airflow obstruction that is not fully reversible, even after bronchodilator administration. The 2024 update of the Global Strategy for Asthma Management and Prevention provides guidelines for spirometric measurements in asthma. They advise that a post-bronchodilator increase in $FEV_1 \geqslant 12\%$ and 200 mL from baseline is typical for asthma but may not be present when asthma is well-controlled. They also report that this degree of reversibility is commonly seen in COPD when there is a decreased FEV_1. However, a post bronchodilator increase in $FEV_1 > 12\%$ and 400 mL from baseline is highly probable for asthma and uncommon in COPD [23].

Since bronchodilator responsiveness may be absent in some asthma patients and present in some COPD patients, further evaluation with diffusion capacity of the lung for carbon monoxide (D_{LCO}) and measurement of fractional exhaled nitric oxide can help further identify treatable traits such as emphysema or type 2 inflammation in patients with obstructive lung disease.

Analysis of the flow–volume loop in spirometry can reveal underlying causes of breathlessness. In addition to indicating airflow obstruction, flow–volume loops can suggest restrictive lung disease through a normal shape with reduced volumes, upper airway obstructions through early plateauing of the inspiratory or expiratory limbs and conditions like excessive dynamic airway collapse, often demonstrating saw-toothing of the expiratory limb.

Lung volume measurement through plethysmography or gas dilution provides valuable insights into both obstructive and restrictive lung diseases. In obstructive disease, residual volume, total lung capacity (TLC), and functional residual capacity are often elevated, especially in emphysema, identifying patients who might benefit from lung volume reduction. In restrictive lung disease, TLC is reduced due to decreased lung compliance, leading to a lower FVC while the FEV_1/FVC ratio typically remains normal or elevated. TLC is calculated as the sum of functional residual capacity and inspiratory capacity.

Another key aspect of PFTs is the D_{LCO}, which assesses gas transfer efficiency in the lungs. A reduced D_{LCO} suggests issues at the alveolar–capillary interface and is commonly found in conditions like interstitial lung disease (ILD), emphysema and pulmonary vascular diseases.

In addition to helping establish a diagnosis, these tests also allow for monitoring the progression of chronic lung conditions. In a study by TZANAKIS *et al*. [24] that evaluated the correlation of dyspnoea scale scores with PFTs in patients with idiopathic pulmonary fibrosis, they reported lung volumes (FVC and TLC) correlated significantly with the Saint George's Respiratory Questionnaire and all dyspnoea scales (Borg, oxygen-cost diagram and mMRC) showed a significant correlation with diffusion capacity. Regular assessment of lung function helps in tailoring treatment strategies and assessing the response to therapy.

Whilst spirometry, lung volumes and D_{LCO} provide comprehensive information on lung function, their interpretation can be complex. In a recent UK-based study, approximately 30% of patients diagnosed with

COPD in primary care had PFTs that were not consistent with obstructive airway disease [25]. Interpreting PFTs requires a comprehensive view of the patient's overall clinical picture, incorporating history, physical examination and other diagnostic findings. If there are mild or non-specific abnormalities on PFTs and they do not align with the patient's symptoms, it follows that treating these findings alone may not resolve their symptoms. Effective management hinges on identifying the true cause of symptoms to ensure targeted, meaningful interventions.

Thoracic imaging

Thoracic imaging is essential for evaluating breathlessness, revealing structural abnormalities in the lungs, pleura and surrounding tissues.

A chest radiography, typically the first imaging step, can identify conditions like pneumonia, pleural effusion, pneumothorax, pulmonary oedema and masses.

Computed tomography (CT) scans offer detailed imaging, aiding in the diagnosis of emphysema, ILD, pulmonary embolism, lung cancer and pleural diseases. A recent multicentre prospective study found that cross-sectional imaging altered the primary diagnosis in 42% of emergency department patients presenting with dyspnoea or chest pain by confirming or ruling-out 95% of alternate diagnoses [26]. High-resolution CT is the gold standard for assessing ILD, identifying patterns such as bronchiectasis, honeycombing, ground-glass opacities, cysts and nodularity. A 2011 joint consensus by the ATS, European Respiratory Society (ERS), Japanese Respiratory Society and Asociación Latinoamericana de Tórax updated diagnostic criteria for idiopathic pulmonary fibrosis, allowing diagnosis without biopsy if high-resolution CT shows a definitive usual interstitial pneumonia pattern [27].

Ventilation–perfusion scanning assesses lung ventilation and perfusion and is particularly useful for diagnosing pulmonary embolism, where ventilation–perfusion mismatch can indicate emboli. The 2022 European Society of Cardiology/ERS Guidelines recommend a ventilation–perfusion scan as the first-line imaging for chronic thromboembolic pulmonary hypertension, with a sensitivity of 96–97% and specificity of 90–95% [28].

Laboratory tests

Laboratory tests are crucial initial investigation in the evaluation of the underlying causes of dyspnoea.

Arterial blood gases provide essential information on oxygenation, ventilation and acid–base status. Severe respiratory conditions commonly present with respiratory failure, characterised by hypoxaemia, with or without hypercapnia. Arterial blood gases differentiate Type 1 from Type 2 respiratory failure and guide oxygenation and ventilation needs. The A–a gradient (alveolar–arterial gradient) measures the difference between alveolar (P_{AO_2}) and arterial (P_{aO_2}) oxygen levels: A–a gradient=((F_{IO_2})×(atmospheric pressure − H_2O pressure) − (P_{aCO_2}/0.8)) − P_{aO_2}. It can be used to differentiate between the five mechanistic causes of hypoxia (table 1). Arterial blood gases can confirm extrapulmonary dyspnoea causes, such as Kussmaul breathing from metabolic acidosis or rare conditions like methaemoglobinaemia.

A full blood count can be useful in evaluating patients with breathlessness. Anaemia will reduce the oxygen carrying capacity, increased white blood cell count may suggest an underlying infection and eosinophils are important in obstructive lung disease, indicating type-2 inflammation, a well-established treatment target in asthma. Recent evidence shows that blood eosinophil counts can guide therapy in COPD, as patients with eosinophilia (>300 cells·μL^{-1}) respond better to inhaled corticosteroids in combination with long-acting bronchodilators, with a symptomatic improvement and reduced exacerbations [29].

TABLE 1 Causes of hypoxia

	Alveolar–arterial oxygen gradient	Corrected with increased inspiratory oxygen fraction
Ventilation–perfusion mismatch	Elevated	Yes
Right-to-left shunt	Elevated	Limited
Diffusion impairment	Elevated	Yes
Alveolar hypoventilation	Normal	Yes
Decreased partial pressure of oxygen	Normal	Yes

Alpha-one antitrypsin levels should be checked in patients diagnosed with COPD. Augmentation therapy can significantly improve survival by slowing disease progression, especially if started before severe damage has occurred [30].

Elevated levels of B-type natriuretic peptide (BNP) are typically indicative of heart failure and troponin is a key marker for myocardial infarction. However, elevated BNP and troponin levels may be seen with large pulmonary emboli or advanced pulmonary hypertension.

D-dimer, a fibrin degradation product, is elevated in thrombotic conditions such as pulmonary embolism. While a negative D-dimer has a high negative predictive value in low-risk patients, it is not definitive. A post-hoc analysis of six studies involving 7268 patients found that D-dimer levels below 750 $\mu g \cdot L^{-1}$ had a negative predictive value of 79–96% [31]. This underscores that, despite its utility, a negative D-dimer alone cannot reliably exclude venous thromboembolism and must be interpreted within the broader clinical context, considering risk factors and clinical findings.

Cardiac imaging

Echocardiography is vital for assessing cardiac causes of breathlessness, evaluating ventricular function, valvular disease and markers of pulmonary hypertension. Agitated saline administration can confirm intra- and extracardiac shunting [32].

Electrocardiography is a key test in evaluating patients with intermittent breathlessness. Dyspnoea is often a presenting symptom in newly diagnosed atrial fibrillation [33], and other dysrhythmias may also manifest with dyspnoea as a primary symptom.

Cardiovascular MRI (magnetic resonance imaging) is the gold-standard for calculating left ventricular ejection fraction and offers more detailed cardiac imaging than echocardiography. It is also valuable in diagnosing infiltrative cardiac disorders like sarcoidosis, which often cause pulmonary compromise. Recognising comorbid cardiac disease in patients with respiratory conditions such as COPD or ILD is essential, as these conditions share risk factors like smoking, systemic inflammation and aging. Cardiovascular complications, including heart failure and ischaemic heart disease, are common in respiratory patients, significantly impacting prognosis and treatment. Early identification and management of cardiac conditions in these patients can improve outcomes and reduce mortality [34–36].

Tier 2 conclusion

PFTs, thoracic imaging, laboratory tests and cardiac imaging are essential in the secondary evaluation of dyspnoea, particularly when causes are multifactorial. A study by Öcal *et al*. [37] found that spirometry and echocardiography identified pulmonary and/or cardiac disease in 83% of 250 patients with unexplained chronic dyspnoea. Additionally, nearly 40% had multimorbid breathlessness, with both cardiac and pulmonary factors contributing to symptoms.

Similarly, Pedersen *et al*. [38], in a study of 129 elderly primary care patients with chronic dyspnoea, found that PFTs, basic laboratory tests, echocardiograms and electrocardiograms provided a diagnosis in 63% of cases. This underscores the importance of thorough and systematic investigations at this tier, which can lead to a definitive diagnosis in a substantial majority of cases, facilitating timely and targeted management of dyspnoea.

Tier 3: dynamic tests

Breathlessness typically worsens with exertion and is often alleviated, or even absent, at rest. Traditional diagnostic tests, including PFTs, radiological imaging and blood tests are generally performed while the patient is at rest and may be asymptomatic.

Normal results from these resting tests, whilst generally reassuring, often fail to explain why a patient experiences debilitating breathlessness and may overlook conditions like dynamic hyperinflation, cardiac ischaemia or right-to-left shunting that only manifest under exertion.

Conducting a complete evaluation whilst symptomatic not only provides a more comprehensive understanding of the patient's experience but also helps them engage with diagnoses like breathing pattern disorders or inducible laryngeal obstruction. Additionally, negative results from static testing performed at rest may leave patients feeling that their concerns have not been fully addressed, potentially hindering effective management of what can be a profoundly limiting symptom. Incorporating dynamic testing into the diagnostic process enhances the ability to detect exercise-induced pathologies, leading to more accurate diagnoses and tailored treatment strategies for patients experiencing exertional breathlessness.

6-minute walk test

The 6-minute walk test (6MWT) is a straightforward and practical assessment in patients with dyspnoea, measuring the distance a patient can walk in six minutes while monitoring oxygen saturation, heart rate, symptom burden and breathing pattern. It is particularly useful for patients with chronic respiratory or cardiac conditions, aiding in decisions regarding ambulatory oxygen needs and pulmonary rehabilitation. A benefit of the 6MWT is its repeatability allowing for monitoring disease progression and exercise tolerance over time or following interventions. The ATS recommends that the 6MWT serve as an adjunct to cardiopulmonary exercise testing (CPET) rather than as a standalone investigation [39].

Cardiopulmonary exercise stress test

CPET offers a comprehensive evaluation of a patient's cardiac and respiratory function during physical exertion, particularly when they are symptomatic or nearing their maximum workload. While CPET may not always yield a specific diagnosis, it can guide clinicians toward the underlying cause, especially in patients who present with normal results from static tests. A normal CPET can offer reassurance, whereas abnormal findings may justify further, more invasive, system-specific evaluations. The ERS has established a standardised protocol for conducting CPET, particularly in patients with chronic lung diseases. This protocol, based on a systematic review involving over 26 000 subjects, ensures consistency and reliability in test results, which is crucial for accurate diagnosis and management [40].

During CPET, several key physiological parameters are measured:

- Minute ventilation ($\dot{V}_E$): The total volume of air inhaled and exhaled per minute.
- Heart rate (HR): The number of heart beats per minute.
- Carbon dioxide production ($\dot{V}_{CO_2}$): The amount of CO_2 produced by the body during metabolism.
- Oxygen consumption ($\dot{V}_{O_2}$): The volume of oxygen utilised by the body, a critical indicator of aerobic capacity.

From these primary measurements, additional metrics are derived:

- Respiratory exchange ratio (RER): The ratio of $\dot{V}_{CO_2}$ to $\dot{V}_{O_2}$, reflecting the balance between CO_2 production and O_2 consumption. This ratio provides insights into the metabolic substrates being utilised (*e.g.*, carbohydrates *versus* fats) and helps determine the onset of anaerobic metabolism.
- O_2 pulse: Calculated as $\dot{V}_{O_2}$ divided by HR, representing the amount of oxygen consumed per heartbeat. It serves as a surrogate for stroke volume, offering insight into cardiac efficiency during exercise.
- Ventilatory equivalents: These include the ratios of ventilation to oxygen consumption ($\dot{V}_E/\dot{V}_{O_2}$) and ventilation to carbon dioxide production ($\dot{V}_E/\dot{V}_{CO_2}$). They assess the efficiency of gas exchange and ventilatory control, highlighting any abnormal respiratory responses during exercise.

CPET also identifies critical thresholds:

- Anaerobic threshold: The point at which lactate begins to accumulate in the blood, indicating a shift to anaerobic metabolism.
- Respiratory compensation point: The stage where ventilation increases disproportionately to CO_2 production, signifying metabolic acidosis.

In the absence of significant cardiopulmonary disease, individuals should reach 80% or more of their predicted $\dot{V}_{O_2}$ max during maximal exercise. This should be accompanied by achieving 80% or more of their target heart rate, calculated as 220 minus age, indicating that cardiovascular capacity is the primary limiting factor during intense physical activity.

Conversely, the ventilatory system usually maintains a significant reserve; individuals should not typically reach 80% of their predicted maximal voluntary ventilation during exercise. Maximal voluntary ventilation can be estimated by multiplying the FEV_1 by 35.

By analysing these parameters, CPET can provides valuable insights into the integrative responses of the cardiovascular and respiratory systems during exercise, focusing the diagnostic pathway.

Dynamic expiratory-phase CT

Dynamic expiratory-phase CT is a specialised imaging technique used to assess the anatomy of the lungs during expiration. Unlike traditional CT scans, which are typically performed at peak inhalation to best visualise structures, dynamic expiratory-phase CT focuses on capturing images while the patient exhales, demonstrating anatomical variations during normal breathing and forced manoeuvres that would otherwise be unseen.

In patients with unexplained dyspnoea, expiratory-phase CT is particularly useful for detecting air trapping, where pockets of air remain in the lungs during exhalation due to obstructed or collapsed airways. This is seen in diseases like COPD, asthma, bronchiolitis and hypersensitivity pneumonitis. It can also identify excessive central airways collapse wherein there is abnormal narrowing of the central airways during expiration. This can result from tracheobronchomalacia, where weakened cartilaginous structures in the airways lead to excessive collapse of the anterior and lateral walls. Another condition, excessive dynamic airway collapse, involves abnormal bulging of the posterior tracheal wall into the airway lumen during expiration [41].

Excessive central airway collapse was traditionally diagnosed at bronchoscopy. However, evaluating sedated patients led to overdiagnosis, and there is poor inter-operator agreement [42], while unsedated bronchoscopy could be poorly tolerated by patients.

A recent systematic review of over 40 studies involving more than 10 000 patients found that, while bronchoscopy has traditionally been regarded as the gold standard for diagnosing large airway collapse, CT was used in 80% of the studies, with only three including bronchoscopic evaluations. This highlights a shift toward dynamic expiratory CT as the preferred diagnostic modality in clinical practice [43].

Tier 3 conclusion

The third tier of dyspnoea assessment comprises dynamic tests like the 6MWT, CPET and dynamic expiratory-phase CT. These tests are crucial when dyspnoea remains unexplained after initial evaluations, providing essential insights into the cardiovascular and respiratory systems under stress rather than at rest.

The diagnostic algorithm of Pratter *et al.* [16], which included advanced thoracic imaging and CPET, demonstrated the effectiveness of these dynamic tests by achieving a diagnosis in 99% of cases. Similarly, DePaso *et al.* [44] showed a significant increase in diagnostic yield from 7% to 81% by incorporating dynamic testing such as CPET in a study of 72 patients with unexplained dyspnoea. Furthermore, a study by Elbehairy *et al.* [45] highlighted that smokers with dyspnoea but normal spirometry exhibited higher levels of inspiratory resistive work during CPET and reported greater dyspnoea intensity during exercise compared to healthy individuals. These findings illustrate the enhanced sensitivity of dynamic tests compared to static assessments.

Future direction

Future research should focus on standardising dyspnoea assessment tools to improve diagnostic accuracy and comparability across studies. Current tools vary in their ability to capture the multidimensional nature of dyspnoea, highlighting the need for validated, universally accepted measures. Additionally, as discussed in this review, exertional dyspnoea remains challenging to diagnose and advances in dynamic tests are essential. Advancing portable, real-time monitoring technologies could enhance early disease detection and improve diagnostic sensitivity for exercise-induced conditions. The integration of digital health technologies, such as wearable sensors and remote monitoring, may also facilitate longitudinal tracking of dyspnoea progression, enabling earlier intervention and more personalised management strategies.

Conclusion

This narrative review presents a structured, tiered approach to the assessment of dyspnoea.

This approach aligns with several key literature reviews and guidelines, each providing robust statistical evidence supporting similar strategies.

Laviolette and Laveneziana [2], in their article "Dyspnoea: a multidimensional and multidisciplinary approach", emphasise that dyspnoea is not a single sensation but a complex symptom with multiple dimensions, including sensory–perceptual intensity, affective distress, and its impact on daily life. They advocate for a multidisciplinary approach to managing dyspnoea, incorporating interventions that address the physiological and psychological aspects of the condition. The authors also highlight the need for better dyspnoea assessment tools and the potential for personalised treatments based on a deeper understanding of dyspnoea's underlying mechanisms. They note that, despite advances, relieving chronic dyspnoea remains challenging, requiring further research to improve clinical outcomes. This perspective is consistent with the comprehensive approach advocated in our review, where addressing the multifaceted nature of dyspnoea is key to improving patient care.

The ATS update on the "Mechanisms, Assessment, and Management of Dyspnoea" offers a detailed analysis of dyspnoea's complex neurophysiological mechanisms, including the involvement of cortico-limbic brain structures that parallel those in pain perception [1]. The review emphasises that dyspnoea is often multifactorial, requiring a broad range of diagnostic approaches. It highlights the critical role of CPET in situations where initial evaluations are inconclusive or where multiple conditions may be contributing simultaneously. They advocate for integrating various diagnostic tools concurrently to effectively capture the diverse causes of dyspnoea. This approach is reflected in our review, which also stresses the importance of utilising diverse and simultaneous investigations to ensure a comprehensive assessment of dyspnoea.

A literature review by Sunjaya *et al*. [46] evaluated the effectiveness of clinical algorithms in diagnosing chronic dyspnoea across eight studies involving 2026 patients aged 20 to 80 years. The review highlighted the need for a validated algorithm integrated into a clinical decision support system for primary care. The authors proposed a stepwise diagnostic pathway, starting with non-invasive tests like spirometry and electrocardiogram, progressing to advanced investigations like echocardiography and thoracic CT. Their findings showed this approach could diagnose 35% of cases in the first stage, 83% by the third stage and over 90% in the final stage. This aligns with the emphasis of our review on structured diagnostic escalation and the importance of dynamic assessments in improving outcomes for challenging dyspnoea cases.

Additionally, a review of 47 publications by Ferry *et al*. [14] explored the diagnostic challenges of chronic dyspnoea, identifying significant gaps in referral and diagnostic accuracy. Only 51% of patients were correctly referred to specialists, and less than half of primary care diagnoses aligned with specialist outcomes. "The British Lung Foundation's Breath Test", based on responses from over 350 000 participants, showed that 58% of patients reported ineffective healthcare advice [47]. Ferry *et al*. [14] proposed a tiered diagnostic pathway, progressing through clinical evaluation, primary investigations (*e.g.*, electrocardiogram, spirometry), secondary investigations (*e.g.*, echocardiography, thorax CT) and tertiary tests (*e.g.*, CPET, cardiac MRI). Studies cited by Ferry *et al*. [14] showed that systematic diagnostic algorithms can achieve diagnosis rates up to 99%. Their pathway emphasises specialist consultation for unresolved cases, including consideration of non-cardiopulmonary causes like obesity or psychogenic dyspnoea. This structured approach complements our review, highlighting the importance of comprehensive and methodical diagnostic strategies.

In conclusion, the ATS update, ERS statement, and the statistical evidence from these literature reviews validate the tiered diagnostic approach advocated in this review. By combining systematic assessment strategies with patient-centred care and incorporating both static and dynamic diagnostic tools, this review aims to enhance the accuracy of diagnosing dyspnoea and improve patient outcomes.

Key points

- Dyspnoea, or breathlessness, is a subjective experience influenced by complex interactions between the respiratory, cardiovascular and nervous systems.
- The initial consultation should focus on detailed history-taking, physical examination and assessment tools to identify potential causes and the severity of dyspnoea.
- Pulmonary function tests and thoracic imaging are critical early investigations for diagnosing and characterising lung diseases that cause dyspnoea.
- Dynamic tests, such as the 6MWT, dynamic expiratory phase CT or CPET can provide valuable data on the functional impact and underlying causes of unexplained dyspnoea.

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