Assessment of breathlessness: a cardiologist's perspective

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Shareable abstract (@ERSpublications)
Breathlessness is a multifaceted symptom. A systematic approach is recommended. From a cardiologist's perspective, we can decipher between cardiac and pulmonary causes with the clinical history, examination and first-line investigations. https://bit.ly/4hVRUDy

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Abstract

"Breathlessness" or dyspnoea is a common, subjective symptom that can be multifactorial. It is a frequent complaint encountered by cardiologists, both in the outpatient and inpatient clinical setting. It requires a comprehensive clinical evaluation including accurate history taking and pursuing appropriate clinical investigations. It is imperative to distinguish cardiac causes of dyspnoea from other causes, including pulmonary, neurological and other systemic conditions. In this review we attempt to summarise the approach to the evaluation of dyspnoea.

Educational aims

- To understand the importance of clinical evaluation and identify the important aspects of history and examination.
- To identify the diagnostic tools required to assess breathlessness and to use them in the appropriate setting.
- To compose a differential diagnosis based on clinical evaluation.
- To implement an appropriate management plan based on the diagnosis.
- To understand the pathophysiology of dyspnoea in relation to cardiac aetiologies.

Introduction

"Breathlessness" or dyspnoea is a common, subjective symptom that can be multifactorial. It is a frequent complaint encountered by cardiologists, both in the outpatient and inpatient clinical setting. It requires a comprehensive clinical evaluation including accurate history taking and pursuing appropriate clinical investigation. It is imperative to distinguish cardiac causes of dyspnoea from other causes, including pulmonary, neurological and other systemic conditions [1, 2]. We attempt to summarise the approach to the evaluation of dyspnoea, in this clinical review.

Pathophysiology of breathlessness

There is concomitant involvement between the respiratory and cardiovascular systems when understanding the pathophysiology of breathlessness. Cardiac causes can be due to many factors including elevated pulmonary capillary wedge pressure (PCWP) secondary to left ventricular dysfunction or reduced cardiac output leading to pulmonary congestion [3, 4]. Coronary syndromes, either acute or chronic, can lead to myocardial ischaemia and subsequent dyspnoea.

Clinical evaluation

History taking is the cornerstone for any presenting complaint (figure 1). A detailed history, addressing the key components of "breathlessness" is crucial and will include the following:

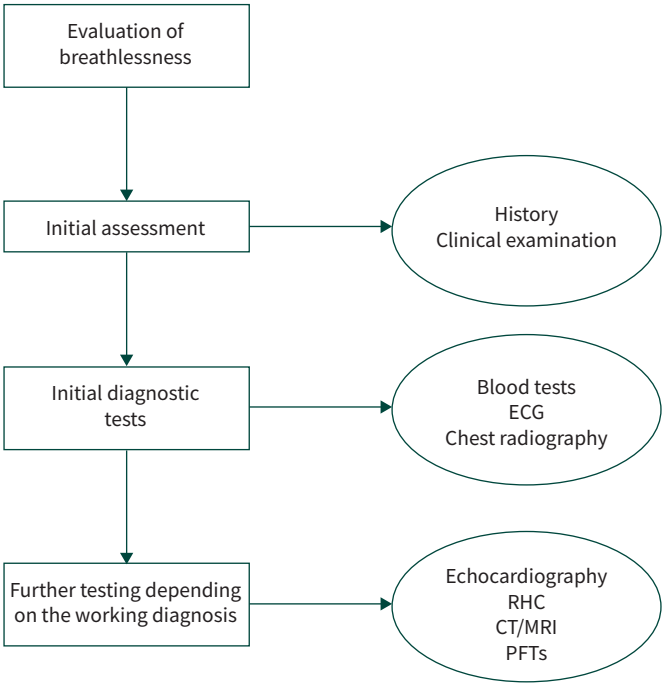

FIGURE 1 Algorithm for breathlessness assessment. RHC: right heart catheterisation; CT: computed tomography; MRI: magnetic resonance imaging; PFTs: pulmonary function tests.

- Breathlessness is an important angina equivalent symptom, particularly in patients who may not experience typical cardiac chest pain. This form of atypical angina is more prevalent in women, the older patient and patients with diabetes.
- Timing: onset, duration and progression of symptoms.
- Associated symptoms: chest pain, palpitations, presyncope and symptoms of cardiac failure (*e.g.* paroxysmal nocturnal dyspnoea, orthopnoea or pedal oedema).
- Exacerbating factors: exertional or present at rest.
- Background medical history, including any previous cardiac history and other comorbidities.
- Social history: smoking, occupational exposure.
- Medication use.

A physical examination can clinch the diagnosis in many cases:

- A thorough cardiovascular examination is important, including confirming any clinical signs of heart failure: jugular venous distension; peripheral oedema; S3 or gallop on auscultation of the heart sounds; and crackles on auscultation of the lung bases suggestive of pulmonary oedema.
- Respiratory signs may also be present and lead to the diagnosis. Fine crepitations on auscultation of the lung bases are suggestive of interstitial lung disease, while an expiratory wheeze is suggestive of COPD.
- Finger clubbing may be secondary to underlying pulmonary or cardiac disease.
- Examining for signs of anaemia, thyroid dysfunction and other systemic conditions can aid in diagnosing the aetiology of breathlessness [5].

Investigations

1) Blood results

- N-terminal pro-brain natriuretic peptide (NT-proBNP) is very useful for the diagnosis of heart failure and has demonstrated a very high negative predictive value (NT-proBNP <300 pg·mL^{-1}) [6].
- High sensitivity troponin levels can evaluate for underlying ischaemia, although this is more relevant in the acute setting.
- A full blood count can detect anaemia.
- Other blood tests, such as renal function, thyroid function tests and B12, ferritin and folate levels, can evaluate for other contributing factors.

2) Rhythm analysis

- ECG is an essential initial screening test and can demonstrate ischaemia, conduction disease or signs of left ventricular hypertrophy, which could all reveal the underlying diagnosis [7]. Underlying atrial fibrillation or high degree atrioventricular block may be the cause of breathlessness.
- Continuous ambulatory rhythm monitoring with both Holter monitoring and implantable loop recorder devices can detect conduction disorders and arrythmias that may not be captured on routine ECG.

3) Chest radiography

Chest radiography is a simple imaging tool that can identify a multitude of abnormalities of breathlessness, including pulmonary oedema, pleural effusions and cardiomegaly. It can also ascertain if there are any non-cardiac causes at play such as lower respiratory tract infection, interstitial lung disease or lung masses [8].

4) Transthoracic echocardiogram

Transthoracic echocardiogram is a vital diagnostic tool that will assess cardiac function. It will provide information on both systolic and diastolic cardiac function, valvular status and an estimation of pulmonary artery pressure with right ventricular systolic pressure. From a cardiac perspective, it is often the most informative non-invasive diagnostic test for evaluating cardiac breathlessness [9]. A transoesophageal echocardiogram may be required for further valvular assessment if a valvular abnormality is detected on a transthoracic study. This is particularly useful for regurgitant valvular disease.

5) Advanced imaging modalities

- Computed tomography (CT) assessment of the lung parenchyma can be useful if an underlying pulmonary condition is suspected. CT coronary angiogram can be used for coronary assessment if this is a clinical concern. It is recommended as a first-line diagnostic test for the evaluation of angina-equivalent symptoms such as exertional breathlessness [10].
- Cardiac magnetic resonance imaging (MRI) can further assess left and right ventricular function, myocardial ischaemia and identify any infiltrative disease. In particular, it provides detailed information on the size and function of the right heart which can be useful when pulmonary hypertension is a concern [11].

6) Pulmonary function tests

- Spirometry, lung volume measurement and flow–volume loops are useful diagnostic tests if an underlying pulmonary aetiology is suspected.
- Cardiopulmonary exercise testing (CPET) can give a comprehensive assessment of unexplained dyspnoea [12]. It can aid in identifying an underlying cardiac or pulmonary diagnosis. CPET also provides insight into pulmonary vascular limitations as an explanation for dyspnoea [13].
- Plethysmography measures lung volumes and airway resistance, which gives a detailed description of a patient's lung mechanics. Both the American Thoracic Society and European Respiratory Society (ERS) have established guidelines on its use [14].

7) Invasive coronary angiography

Invasive coronary assessment may be required if coronary artery disease is suspected. It can follow on from a CT coronary angiogram which has demonstrated a coronary lesion, or cardiac MRI that has demonstrated ischaemia. It may also be the first-line investigation if there is a high pre-test probability for significant coronary artery disease or in elderly patients [15].

8) Right heart catheterisation

Right heart catheterisation (RHC) is the gold standard for diagnosing pulmonary hypertension and differentiating between pre- and post-capillary forms of pulmonary hypertension. It should be performed in an experienced catheterisation lab or pulmonary hypertension centre and ideally include exercise testing [16].

Transthoracic echocardiogram

The echocardiogram is an excellent tool in the cardiologist's toolbox, and can evaluate many causes of dyspnoea from a cardiovascular perspective.

- Left ventricular function: One of the first aspects of the echocardiogram is evaluation of left ventricular systolic and diastolic function. Systolic dysfunction, as indicated by a reduction in ejection fraction, is a critical diagnosis that warrants further investigation from a cardiovascular perspective. Diastolic dysfunction, which leads to heart failure with preserved ejection fraction, is identified on the echocardiogram by looking at mitral flow Doppler patterns, left atrial size and left ventricular

relaxation. This is important to diagnose as diuretics are the mainstay of treatment, which may improve breathlessness.

- Right ventricular function: The right heart is often termed the "forgotten ventricle" when evaluating cardiac status and echocardiographic parameters. Right ventricular function is particularly important in patients with suspected pulmonary hypertension or those with chronic lung disease and cor pulmonale. This is assessed by evaluating the tricuspid annular plane systolic excursion (TAPSE) and the size of the right ventricular cavity, which may be dilated with elevated pulmonary pressures. We can also assess pressure and volume overload on right ventricular assessment.
- Pulmonary artery systolic pressure (PASP): Doppler assessment of the tricuspid regurgitation jet estimates PASP by evaluating right ventricular systolic pressure (RVSP), which is added to an estimate of right atrial pressure by assessing the inferior vena cava. An elevated PASP on echocardiogram suggests a high probability for pulmonary hypertension.
- Valvular heart disease: Valvular abnormalities and their severity are identified with echocardiography. This guides appropriate further investigation and intervention.
- Pericardial disease: Effusions and their effect on cardiac physiology are identified with echocardiography. We can quantify the size of effusions and identify the presence of cardiac tamponade by assessing for right ventricular or right atrial diastolic collapse, in addition to assessment of mitral and tricuspid inflow velocity variation and inferior vena cava dilatation. Constrictive and restrictive pericarditis physiology can be assessed, which prompts further investigation.
- Stress echocardiography: Dobutamine stress echocardiography can be used if underlying ischaemic heart disease is suspected. It is also a useful tool to assess the severity of aortic stenosis in the clinical scenario of low-flow, low-gradient aortic stenosis, when there is left ventricular dysfunction and a falsely low aortic valve gradient.

Echocardiography is a critical diagnostic tool for the investigation of breathlessness, particularly when cardiac aetiologies are suspected. It provides a significant amount of diagnostic information, not only the assessment of left ventricular ejection fraction. It provides a comprehensive assessment of function, valvular status, pulmonary pressures and pericardial pathology.

Right heart catheterisation

RHC is an invasive diagnostic investigation, performed in the catheterisation laboratory by a cardiologist. It involves accessing the venous circulation, *via* the brachial, femoral or internal jugular veins, and passing a Swan–Ganz catheter through the right heart and pulmonary arteries for pressure assessment. It provides direct haemodynamic assessment of the right atrium, right ventricle, pulmonary artery and PCWP, which is a surrogate for left atrial pressure. It is particularly useful when echocardiography suggests an underlying pathology such as pulmonary hypertension, pericardial pathology or intracardiac shunt.

- Pulmonary hypertension: As per the 2022 European Society of Cardiology/ERS pulmonary hypertension guidelines, the diagnosis of pulmonary hypertension is defined by a mean pulmonary arterial pressure >20 mmHg (table 1) [17].
- Valvular heart disease assessment: We can assess the severity of valvular heart disease by evaluating the pressure wave form. Large V waves on the right atrial pressure wave form demonstrates regurgitation into the right atrium during systole and occurs with severe tricuspid regurgitation. Large V waves on the PCWP pressure wave form, which is a marker for left atrial pressure, demonstrates regurgitation into the left atrium during systole, which occurs with severe mitral regurgitation.
- Shunt assessment: Cardiac shunting is evaluated by measuring the oxygen saturation in each of the chambers. A step up of 5% in saturation is suggestive of a shunt. A step up in saturation between the superior vena cava and the right atrium is suggestive of an atrial septal defect. A step up between the right atrium and the right ventricle is suspicious for a ventricular septal defect. We can assess the

TABLE 1 Definition of pulmonary hypertension, as per the 2022 European Society of Cardiology/European Respiratory Society pulmonary hypertension guidelines

	Haemodynamic characteristics
Pre-capillary pulmonary hypertension	mPAP >20 mmHg, PCWP ⩽15 mmHg, PVR >2 WU
Isolated post-capillary pulmonary hypertension	mPAP >20 mmHg, PCWP >15 mmHg, PVR ⩽2 WU
Combined post- and pre-capillary pulmonary hypertension	mPAP >20 mmHg, PCWP >15 mmHg, PVR >2 WU

mPAP: mean pulmonary arterial pressure; PCWP: pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance; WU: Wood unit. Information from [17].

clinical significance of a shunt by measuring the Qp:Qs ratio (pulmonary blood flow/systemic blood flow). A Qp:Qs ratio >1.6 indicates a significant left-to-right shunt and <1 is indicative of a significant right-to-left shunt. This occurs in Eisenmenger syndrome secondary to pulmonary hypertension.

- Cardiac output: This is a crucial parameter in evaluating heart function with assessment *via* thermodilution or Fick's principle being the most commonly used methods in clinical practice. Each method must be used with consideration of the clinical context as both methods have their limitations. Thermodilution can be affected by right heart dysfunction, thermal losses and improper injection technique. It tends to overestimate in low cardiac output states and is inaccurate if there is significant tricuspid regurgitation. Fick's method assumes oxygen consumption, which may be inaccurate in critically unwell patients.

RHC is particularly useful when non-invasive investigations, such as echocardiography, are inconclusive. It provides a direct measurement of cardiac pressures and guides both the diagnosis and management of complex cardiac and pulmonary conditions. It can help differentiate between a pulmonary and cardiac aetiology of breathlessness.

Differential diagnoses

The differential diagnosis for breathlessness is broad and includes both cardiac and pulmonary causes (table 2), as well as a range of other systemic conditions. Note that table 2 does not present an exhaustive list.

Management

The general management of these patients involves addressing the symptoms themselves, as well as attempting to treat the underlying cause. In patients with cardiac-related breathlessness this involves a multidisciplinary approach in conjunction with medical management.

Heart failure management

The management of heart failure is dependent on the type of heart failure (*e.g.* preserved or reduced ejection fraction) and if there any other concomitant issues such as valvular or ischaemic heart disease.

Pharmacological therapy for heart failure:

- Diuretic therapy is the mainstay of treatment for improving breathlessness, if pulmonary congestion is the cause. Loop diuretics are first line, with the addition of thiazide or thiazide-like diuretics if required [18].
- Angiotensin-converting enzyme inhibitors/aldosterone receptor blockers reduce afterload and can improve symptoms. They have also been proven to decrease mortality in patients with heart failure with reduced ejection fraction as proven in the SOLVD trial [19].
- Mineralocorticoid receptor antagonists, such as spironolactone, have been proven to reduce morbidity and mortality in patients with heart failure as described in the RALES trial [20].
- Angiotensin receptor neprilysin inhibitors (*e.g.* sacubitril–valsartan) have been shown to be superior to enalapril in reducing hospitalisation and death in the PARADIGM-HF trial [21].
- Sodium glucose co-transporter 2 inhibitors have been proven beneficial in both heart failure with reduced ejection fraction (DAPA-HF [22], EMPEROR-Reduced [23] trials) and heart failure with preserved ejection fraction (EMPEROR-Preserved [24] trial).

TABLE 2 The differential diagnosis for breathlessness

Cardiac	Pulmonary	Others
Heart failure: systolic or diastolic dysfunction	COPD	Anaemia
Valvular heart disease	Asthma	Obesity
Arrythmias	Interstitial lung disease	Deconditioning
Conduction disorder	Pulmonary hypertension	Neuromuscular disease
Pericardial disease	Pulmonary embolism	
Ischaemic heart disease	Respiratory tract infection	
	Pneumothorax	
	Pleural effusion	
	Musculoskeletal disorders	
	Psychogenic: functional disorders	

Device therapy is also a consideration for heart failure management in order to address symptoms of breathlessness. Cardiac resynchronisation therapy has been shown to improve dyspnoea and improve pulmonary function tests in patients with heart failure [25].

Ischaemic or structural heart disease management

These patients may require invasive coronary revascularisation or coronary artery bypass grafting, as well as medical management of symptoms with anti-anginal medications. These medications include β-blockers, calcium channel blockers and nitrates as described in the 2024 European Society of Cardiology guidelines for chronic coronary syndrome [26]. Valvular heart disease may require surgical or percutaneous management depending on the particular disease.

Arrythmias

Cardiac arrythmias can be managed with a rate- or rhythm-control strategy, with a tailored approach considering the patient and taking into account their age and underlying comorbidities. Device therapy may also be warranted in this cohort. Invasive ablation strategies can also be used, again this should be on an individualised basis.

Conduction disorders

Conduction disorders may respond to ceasing of an offending rate control agent, but may require pacing device insertion.

Pericardial disease

A pericardial effusion may require pericardiocentesis for resolution of symptoms. Constrictive pericarditis requires treating the underlying cause, with surgical pericardiectomy reserved for refractory cases.

Summary

Breathlessness is a multifaceted symptom, which cardiologists are faced with on a daily basis. A systematic approach is recommended in order to identify the underlying cause. From a cardiologist's perspective, we can decipher between cardiac and pulmonary causes with the clinical history, examination and first-line investigations. This combines an accurate clinical history and examination, with a tailored approach recommended for further investigations. We can conclude that breathlessness is non-cardiac with a reassuring NT-proBNP, electrocardiogram and echocardiogram in most cases. This will ensure efficiency when identifying the correct diagnosis. Effective management relies on addressing the primary condition while providing symptomatic relief, ultimately improving patient outcomes. This review underscores the importance of a thorough and methodical assessment in achieving optimal patient care.

Self-evaluation questions

1. Which key components should be included in the history taking when assessing a patient with breathlessness?
2. What information can be gained from a thorough clinical examination of a patient with breathlessness?
3. What are the first-line investigations for the assessment of breathlessness?
4. How can echocardiography assist in this assessment?
5. What differential diagnoses should be considered for breathlessness?

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Suggested answers

1. Onset, duration, associated symptoms and background history.
2. Volume status, breath sounds, valvular heart disease, signs of underlying pathology and rhythm.
3. Bloods, chest radiography and ECG.
4. It determines systolic and diastolic function, underlying valvular disease, right heart function and pericardial disease.
5. Heart failure, ischaemic heart disease, conduction disorder and infiltrative disease (from a cardiac perspective).