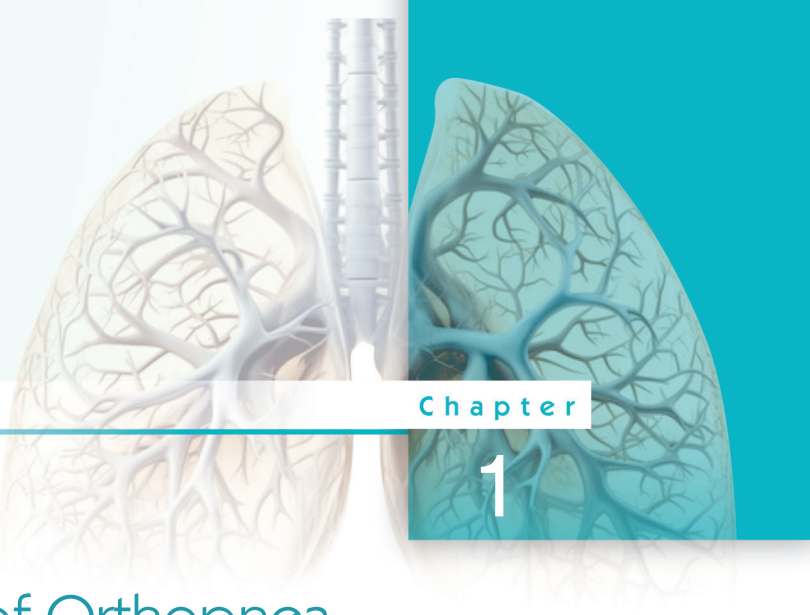

Chapter 1

Approach to a Case of Orthopnea

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LEARNING POINTS

1. Orthopnea is a condition where dyspnea worsens in supine position, and improves in the sitting or propped up position.
2. Etiology for orthopnea is varied and it requires a detailed clinical examination and evaluation to ascertain the correct cause.
3. Common causes of orthopnea include volume overload states, neuromuscular diseases, anterior mediastinal masses, morbid obesity and other causes of raised intra-abdominal pressure.

INTRODUCTION

Orthopnea is a clinical condition, defined as increased sensation of breathlessness in a recumbent position which is relieved by sitting or standing. Etiology for orthopnea is diverse, and includes cardiac dysfunction, diaphragmatic disorders, mechanical causes like mediastinal masses, and severe obstructive airway disease. Here we present a case of orthopnea secondary to diaphragmatic weakness due to motor neuron disease (MND).

CASE VIGNETTE

A retired male, mechanic by profession, in his early sixties presented to us with a history of shortness of breath, dry cough, decreased appetite, unexplained weight loss of around 12 kilograms, severe weakness, significant decline in functional status since last four months. Breathlessness was insidious in onset and gradually progressive. It was aggravated on lying flat and was partially relieved on sitting position. Since one month, he was unable to sleep in recumbent position due to severe distress. He did not have any pedal edema or abdominal distension.

Patient is a known diabetic for 20 years, well controlled on regular medication. He is a reformed smoker, with a 10 pack-year history. He underwent cholecystectomy 10 years ago for cholelithiasis.

At presentation, he had severe orthopnea and was breathless even on minimal exertion. On physical examination, he was afebrile and his vital parameters were within normal range. His room air oxygen saturation in sitting position was 95%. Respiratory system examination revealed bilateral, normal vesicular breath sounds. Cardiac examination revealed normal heart sounds and there were no signs of venous congestion. On lying down, he had paradoxical thoracoabdominal movement, suggestive of diaphragmatic weakness, and he could not lie supine for more than a minute.

Central nervous system (CNS) examination showed wasting of proximal muscles in both upper and lower limbs with spontaneous fasciculations. He also had an exaggerated knee reflex, suggesting upper and lower motor neuron involvement. Head and neck examination revealed bulbar weakness, wasting of muscles and tongue fasciculations. No sensory deficits were observed.

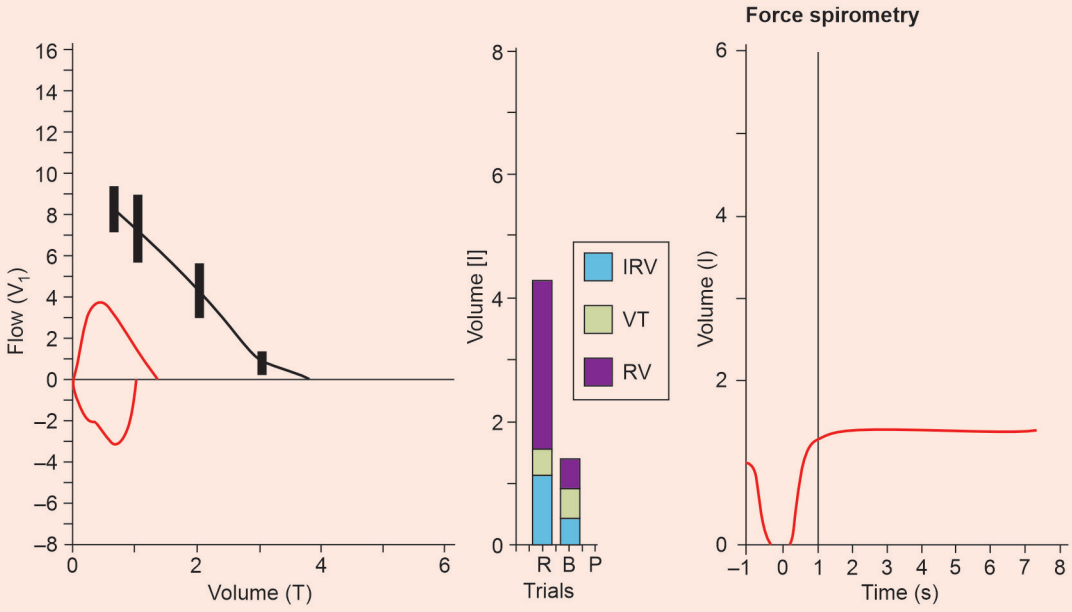
Arterial blood gas analysis on room air (at sea level) revealed presence of compensated chronic type 2 respiratory failure (pH: 7.43; pCO_2: 63 mm of Hg; pO_2: 56 mm of Hg; Bicarbonate: 34 mEq/L). Alveolar-arterial oxygen gradient (A-aDO2) was calculated and was found to be normal (15 mm Hg). Normal A-aDO2 ruled out any significant airway/interstitial or parenchymal disease as the cause of his type 2 respiratory failure. Other laboratory workup were within normal range.

Spirometry showed probable severe restriction with a reduced forced expiratory volume 1 (FEV1) of (1.32L, 42%), forced vital capacity (FVC) of (1.39 L, 35%), and a normal FEV1/FVC ratio (95.35%) (Fig. 1.1). Supine pulmonary function testing and magnetic resonance imaging (MRI) brain and spine could not be done because of severe dyspnea in the recumbent position. Ultrasonography (USG) chest showed elevated left hemi diaphragm with absent movements, and reduced movements on the right side.

Nerve conduction study (NCS) was suggestive of moderate symmetrical sensory and motor axonal polyradiculoneuropathy involving the lower limbs more than the upper limbs. Electromyography study (EMG) was suggestive of preganglionic neurogenic lesion with evidence of active denervation and reinnervation in the muscles tested. A diagnosis of motor neurone disease was confirmed. Orthopnea was attributed to bilateral diaphragmatic paresis, and type 2 respiratory failure was attributed due to respiratory muscle weakness.

To rule out secondary causes of motor neuron disease, antinuclear antibody (ANA) profile, autoimmune encephalitis panel, and rheumatoid factor were done and found to be negative. Serum protein electrophoresis and cerebrospinal fluid (CSF) analysis were within normal limits. A final diagnosis of primary motor neuron disease with respiratory muscle involvement was made.

Patient was initiated on non-invasive positive pressure ventilation with an intelligent volume assured pressure support (IVAPS) mode. Minute ventilation was set at 9 L/minute with an expiratory positive airway pressure (EPAP) at 6 cm H_2O. He was advised to use IVAPS continuously during nighttime and intermittently during daytime, with which he was comfortable and able to lie supine. He was also initiated on tablet Riluzole (a benzothiazole derivative) at 50 mg twice a day. In the initial review visit after four weeks, the patient was symptomatically better. Orthopnea had significantly reduced with the use of assisted ventilation. Patient was continued on IVAPS and Riluzole and was advised to be on regular follow up.



		Pred	LLN	Pre	%Pred	Z-Score
FVC	[L]	4.01	3.08	1.39	35%	-4.7
FEV 1	[L]	3.13	2.32	1.32	42%	-3.5
FEV1% FVC	[%]	78.04	66.59	95.35	122%	2.9
PEF	[L/s]	8.19	6.20	3.69	45%	-3.7
MMEF	[L/s]	2.60	1.23	2.49	96%	1-0.1
FET	[Sec]	-	-	7.34	-	
EV	[L]	-	-	0.08	-	

Fig. 1.1: Spirometry showing preserved FEV1/FVC ratio with severely reduced FEV1 and FVC which may be suggestive of a restrictive ventilatory defect.

DISCUSSION

Orthopnea refers to the sensation of breathlessness in recumbent position, relieved in the sitting or standing position. Spontaneous respiration is controlled by neural and chemical mechanisms. There are varied causes for orthopnea, and each cause has a unique mechanism which contributes to orthopnea (Tables 1.1 and 1.2). The most common causes of orthopnea encountered in routine practice includes heart failure, obesity, diaphragmatic weakness (either due to phrenic nerve damage or due to intrinsic muscle or a motor neuron diseases [MND]), advanced chronic obstructive pulmonary disease (COPD) and anterior mediastinal masses.

A. Orthopnea due to Left Heart Disease/Volume Overload States

The most common cause of orthopnea encountered in clinical practice is due to left heart dysfunction. Whenever a patient complains of orthopnea, it is important to assess for features of volume overload state (pedal edema, elevated JVP, bibasal fine end inspiratory

Table 1.1: Causes of orthopnea	
Pathophysiologic condition	***Diseases***
Left heart failure (pulmonary edema)	Left ventricular systolic failure Left ventricular diastolic dysfunction Left heart inflow or outflow tract obstruction
Other causes of pulmonary edema	Kidney failure Chronic liver disease Capillary leak syndromes
Diaphragmatic paralysis	Bilateral diaphragmatic paralysis (neurogenic or a muscular cause) Unilateral diaphragmatic paralysis associated with other pulmonary/cardiac pathology Motor neuron diseases
Elevated abdominal pressure	Massive ascites Large intra-abdominal masses Morbid obesity
Anterior mediastinal masses	Thymoma Lymphoma Any anterior mediastinal mass
End stage respiratory failure	Any cause of end stage respiratory failure (severe COPD, ILD)

Table 1.2: Causes of orthopnea and physiologic mechanisms for orthopnea	
Disease condition	***Pathophysiologic mechanism for orthopnea***
Left heart failure	Redistribution of blood from lower extremities and splanchnic beds to the pulmonary vasculature leads to development of pulmonary congestion in the presence of a poorly functioning left heart.
Bilateral diaphragmatic paralysis	Movement of diaphragm more cephalad due to lack of gravity leads to a fall in forced vital capacity and leads to orthopnea. This happens only when the diaphragm is paralyzed/paretic and cannot contract to maintain its position.
Anterior mediastinal masses	Direct compression of the trachea when in supine position
Abdominal masses/raised abdominal pressure	Any cause of raised abdominal pressure will push the diaphragm more cephalad in supine position leading to worsening dyspnea
End stage respiratory failure	Inspiratory respiratory muscles have a mechanical advantage in sitting and tripod position. This is lost in a lying position, and in the presence of a compromised respiratory reserve, can lead to orthopnea.

crepitations). Presence of such features should prompt immediate evaluation for cardiac status by 2D echocardiography, electrocardiography and a serum N-terminal pro B-natriuretic peptide (NT pro BNP) level. If cardiac function is normal, other causes of a volume overload state like renal failure or liver failure have to be considered.

Mechanism of orthopnea in left ventricular failure (LVF) is the development of pulmonary vascular congestion during recumbency. In the horizontal position there is redistribution of blood from the lower extremities and splanchnic beds to the lungs. In normal patients this has little or no effect. In case of patients with LVF, as the additional volume cannot be pumped out by the left ventricle, there is significant reduction in vital capacity and

pulmonary compliance resulting in shortness of breath. Pulmonary congestion decreases when the body assumes a more erect position, and this is accompanied by an improvement in the symptoms.

B. Orthopnea due to Neuromuscular Diseases

Mechanism of dyspnea in neuromuscular diseases is attributed to weakness of the inspiratory muscles (diaphragm, external intercostals, scalene, sternocleidomastoids and trapezii). This results in a decline in tidal volume with an increase in respiratory frequency to compensate and maintain alveolar ventilation. Patients with respiratory muscle weakness rely on gravity to assist in diaphragmatic movement. When lying down, gravity assisted caudal movement of the diaphragm is lost, and the position of the diaphragm becomes more intrathoracic. This leads to a further loss in FVC and results in orthopnea. Inadequate ventilation during sleep (nocturnal hypoventilation) is the initial symptom to manifest in diseases affecting respiratory muscles. Inspiratory muscle weakness as it worsens, produces shortness of breath and hypoventilation when awake also.

C. Orthopnea due to Respiratory Diseases

Dyspnea is one of the most common symptoms in a patient with COPD and in patients with other causes of severe airflow obstruction. In such patients breathing discomfort can be further amplified in the supine position. Though the exact mechanism of orthopnea is unknown, the following mechanism has been proposed. This includes impedance of diaphragmatic motion in the supine position, which results in further mechanical disadvantage requiring compensatory increase in ribcage and accessory muscle activity to maintain ventilation. Studies have shown lower maximum inspiratory mouth pressure (MIP) and lower expiratory mouth pressure (MEP) in supine versus sitting position in patients with advanced COPD, reflecting functional weakness of various respiratory muscles in the supine position.

In addition to the above, worsening pulmonary gas exchange abnormalities due to gravitational effect and cephalad shift of abdominal contents, could potentially stimulate chemoreceptors to increase inspiratory neural drive (IND), further compounding respiratory discomfort in some patients. Advanced COPD showed higher rates of IND at rest (estimated by diaphragm electromyography) compared to healthy individuals. Thus, it is postulated that orthopnea in advanced COPD is secondary to acute amplification of IND and neuro-mechanical dissociation (NMD) due to sudden deterioration of load capacity ratio of already compromised inspiratory muscles in supine position.

D. Orthopnea due to Anterior Mediastinal Masses

Any large anterior mediastinal mass (thymoma, lymphoma, germ cell tumors, etc.) can cause direct compression of the large airways which is aggravated in the lying down position (due to assisted gravity). In any individual with unexplained orthopnea or associated stridor, we must examine the mediastinum on chest X-ray. A contrast enhanced CT chest will confirm the presence of anterior mediastinal mass and help characterize the lesion.

E. Orthopnea due to Morbid Obesity/Raised Intra-abdominal Pressure

Morbid obesity is another reason for orthopnea in some individuals. Morbidly obese patients breathe at a low lung volume with a reduced expiratory reserve volume (ERV). Hence during tidal breathing expiratory flow volume is decreased promoting expiratory flow limitation

which is further exacerbated in supine position when the functional residual capacity(FRC) decreases because of the gravitational effect of the abdominal contents.

Any cause of raised intra-abdominal pressure (ascites, large masses) can cause a sensation of orthopnea due to a more cephalad position of diaphragm secondary to the raised abdominal pressure.

Approach to a Case of Orthopnea

A detailed history and clinical examination often is helpful in identifying the possible cause of orthopnea. An algorithm for evaluating the cause is proposed in Fig. 1.2. Focussed investigations are helpful in confirming the etiology.

Of the causes of orthopnea, neuromuscular causes of orthopnea are often missed/under diagnosed. Initial diagnostic tests in patients with motor neuron disease (MND)/suspected neuromuscular diseases include pulmonary function testing (PFT) (spirometry–supine and sitting, maximal inspiratory and expiratory pressures (MIP, MEP), and sniff nasal inspiratory pressure (SNIP)), radiology (chest X-ray, fluoroscopic assessment of diaphragmatic motion and ultrasound of diaphragm), and arterial blood gas analysis (ABG) analysis.

A restrictive defect is typical in case of patients with respiratory muscle weakness, identified by reduced forced expiratory volume in one second(FEV1), reduced forced vital capacity (FVC) and with a normal FEV1/FVC ratio (more than 70% predicted) and a reduced total lung capacity(TLC). Spirometry is to be performed in supine and upright position. Though obtaining a supine PFT in these patients can be practically challenging, a fall in VC greater than 30% in the supine as compared to the upright position is suggestive of bilateral diaphragmatic weakness.

A brief summary of investigations which help in confirming the diagnosis are listed in Table 1.3.

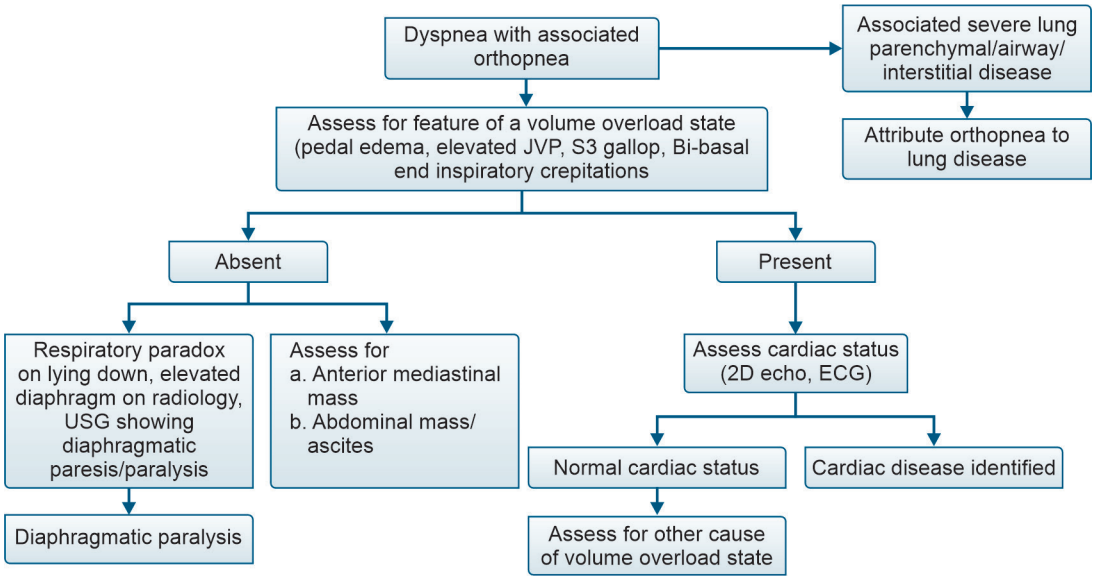


Fig. 1.2: Algorithmic approach to orthopnea

Table 1.3: Investigations and interpretation in a case of orthopnea	
Chest radiograph	Often the first test performed. Careful examination of the mediastinum, diaphragmatic position and costo-phrenic angles (for effusion) is needed. Presence of cardiomegaly and features of pulmonary edema point towards a cardiac cause of orthopnea. Most causes of orthopnea except COPD will have reduced lung volumes on a chest radiograph
Spirometry	Most causes of orthopnea will show a restrictive defect on spirometry (except COPD and airway diseases). A supine spirometry will be helpful when suspecting diaphragmatic weakness as the cause of orthopnea. Fall in FVC by 30% or more points to bilateral diaphragmatic weakness/dysfunction as the possible cause. Flow volume loops may show flattening of one or more limbs when there is a central airway obstruction due to compression by anterior mediastinal masses.
Arterial blood gas analysis	Will help in identifying associated hypercapnia. A normal (A-a) DO2 will help in ruling out significant airway/parenchymal or vascular causes of dyspnea. Hypoxemia/hypercarbia with a normal (A-a) DO2 will point towards a central/neuromuscular cause of respiratory failure
High resolution CT (HRCT) of the chest	Will help in identifying most causes of orthopnea. Features of pulmonary edema (smooth interlobular septal thickening, bilateral pleural effusion) point towards a volume overload state. Lung parenchymal/airway changes (emphysema, small airway disease and interstitial lung diseases) can be identified. A contrast scan is necessary in cases of anterior mediastinal masses for detailed assessment. A normal HRCT chest can indicate a neuromuscular/abdominal cause of orthopnea.
Other tests for assessment of diaphragm	a. Ultrasonography of diaphragm (diaphragmatic thickness and movement with respiration). b. Fluoroscopic assessment of diaphragmatic motion (Sniff test–useful in unilateral diaphragmatic paresis). c. Respiratory muscle strength assessment (MIP, MEP and SNIP test*)

*SNIP test is useful in patients with bulbar weakness who have difficulties in creating a tight seal around the mouth piece to perform routine PFT or MIP or MEP.

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