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LITERATURE REVIEW

Management of restrictive and obstructive lung disease in intensive care unit: a review

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ABSTRACT

Lung disease is broadly divided into obstructive lung disease (OLD) and restrictive lung disease (RLD). The latter is a disorder of the parenchyma, pleura, thorax, or neuromuscular walls of the lungs, characterized by decreased total lung capacity due to reduced lung distensibility. Meanwhile, OLD causes increased resistance to flow due to the blockage of part or all of the respiratory tract from the trachea to the terminal bronchioles. These two diseases' initial symptoms and signs are common, such as shortness of breath, coughing, cyanosis, respiratory muscle retractions, snoring, and fever. Early detection is needed to recognize differences in symptoms and signs, establish a diagnosis, and carry out appropriate treatment. It is essential to differentiate between RLD and OLD because they have different therapeutic management. This review aims to discuss the management of restrictive and obstructive lung disease in intensive care unit It is drawn upon various sources, including case reports, literature reviews, systematic reviews, and meta-analyses, to provide an overview of the difference between RLD and OLD to help clinicians differentiate between RLD and OLD and provide appropriate therapeutic management. Although RLD and OLD have similar signs and symptoms, they have different pathologic processes. The leading cause of RLD is a pathological condition that causes a decrease in lung compliance. Meanwhile, the primary pathological process of OLD is an increase in airway resistance, which causes typical obstructive symptoms. Addressing this area of interest can help clinicians to provide appropriate management of both pharmacotherapy and mechanical ventilation and monitoring of respiratory mechanisms.

1. Introduction

Lung disorders are divided into two significant spectrums: obstructive lung disease (OLD) and restrictive lung disease (RLD). The latter is caused by alteration of parenchymal, pleural, thoracic wall of the lungsor neuromuscular disorders. These conditions may cause a reduction in lung compliance, resulting in a decrease in lung volume, particularly total lung capacity. The underlying causes of RLD can be categorized as intrinsic factors (damage to the lung parenchyma), extrinsic factors (disorders outside the parenchyma), or neurological factors (disorders of the central nervous system) (Hammer & McPhee, 2019). It is characterized by increased resistance due to partial or complete obstruction of the respiratory tract. Resistance causes air-trapping, especially during exhalation, causing excessive lung inflation so that the thoracic cavity tends to take an inspiratory position, and the diaphragm becomes lower and flatter (Augusti

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et al., 2020).

Previous studies showed that RLD has a prevalence rate of 3-6 cases per 100,000 population (Hutchinson *et al.,* 2019). According to the World Health Organization (WHO), chronic obstructive pulmonary (COPD) ranked 3rd in the leading cause of death throughout the world in 2019, notably in developing countries (WHO, 2020). In Southeast Asia, the estimated prevalence of COPD is 6.3%, with the highest in Vietnam (6.7%). The incidence of COPD is more common in men (11.8%) than women (8.5%) (Kemenkes, 2019). According to the 2023 Indonesian Health Survey (SKI), pneumonia is 10.8%, with the province of East Nusa Tenggara (NTT) being the province with the highest prevalence. The prevalence of COPD in Indonesia accounted for 3.7% or 9.2 million people, with the province first ranked in the number of COPD cases in NTT province. Meanwhile, the prevalence of asthma is 1.6%, with a recurrence rate of 58.3% in Indonesia (Kemenkes RI., 2023).

It is essential to recognize the signs and symptoms of both spectrums early. However, they may resemble each other, so accuracy and understanding will be needed to differentiate RLD from obstructive lung disease and provide appropriate management. This literature review acts as a guide to determine the difference between RLD and OLD so early diagnosis can be done, and proper management can immediately be done in the intensive care room.

2. Method

The method used in this study is a literature review. The literature is selected using the method of clinical studies in the form of case reports, books, guidelines, literature reviews, systematic literature, and meta-analysis. The literature search for supporting data was conducted on PubMed and Google Scholar databases. The Boolean operators ("AND," "OR," and "NOT") were applied to filter the search. Articles relevant to the topic of management of OLD and RLD in intensive care units or critically ill patients are included in this literature review.

3. Result

Based on our literature search, we included thirty-one research articles discussing definitions, respiratory system physiology, pathophysiology, etiology, symptoms and signs, diagnosis, and pharmacological and non-pharmacological management of restrictive lung disease (RLD) and obstructive lung disease (OLD).

3.1. Definition

Restrictive lung disease RLD is characterized by increased elastic recoil of the lungs, decreased lung compliance, air and lung volume mismatch, and V/Q mismatch. This situation decreases gas exchange. Restrictive lung disease is categorized into 2 types based on the causal factors: intrinsic (intrapulmonary) or extrinsic factors (extrapulmonary) (Dillane, 2021).

Meanwhile, obstructive lung disease increases resistance to expiratory airflow due to a decrease in the diameter of the conducting airways. This condition may be caused by abnormalities in the lumen, airway walls, and/or supporting structures surrounding the airway (Sparling & Melo, 2021). Obstructive pulmonary disease is divided into asthma and COPD, including chronic bronchitis and pulmonary emphysema (Novelli *et al.,* 2022).

3.2. The Physiology of the Respiration System

Lung volume can be dynamic or static; both are essential for evaluating obstructive and restrictive ventilation defects. Static lung volume includes tidal volume (TV), inspiratory reserve volume (IRV), expiratory reserve volume (ERV), and residual volume (RV). In contrast, static lung capacity is divided into inspiratory capacity (IC), functional residual capacity (FRC), vital capacity (VC), and total lung capacity (TLC). Dynamic lung volume depends on the airflow rate and mostly comes from VC. (Lutfi, 2017). Figure 1 shows standard lung volumes and capacities from spirometer traces, where solid black and gray arrows indicate lung volumes and capacities, respectively.

End-expiratory recoil causes the lungs to collapse as if they are being sucked in while the chest wall is pulled outwards, causing negative pressure in the potential space between the parietal and visceral pleura. Intrapleural pressure (P_{PI}) is essential to maintaining respiratory tract patency. Rhythmic contractions of the inspiratory muscles cause cyclic changes in the chest cavity that correspond to the cyclic height of P_{PI} (Praud & Redding, 2019). During inspiration, a decrease in P_{PI} causes intra-alveolar pressure (P_{alv}) to fall, allowing the air to enter the alveoli.

A decrease in P_{PI} reduces airway resistance, dilating the small airways and causing further airflow into the alveoli. The opposite mechanism occurs in expiration. When the inspiratory muscles relax, the dimensions of the thorax decrease, P_{PI} increases, and Palv increases, causing air from the alveoli to exit following the pressure gradient. The airway pressure (P_{aw}) is always higher during the respiratory process than P_{p1}—the gradual decrease in P_{aw} results from a secondary increase in airway resistance to the trachea. P_{p1} is relatively constant around the lungs, so each tiny airway can be further divided into three segments: the rising segment, where P_{p1} is lower than P_{aw}; a point with the same pressure between P_{p1} and P_{aw}, and the

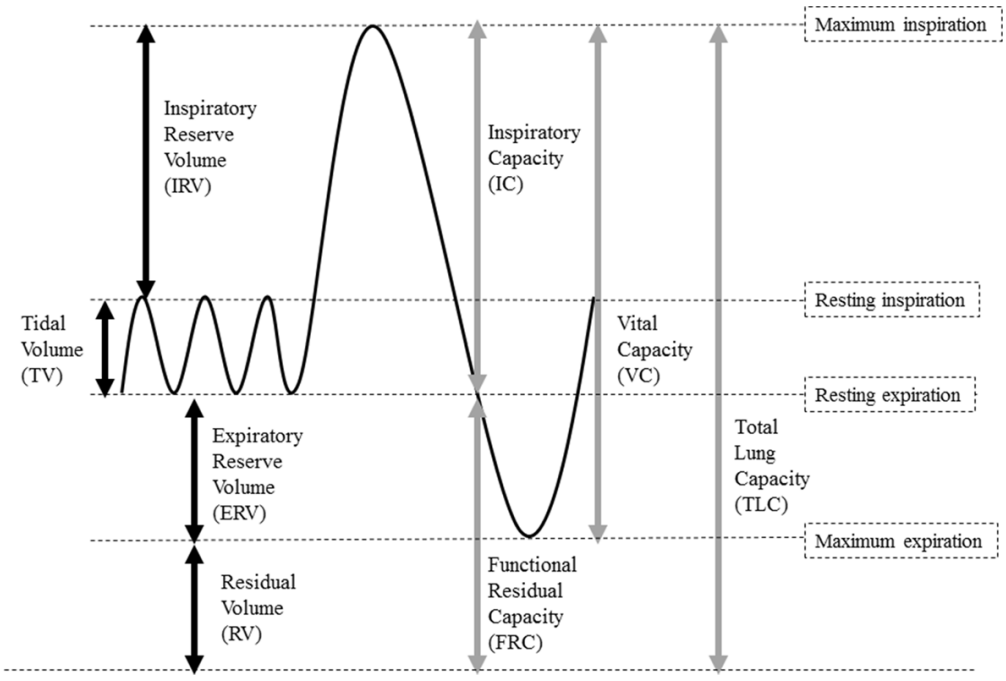

Figure 1. Lung volume and lung capacity from a spirometer trace (Lutfi, 2017).

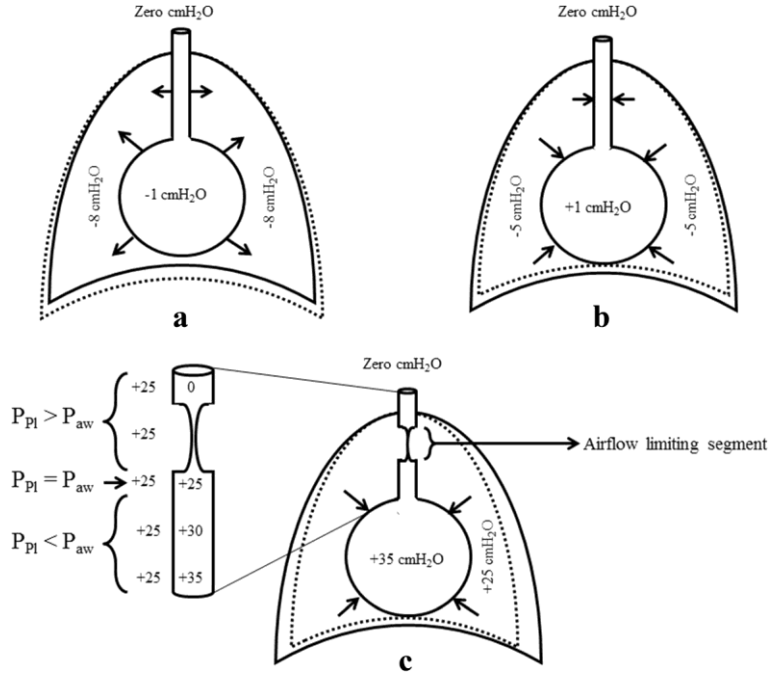

Figure 2. P_{Pl} and P_{aw} towards the end of normal inspiration (a), normal expiration (b), and strong expiration (c) (Lutfi, 2017).

airflow limiting segment, where P_{p1} is higher than P_{aw}. This is because the development of segments that restrict airflow occurs in small airways that do not have cartilage support so that the lungs cannot be emptied (Figure 2) (Lutfi, 2017).

Pulmonary ventilation is determined by airway resistance, lung compliance, and thoracic cavity. Lung volume is inversely proportional to airway resistance. During the inspiratory phase, Pp1 decreases significantly, increasing airway distension, especially in small bronchioles. The higher the lung volume, the more the alveolar walls will pull and separate the small airways, resulting in an increase in P_{pi}, which will cause a decrease in airway resistance. Figure 3 shows that the lungs' entire pressure volume static (PVC) is in the positive part of P_{aw}. This shows the tendency of the lung to collapse at any level of lung inflation.

Pulmonary compliance helps predict changes in lung volume per unit and transpulmonary pressure (PT). transpulmonary pressure is measured in dynamic and

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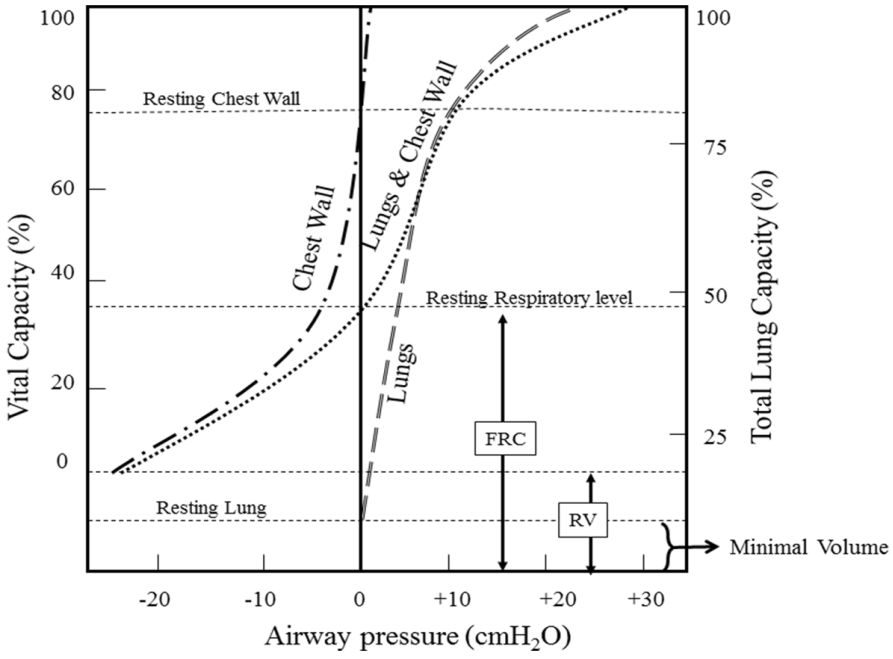

Figure 3. PVC curve of the chest wall and lungs (Lutfi, 2017)

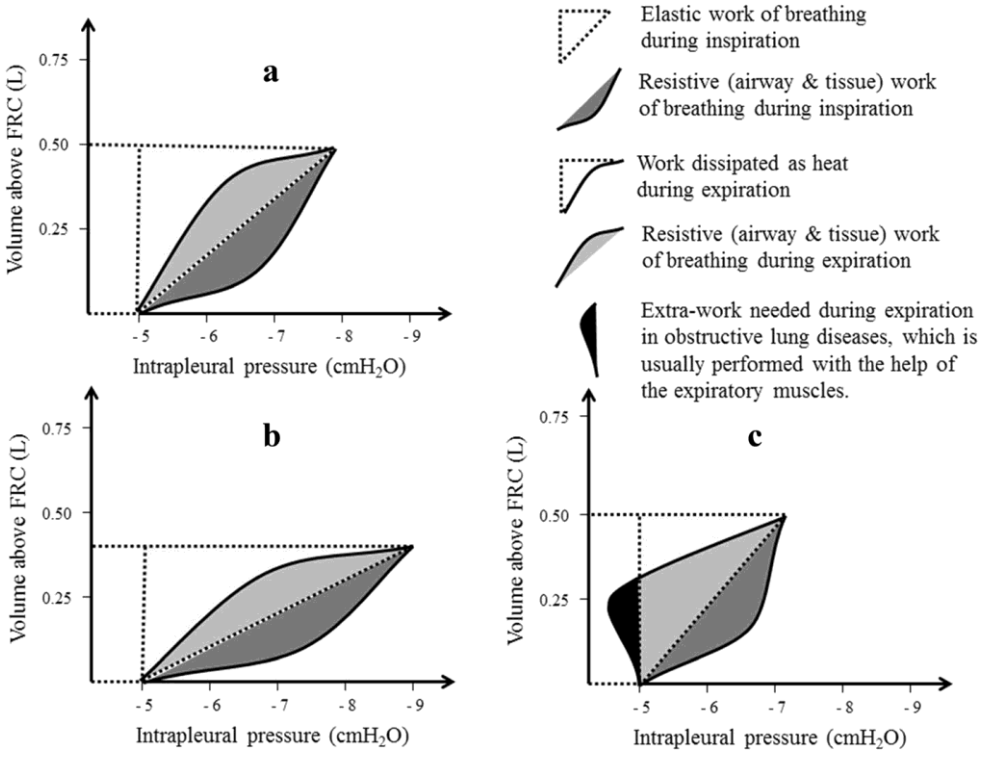

Figure 4. Work of breathing; (a) Normal subjects; (b) RLD; (c) OLD (Lutfi, 2017).

static conditions. PT is the pressure difference between the two sides. Calculate PT, trans-chest wall pressure, and trans-respiratory pressure using the formulas Palv–PPl, PPl–Patm and Palv–Patm. Dynamic compliance describes compliance measured during breathing, while static compliance describes lung compliance when airflow is nonexistent. The relationship between lung compliance, pressure (P), and volume (V) is calculated using the formula C = V/P. The entire lung pressure-volume curve is in the positive part of P_{aw}, indicating a tendency for the lung to collapse at any lung inflation rate, and PT never reaches zero (Lutfi, 2017).

3.3. Pathophysiology

RLD decreases the lung, chest wall, or both compliances, reducing the static pressure-volume curve. Lung volume will decrease due to limited lung expansion (low FVC and TLC). Decreased pulmonary compliance

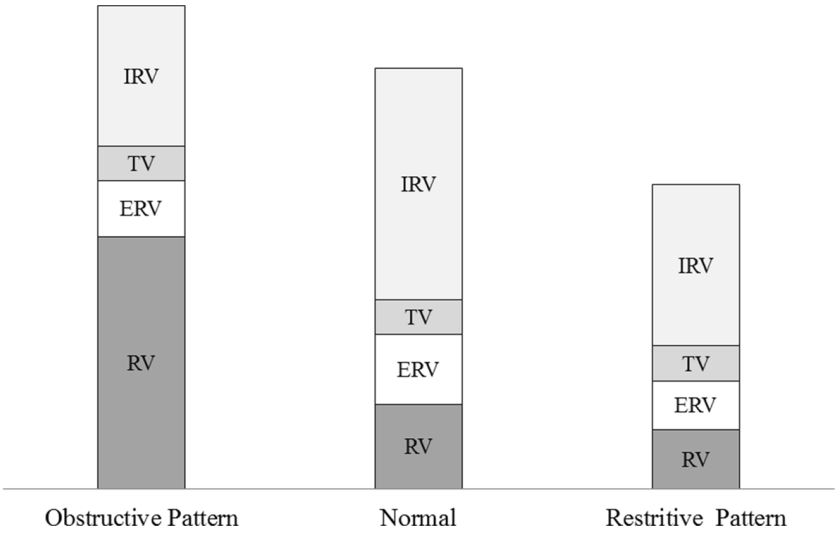

Figure 5. Volume and static capacity changes in RLD and OLD (Lutfi, 2017).

increases the Pp1 required for tidal inspiration, but TV remains below the expected average. Shifting the dynamic lung compliance curve to the right can increase the elastic work of breathing required for inspiration so that rapid breathing occurs as compensation. Figure 4 shows a graph of the breathing work in normal subjects, patients with RLD, and patients with OLD.

Obstructive lung disease occurs due to an obstruction to the airflow, where airflow stops earlier than expected with high lung volume, causing air to be trapped in the lungs (air-trapping). Lung compliance in OLD can be normal or increased, especially if there are structural changes in the emphysematous lung. A non-negative P_{p1} is necessary because the dynamic pulmonary complaint curve does not shift or shift to the left if emphysematous lung changes occur. Increased airway resistance is the primary abnormality in OLD. Changes in volume and static capacity in RLD and OLD can be seen in Figure 5.

3.4. Etiology

The leading causes of RLD includeintrinsic (intrapulmonary) and extrinsic restrictions. Intrinsic restriction is caused by an inflammation in the lung tissue due to interstitial lung disease. This process causes the tissue to become stiff, thereby reducing the distensibility of the lungs. Idiopathic fibrosis, involving acute interstitial pneumonia, lymphocytic interstitial pneumonitis, desquamative interstitial pneumonitis, and sarcoidosis, usually causes intrinsic RLD. Meanwhile, extrinsic restrictions may be caused by disorders originating from outside the lungs that may increase pressure on the lung parenchyma so that the distensibility of the lungs is reduced. Decreased lung distensibility causes lung volume to decrease, particularly total lung capacity. Diseases that further increase the risk of extrinsic RLD include scoliosis, obesity, pleural effusion, neoplasms, ascites, pleuritis, rib fractures, and neuromuscular disorders (diaphragmatic paralysis, Guillain-Barre Syndrome, myasthenia gravis, muscular dystrophy, Amyotrophic lateral sclerosis (Lou Gehrig's Disease) (Shorr M D, 2009).

Obstructive lung disease is caused by inflammation of the airways. This condition can occur due to exposure to tobacco smoke, air pollution, or alpha-1 antitrypsin deficiency. Moreover, it can be triggered by airway hyperresponsiveness, which causes chronic inflammation and airway obstruction. This condition can be found in cases such as asthma and COPD. Asthma may be triggered by upper respiratory tract infections, physical activity, cold temperatures, and exposure to cigarette smoke or other pollutants (Porsbjerg & Westergaard, 2021). Interactions between the environment and genetics can cause COPD. This occurs throughout a person's life, causing damage to the lungs or aging or altering normal development. The main environmental factors that cause COPD are smoking and inhaling toxic particles and gases from air pollution. The most relevant genetic factor in COPD is the SERPINA1 gene mutation, which causes α1-antitrypsin deficiency, resulting in decreased lung function and the risk of COPD (Gold, 2022).

3.5. Signs and Symptoms

Patients with RLD may experience shortness of breath, dry cough, productive cough (a diffuse lung parenchymal disorder), hemoptysis, wheezing and pleuritic chest pain (rare manifestations), dyspnea, respiratory failure due to muscle weakness, ventilation disorders (Porsbjerg and Westergaard, 2021). Physical examination of intrinsic disorders may reveal velcro crackles, crackles, cyanosis (manifestation in severe

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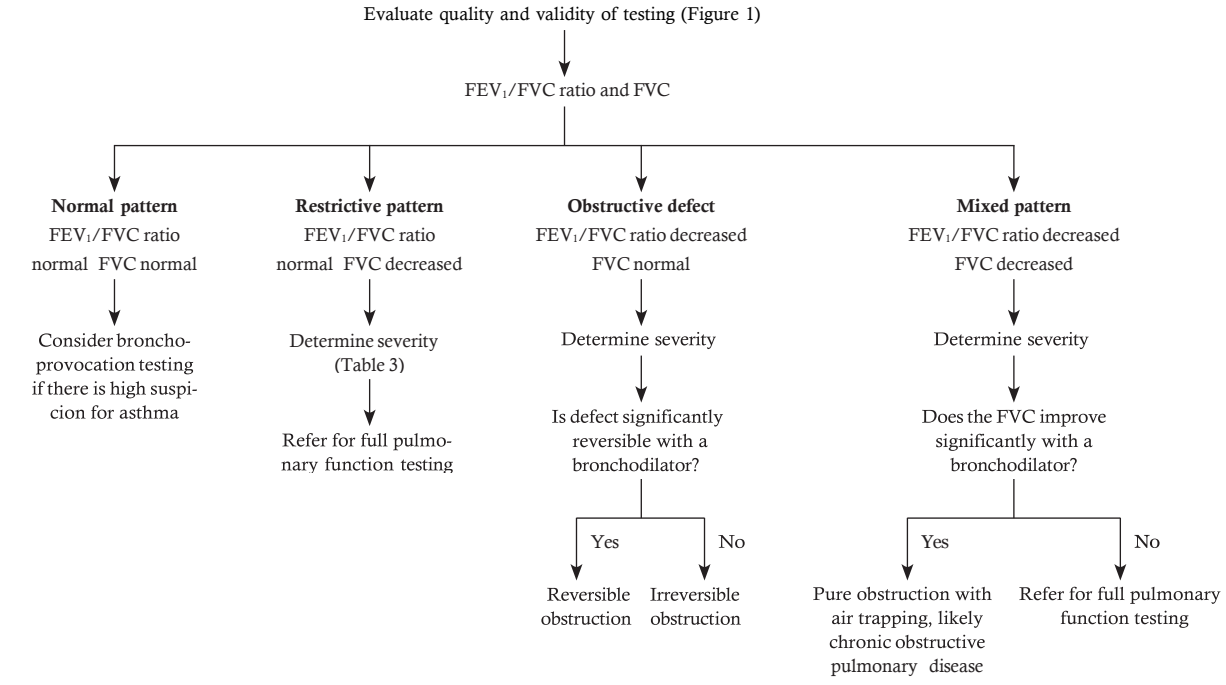

FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity.

Figure 6. Spirometry interpretation algorithm (D'urzo *et al.,* 2020).

Table 1. Spirometry Interpretation (D'urzo *et al.,* 2020).

Classification	FEV1/FVC (%)	FEV1 (%)	FVC (%)
Normal	> 70%	>80%	>80%
Obstructive	< 70%	<80%	>80%
Restrictive	> 70%	<80%	<80%
Mixed	>70%	<80%	<80%

conditions), clubbing fingers (often found in idiopathic pulmonary fibrosis), erythema nodosum (as a sign of sarcoidosis), pulmonary hypertension, and cor pulmonale characterized by the presence of shift of heart to the right and gallop sound. Extrinsic disorders include decreased fremitus strem, tympanic, loss of respiratory sounds, use of accessory muscles to breathe, and rapid and shallow breathing.

Meanwhile, OLD has several different symptoms; for example, the patient may experience dyspnea, tachypnea, chest tightness, wheezing, coughing, hypercapnia, tachycardia, pulsus paradoxus, respiratory acidosis in cases of asthma (Porsbjerg & Westergaard, 2021). In other diseases, such as chronic bronchitis type COPD, we may find productive cough, dyspnea, tachypnea, wheezing, rough crackles on inspiration and expiration, and tachycardia. In emphysema type, COPD patients may experience decreased intensity of breath sounds, prolonged expiratory time, lung hyperinflation, wheezing, rough wet crackles or dry crackles if there is an accompanying disease of lung infection or pulmonary edema, tachypnea, tachycardia, barrel chest, increased jugular venous pressure and peripheral edema (rare) (Augusti *et al.,* 2020).

3.6. Diagnosis

1. Laboratory Findings

Some routine blood tests are worth noting. Leukocyte count indicates the presence of infection, characterized by an increase in the type of polymorphonuclear leukocytes (PMN) for acute infections and mononuclear for chronic infections. In addition, hemoglobin levels help to determine the presence of chronic hypoxemia, and erythrocyte sedimentation rate (ESR) levels help to determine the presence of inflammation. C-reactive protein (CRP) levels can also help to determine ongoing inflammation for management consideration (Porsbjerg & Westergaard, 2021).

2. Chest X-Ray

The diagnosis of lung disease is based on abnormal chest imaging, with only about 10% of chest X-rays being normal. Imaging of RLD, as in IPF, shows a reticulonodular ground-glass appearance (Gruden *et al.,* 2022). Meanwhile, imaging of OLD

as in COPD shows a picture of lung hyperinflation, pendulum heart, widened rib gaps, flat diaphragm structure due to lung enlargement, and an increase in anteroposterior diameter (Myc *et al.,* 2019). In bronchial asthma, plain chest X-rays are used as an initial imaging evaluation to determine complications and rule out other causes of wheezing. In most asthmatic patients, chest radiographic findings are normal. Because pneumonia is one of the most common complications of asthma, chest X-rays are indicated in patients with fever to rule out pneumonia (Gulhane & Chen, 2021).

3. Blood-Gas Analysis

Hypoxemia may be detected in RLD due to ventilation-perfusion disorders caused by an underlying disease and the formation of a shunt. At the same time, the rise in arterial PaCO2 levels can typically be found in OLD. These conditions will cause respiratory acidosis. The severity goes hand in hand with the severity of obstruction (Glick *et al.,* 2020; Gold, 2022).

4. Pulmonary Function Tests/Spirometry

In RLD patients, there is a decrease in functional residual capacity (FRC), total lung capacity (TLC), and residual volume (RV). A reduction in Forced Vital Capacity (FVC) and Forced Expiratory Volume in one second (FEV1) to normal values or an increase in the FEV1/FVC ratio indicates the presence of a restrictive condition. In addition, in patients with RLD, iTLC is decreased. In contrast, OLD is characterized by a reduction in the FEV1/FVC ratio with a value <0.7 (Porsbjerg & Westergaard, 2021). The spirometry interpretation algorithm is presented in Figure 6.

5. High-Resolution Computed Tomography (HRCT)

A high-resolution chest CT scan can confirm RLD. Idiopathic pulmonary fibrosis (IPF) diagnosis can be confirmed through clinical evidence and with a CT scan, without a biopsy required. The basal peripheral lung zone is a zone that can be found in IPF, asbestosis, connective-tissue disease, and eosinophilia pneumonia. Upper lung disorders are often found in sarcoidosis, while IPF, asbestosis, and rheumatoid arthritis lung disease are often found in the lower lung zone. Peripheral and lower zone infiltration is often found in IPF and asbestosis.

6. Bronkoalveolar lavage (BAL)

Bronkoalveolar lavage (BAL)is a minimally invasive method that provides essential information about immunological, inflammatory, and infectious processes at the alveolar level through bronchoscopy. It has been widely used in patients with various lung diseases (Ren *et al.,* 2023). The advantages of this technique include its non-invasive nature and the ability to sample alveolar contents quickly. Findings in BAL fluid have characteristics that can predict specific lung abnormalities in RLD and OLD. Predominantly lymphocytic BAL findings are sufficient to support a diagnosis of pulmonary sarcoidosis or hypersensitivity pneumonitis in patients with appropriate clinical and imaging findings. Significant BAL eosinophils may indicate acute eosinophilic pneumonia in patients with acute alveolar opacities on chest imaging. In most cases, although the differential cell findings on BAL are often less specific, they are still helpful in ruling out certain disorders such as diffuse alveolar hemorrhage, eosinophilic lung disease, and, to a lesser extent, certain infections, thereby narrowing the diagnosis (Davidson *et al.,* 2020).

7. Lung biopsy.

A lung biopsy examination is not a routine examination to confirm the diagnosis of lung disease. If other tests cannot find the cause of lung disease, it may be necessary to remove a small amount of lung tissue (biopsy lung) (Hirai, 2021). The sensitivity and specificity of lung biopsy ranged from 36% to 48% and 56% to 79%, respectively. Metaplasia and epithelial inflammation are specific to COPD, whereas epithelial desquamation and basement membrane thickening are associated with asthma. Specific histopathological features of asthma and COPD probably exist, but current routine analysis procedures to assess lung biopsy specimens are not sufficiently discriminatory. This might be rectified by improving pathological definitions. According to the guidelines for diagnosing and treating RLDs, a diagnostic lung biopsy may be used to obtain a differential diagnosis of RLD in patients with RLD, which is challenging to differentiate clinically. Histologic findings of interstitial pneumonia include interstitial cellular infiltration and interstitial fibrosis. This causes end-stage honeycomb lung. The findings of eosinophils and macrophages are the dominant alveolar inflammatory cells and extend to the interstitium in eosinophilic pneumonia. In IPF, there is a picture of temporal heterogeneity in subpleural and paraseptal inflammation. The characteristic features of IPF are patchy scar tissue in the lung parenchyma and normal or almost normal alveoli interspersed with fibrotic areas (Hariri *et al.,* 2021; Otsuka *et al.,* 2022).

3.7. Management of RLD and OLD in the ICU

1. Pharmacological Management of RLD

The management of RLD varies depending on the underlying cause. The underlying inflammation requires anti-inflammatory therapy (Vyas *et al.,* 2021).

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Treatment begins immediately when symptoms appear or after there is objective evidence of disease progression or in moderate/severe disease states. The common pharmacotherapy for RLD includes corticosteroids, immunosuppressive, and cytotoxic agents. Idiopathic pulmonary fibrosis (IPF) can be given high-dose steroid monotherapy (0.5-1 mg/kg), although it does not improve survival and is associated with significant morbidity (Wijsenbeek *et al.,* 2022). Autoimmune lung diseases such as interstitial lung disease (ILD) can also be treated with corticosteroids, which have immunosuppressive effects. Apart from corticosteroids, autoimmune disorders in RLD can also be given other immunosuppressive agents such as cyclophosphamide and rituximab (Dsouza *et al.,* 2023).

Obesity hurts static and dynamic lung volumes and causes airway flow limitation and increased airway hyperresponsiveness. Obesity increases the risk of pulmonary hypertension, pulmonary embolism, respiratory tract infections, and hypoxic respiratory and ventilatory failure. The core mechanisms by which obesity causes these widespread respiratory complications include the added physical burden of adipose tissue to the respiratory system and the resulting systemic inflammatory state. Weight loss is the primary therapeutic strategy to alleviate and overcome these adverse effects. For patients who have failed to achieve clinically significant weight loss, defined as ≥ 5% of baseline weight after 6 months of lifestyle interventions, professional organizations, including The Obesity Society, the Endocrine Society, and the American Association of Clinical Endocrinologists

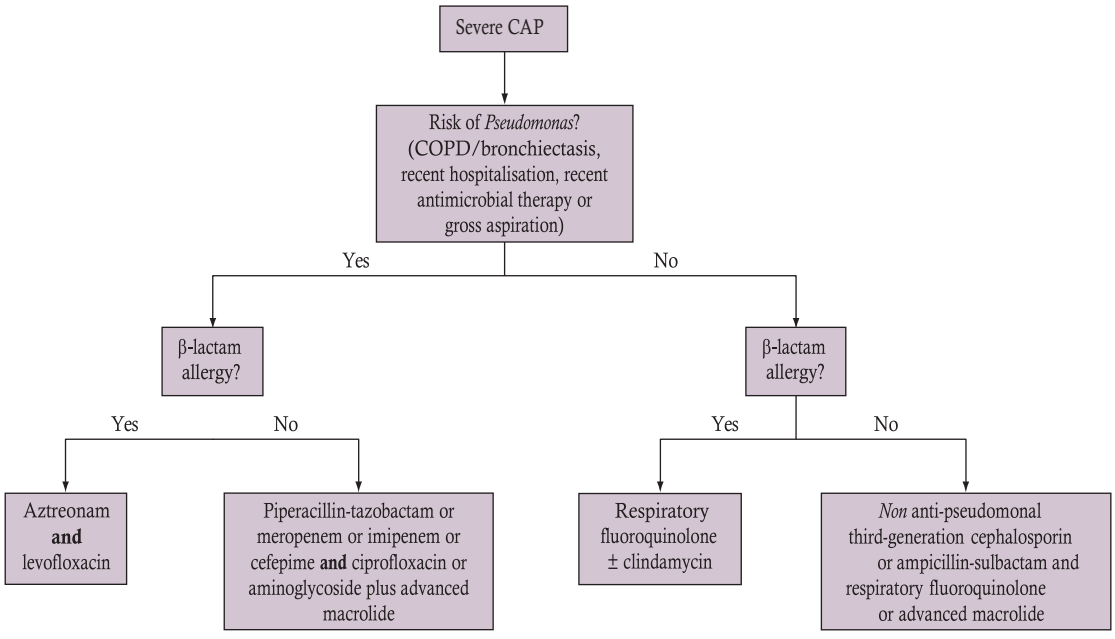

Figure 7. Community-Acquired Pneumonia (CAP) Antibiotic Selection Regimen (Mittal, 2019).

Positioning	Nurse in semirecumbent position (≥30 degrees)
Minimise duration of invasive mechanical ventilation	Assess daily for readiness to wean using spontaneous awakening trials and spontaneous breathing trials Facilitate use of non-invasive ventilation
Suctioning	Use subglottic suctioning in patients expected to be intubated for >72 h Use closed endotracheal suctioning and change catheters only as needed. Use standard precautions while suctioning respiratory tract secretions Avoid non-essential tracheal suctioning
Ventilator circuit	Change ventilator circuits only when damaged or soiled. Remove condensate from circuits, keeping circuit closed during removal and making sure condensate does not drain towards patient Change heat and moisture exchangers every 5–7 days or if clinically indicated
General care	Oral care at least 6 times per day, with chlorhexidine at least twice per day Use an early mobilisation protocol Avoid gastric overdistension
General infection control measures	Perform hand hygiene Avoid use of prophylactic systemic antimicrobials

Figure 8. Consensus Strategy for Prevention of Nosocomial Pneumonia and VAP (Mittal, 2019).

SITUATION	ANTIBIOTICS
No risk factors for multidrug-resistant pathogens	Piperacillin-tazobactam 4.5 g q6h *or* cefepime 2 g q8h *or* Levofloxacin 750 mg q24h *or* meropenam 1 g q8h,imipenam 500 mg q6h
Risk factors for multidrug-resistant organisms: • Prior intravenous antimicrobial therapy within90 days • Hospitalisation for ≥5 days prior to onset of VAP • Septic shock at time of VAP • ARDS preceding VAP • Acute renal replacement therapy prior to VAP onset *or* • High frequency of antibiotic resistance in thelocal ICU/hospital antibiogram • >10%–20% *Staph aureus* isolates being resistantto methicillin • >10% of Gram-negative isolates being resistantto an agent considered for monotherapy) *or* Immunosuppression *or* Bronchiectasis *or* Cystic fibrosis	One of: Antipseudomonal cephalosporin (e.g. cefepime 2g q8h, ceftazidime 2g q8h) *or* Antipseudomonal carbapenem (e.g. meropenem 1 g q8h orimipenem-cilastin 500 mg q8h) *or* ß-lactam/ß-lactamase inhibitor (e.g. piperacillin-tazobactam 4.5g q6h, cefoperazone-sulbactam 2 g q8h) *or* Monobactam (aztreonam 2 g q8h)*PLUS* one of: Aminoglycoside 15–20 mg/kg q24h or Antipseudomonal quinolone (e.g. levofloxacin 750 mg q24h, ciprofloxacin 400 mg q8h) PLUS one of the following for patients at high risk of methicillin-resistant *Staphylococcus aureus* (MRSA)infection: Linezolid 600 mg q12h or vancomycin load 25–30 mg/kg,15 mg/kg q12–8h

Figure 9. Recommended antibiotic regimens for nosocomial pneumonia (Mittal, 2019).

recommend anti-obesity medication (AOM) for individuals with BMI ≥ 30 kg/m2 or BMI ≥ 27 kg/m2 with comorbidities (Apovian *et al.,* 2015). However, the uses and side effects of AOM are still unclear and require further research. Pharmacological therapy, in this case, is symptomatic. Administration of anti-inflammatories such as corticosteroids (prednisone) may be considered (Mafort *et al.,* 2016). Surgical correction of scoliosis is the primary therapy for extrinsic RLD due to scoliosis. Pharmacological treatment in RLD scoliosis is symptomatic as in RLD due to obesity (Tsukahara & Mayer, 2022).

Prednisolone can be given as an alternative (reduced from 0.5 mg/kg/day to 10-20 mg/day) together with azathioprine (2 mg/kg, maximum 150 mg/day) and N-acetylcysteine 600 mg three times daily. These agents have been shown to provide significant effects compared with high-dose steroid monotherapy and have better treatment effects than prednisolone or azathioprine monotherapy alone (Wijsenbeek *et al.,* 2022). IPF patients can also be given new classes of antifibrotic drugs, such as pirfenidone and nintedanib (Spagnolo *et al.,* 2021). Figure 7 shows the antibiotic selection algorithm in CAP.

According to symptoms, RLD caused by bacteria can be treated with antibiotics and symptomatic therapy such as mucolytics, expectorants, and antipyretics. The antibiotic of choice in community-acquired pneumonia (CAP) depends on the severity, risk of pseudomonas infection, and tolerance to β-lactams (Mittal, 2019). RLD patients are at high risk of experiencing nosocomial pneumonia or VAP, so strategies are needed. Figure 8 explains strategies for preventing nosocomial pneumonia and VAP.

If nosocomial pneumonia or VAP occurs, a particular antibiotic regimen is needed. Previous use of intravenous antibiotics within 90 days may cause multi-rug resistant hospital-acquired pneumonia (MDR-HAP), Methicillin-Resistant Staphylococcus aureus (MRSA-HAP/VAP), and MDR pseudomonas HAP/VAP (Mittal, 2019). Figure 9 shows the preferred antibiotic regimen for nosocomial pneumonia.

RLD patients can undergo transplantation if the progression of the disease is advanced (TLCO <40% predicted value) or progressive (decrease in FVC >10% or reduction in FVC >15% during six months of follow-up). Oxygen supplementation in RLD patients may help to maintain SpO2 above 95% (PaO2 >60 mmHg) (Wijsenbeek *et al.*, 2022).

2. Pharmacological Management of OLD

Pharmacological Management of OLD aims to improve airway obstruction, relieve symptoms, prevent exacerbations, and reduce the severity of the disease (Glick *et al.,* 2020).

a. β2-agonis

Bronchodilator agents can relax bronchial smooth muscle tone and reduce dynamic hyperinflation. Short-acting bronchodilator agents usually relieve acute symptoms (Gold, 2022). β2 agonists cause

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bronchodilation by stimulating β2 receptors in airway smooth muscle and can reduce bronchodilation and mucosal edema. Short-acting beta Agonists (SABAs) are the first-line bronchodilator therapy (GOLD, 2022). The agents include salbutamol (albuterol), terbutaline, isoproterenol (isoprenaline), and epinephrine (adrenaline). Salbutamol is the first-choice agent to treat OLD because it has relative β2 selectivity, with reduced β1-mediated cardiac toxicity.

Long-acting β2-agonist drugs (Long-Acting Beta Agonist or LABA) such as salmeterol and formoterol do not play a role in acute exacerbations due to their slow onset of action (Mittal, 2019). Initial therapy can be started with nebulized salbutamol in high doses and repeated. The usual dose in adults is 5–10 mg (in a 2.5 to 5.0 mL volume of diluent) every 2–4 hours, but more frequent dosing with a higher total dose is often necessary in severe asthma. Continuous nebulization appears to be better than intermittent dosing and is generally used early in treatment for severe asthma. The nebulizer is supplied with O2 10–12 L/min and a reservoir volume of 2–4 mL, resulting in particles in the desired 1–3 μm range. The total dose should be adjusted according to the treatment response and the toxic side effects level (Mittal, 2019).

Intravenous administration of β-agonists remains controversial. There is no clear evidence regarding its significant benefits or side effects. However, intravenous β-agonists have the theoretical advantage of additional access to pulmonary units with severe airflow obstruction and poor nebulized drug delivery, and several studies have shown improved response when intravenous beta-agonists are used. Intravenous β-agonists are considered if the patient does not respond to nebulization. Typical doses are 5-20 μg/minute, but doses greater than 10 μg/minute should be used during the first 4-6 hours due to side effects, which should be closely monitored (Mittal, 2019).

Other studies state that the recommended initial therapy for administering albuterol is 2.5-5 mg (0.5-1 mL of 0.5% solution in 5 mL of saline) nebulized every 20 minutes for 3 doses so that optimal administration dilutes the aerosol for at least 3 mL with O2 6–8 L/min followed by 2.5–10 mg every 1–4 hours as needed or 10–15 mg/hour with titration based on response and severity. β-agonist therapy, in the form of subcutaneous epinephrine or terbutaline, can be given at a dose of 0.3–0.5 mL epinephrine with a dilution of 1:1000 (1 mg/mL) and 0.25 mg terbutaline. Both can be repeated as needed up to 3 times at 20-minute intervals. However, both drugs have undesirable adverse effects, especially in patients with cardiac disease, and neither drug has shown superior outcome benefits over inhaled therapy (Vincent *et al.,* 2023).

b. Anticholinergic

The anticholinergic agents have a bronchodilator effect by reducing cholinergic bronchomotor tone mediated by parasympathetic autonomic innervation. Long-acting anticholinergics (LAMAs) include tiotropium, and short-acting muscarinic-anticholinergics (SAMAs) include ipratropium bromide. Ipratropium bromide is the most common anticholinergics used to treat asthma and is a quaternary derivative of atropine. Ipratropium is widely used as a first-line medication along with β-agonist therapy. Numerous studies and meta-analyses show additional benefits and few side effects when adding ipratropium bromide to a β-agonist regimen (Rodrigo, 2018). The regimen of ipratropium bromide 500 mcg is nebulized every 4-6 hours for 24-48 hours with reduced frequency afterward (Mittal, 2019).

Several studies suggest that the use of ipratropium bromide as adjunctive therapy with SABA has limited benefit in patients with mild or moderate attacks. However, in patients with severe attacks, the addition of ipratropium bromide with SABA is more effective than SABA alone. Ipratropium nebulization is given at a dose of 0.5 mg (with albuterol 2.5 mg), with nebulization being more effective. Ipratropium bromide was monitored for urinary tract and ocular side effects. Accidental spraying of ipratropium into the eyes may cause additional toxicity, including mydriasis. Clinical response indicates a combination of albuterol and ipratropium for the first 1-3 hours (Vincent *et al.,* 2023).

c. Corticosteroid

Corticosteroids act as an anti-inflammatory to stabilize and reduce the frequency of exacerbations. It can be administrated via inhalation or systemically. Inhaled corticosteroids are often used with LABAs or LAMAs to reduce inflammation (McCauley & Datta, 2012). The combination of inhaled corticosteroids and LABAs is more beneficial. Systemic corticosteroids are given as therapy for acute exacerbations only.

d. Methylxanthine

The methylxanthines group is often used as additional therapy after the administration of LABAs or LAMA. Methylxanthines relaxes the smooth muscles in the airways, causing mild bronchodilation. This can be made possible by inhibiting phosphodiesterase (PDE) III and IV. Theophylline, combined with salmeterol (including LABAs), has been shown to provide a much more significant increase in FEV1 than salmeterol alone (Singh *et al.,* 2015).

e. Magnesium Sulfate

Magnesium sulfate inhibits calcium channels, reducing smooth muscle bronchoconstriction and

airway parasympathetic tone. This drug can be administered via intravenous infusion or in the form of inhalation and is relatively contraindicated in patients with renal insufficiency. The onset of action is slower than bronchodilators but faster than corticosteroids. A cochrane meta-analysis concluded that intravenous magnesium sulfate (IV MgSO4) improves lung function during severe acute exacerbations. A dose of 1.2 g or 2 g IV MgSO4 over 15-30 minutes improves lung function that is unresponsive to SABAs and corticosteroids. In patients with neuromuscular disease, myocardial damage, and renal disorders, MgSO4 administration is contraindicated. It is essential to monitor serum magnesium (Mg) levels, deep tendon reflexes, blood pressure, respiratory rate, and renal function when administering MgSO4.

f. PDE4 inhibitor

Phosphodiesterase-4 inhibitors can reduce inflammation by inhibiting the breakdown of intracellular cyclic AMP. Oral dosages are given every 24 hours. Roflumilast is a PDE4 inhibitor and has been reported to reduce exacerbations in the population (Facchinetti *et al.,* 2021).

g. Sedation and Paralysis

Sedation provides comfort and patient-ventilator synchronization. Benzodiazepines are a cheaper alternative, although more unpredictable in waking the patients. Opioids may be added to analgesic sedation. Paralysis is indicated when mechanical ventilation can not be achieved with sedation and analgesia alone. Additional therapy for OLD with exacerbations, such as antibiotics and symptomatic treatment such as mucolytics and the antioxidant erdocysteine N-acetyl cysteine, can reduce exacerbations.

3. Non-Invasive Mechanical Ventilation Management

Noninvasive Positive Pressure Ventilation (NPPV) is the most used method for non-invasive ventilation (NIV). It includes continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), or pressure support ventilation (PSV) (McCauley & Datta, 2012). RLD patients with acute hypoxemia will be given oxygen supplementation along with non-invasive ventilation (NIV), one of which is a high-flow nasal cannula (HFNC), which can achieve heated humidified oxygen flow rates, titrated to 100% oxygen fraction (FIO2) (Jentzer *et al.,* 2016). Acute hypoxemic respiratory failure, HFNC, can reduce mortality. The physiological benefits of HFNC are that it reduces dead space and provides small amounts of positive end-expiratory pressure (PEEP), reducing respiratory secretions, decreasing respiratory rate, and reducing respiratory effort (Koyauchi *et al.,* 2018).

The indication for NIV on RLD and OLD is in fully awake patients with specific clinical conditions (such as moderate-severe dyspnea, accessory muscle use, tachypnea, abdominal paradox) and impaired gas exchange (acute or acute on chronic hypercapnic respiratory failure (PaC02>45 mmHg, pH<7.35) and hypoxemia (Pa02/fi02 < 200). The main goals of mechanical ventilation for OLD and RLD are to improve pulmonary gas exchange and to rest compromised respiratory muscles sufficiently to recover from the fatigued state (Branson, 2014; Carbonara & Nava, 2012). NIV may be given to patients with OLD when an exacerbation occurs if respiratory acidosis occurs (pH <7.36) or respiratory problems persist. Oxygen supplementation is indicated in OLD patients with resting PaO2 < 55 mmHg on room air or PaO2 > 56 mmHg and < 59 mmHg with a hematocrit > 55%. SaO2 < 88% during light activity is an indication of O2 supplementation. Indications for noninvasive mechanical ventilation (NIV) include respiratory acidosis (PaCO2 $\geq$ 45 mmHg dan pH arteri $\leq$ 7.35), severe dyspnea with increased work of breathing, or persistent hypoxemia with oxygen supplementation (McCauley & Datta, 2012).

Bilevel Positive Airway Pressure (BIPAP) settings with inspiratory positive airway pressure (IPAP) 10-15 cmH2O and expiratory positive airway pressure (EPAP) 4-6 cmH2O or a combination of pressure support (PS) 10-15 cmH2O and continuous positive airway pressure (CPAP)of 4-8 cm H2O with effective NPPV mode. Pulmonary rehabilitation can be provided to increase functional capacity and reduce symptoms of dyspnea in OLD patients. Installation of an invasive mechanical ventilator may be considered when NPPV fails, severe respiratory acidosis (pH < 7.25), life-threatening hypoxia (PaO2 < 50 mm Hg), and severe respiratory distress accompanied by increased work of breathing and respiratory rate, hemodynamic instability and when there are contraindications. NPPV or in cases of threat of respiratory arrest (McCauley & Datta, 2012).

4. Invasive Mechanical Ventilation Management

The aim is to provide supportive respiratory therapy with moderate to severe respiratory acidosis (pH <7.36) and complex breathing characterized by increased respiratory effort. Indications for invasive mechanical ventilation include decreased consciousness, unstable hemodynamics, persistent inability to excrete secretions, and life-threatening hypoxemia.

Ventilation strategies in patients with impaired lung compliance in RLD are aimed at restoring collapsed lungs, maintaining FRC, and increasing

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oxygenation while reducing the risk of barotrauma. Pressure control mode has been shown to improve oxygenation, improve gas exchange, reduce peak inspiratory pressure, and increase mean airway pressure (Branson, 2014). PEEP settings are essential to increase FRC, improve oxygenation, and recruit collapsed lungs in patients with ARDS or other lung disorders with low compliance (Goligher *et al.,* 2016). ARDSnet protocol on lung protection ventilation strategy with ventilator setting TV 6 ml/Kg, regulating respiratory rate (RR) to maintain optimal minute ventilation (MV), SpO2 88-95, PaO2 55-80mmHg, increasing PEEP with increasing FiO2 (5- 24 cmH2O) according to the sliding scale, target plateau pressure (Pplat) <30cmH2O and target pH = 7.30-7.45 (if pH <7.15 then increase the TV and give NaHCO3). TV can be reduced gradually by 1 mL/kg PBW to a minimum of 4 mL/kg. Increase the TV gradually by 1 mL/kg or TV 6 mL/kg if Pplat < 25 cmH20 to Pplat > 25 cmH20. If TV is 4 mL/kg and pH <7.15, then Pplat >30 cmH20 is allowed. In patients with severe dyspnea, the TV can be increased to 8 mL/kg, and Pplat maintained <30 cmH20 (Branson, 2014; Weiss *et al.,* 2016).

Mechanical ventilation of OLD patients requires constant monitoring due to increased airway resistance and air-trapping, making patients susceptible to intrinsic PEEP. OLD with acute respiratory failure should be given assisted control ventilation mode. A TV of 6 mL/kgBW, as used in ARDS patients, is not mandatory but may be necessary to reduce Positive End-Expiratory Pressure (PEEP). Initial ventilator settings in OLD patients with a respiratory rate of 10-12 breaths/minute, TV 8-10 mL/kgBW, FiO2 as needed to maintain oxygen saturation of more than 90%, and PEEP of 0-5 mmHg. Intrinsic PEEP can be reduced by reducing respiratory rate or TV and adjusting extrinsic PEEP to lengthen breathing time. Aggressive inhaled bronchodilator therapy is administered to reduce airway resistance. Ventilator dyssynchrony should be prevented through adequate sedation, and in some cases, neuromuscular blockade is necessary to overcome patient-ventilator dyssynchrony (McCauley & Datta, 2012). In OLD, the main goals of mechanical ventilation are to reduce inspiratory effort, reduce respiratory distress, minimize dynamic hyperinflation and PEEPi, and reduce respiratory acidosis and hypoxemia. The mechanical ventilation therapy target is achieved if PaCo2 <45 mmHg, Ph >7.35, SaO2 >88%, and Pao2/Fio2 > 200 (Branson, 2014).

3.8. Monitoring Respiratory Mechanisms

1. RC_{EX}, C_{STAT} and R_{INS}

The main of the respiratory system are resistance and compliance. The respiratory system can be measured using airway pressure and airway flow. Static measurements rely on end-expiratory and end-inspiratory occlusion. In contrast, dynamic measurements use the least squares fitting method to assess lung compliance and continuous airway resistance during mechanical ventilation without the need for occlusion (Tawfik *et al.,* 2022; Wang & Sharma, 2017). These methods can only be used passively or with minimal inspiratory effort.

Compliance (C) is defined as the elastic property of the respiratory system, including the chest wall and lungs. Meanwhile, static compliance (C_{STAT}) is the ratio between tidal volume (VT) and changes in transmural pressure (ΔP). ΔP can be calculated as the difference between plateau pressures (P_{PLAT}) and PEEP total ($PEEP_{TOT}$), measured at the end of inspiration and expiration, respectively. From that statement, we get the equation $C_{STAT} = VT/\Delta P = VT/(P_{PLAT} - PEEP_{TOT})$ with a compliance dimension of ml/cmH2O. Elastance (E) is the inverse of static compliance, with eq E= P/ VT.

Static compliance can be measured dynamically and continuously using the least squares fitting (LSF) occlusion (Tawfik *et al.,* 2022; Wang & Sharma, 2017). C_{STAT} in normal lungs with mechanical ventilation is approximately 50-60 mL/cmH_2O. Decreased compliance may occur in atelectasis, pneumothorax, ARDS, pulmonary fibrosis, and chest wall rigidity. ARDS patients have a C_{STAT} of around 35-45 mL/cmH_2O (table 3). The lung compliance monitoring in ARDS patients can provide information regarding aerated lung volume. In pulmonary emphysema, there is increased compliance.

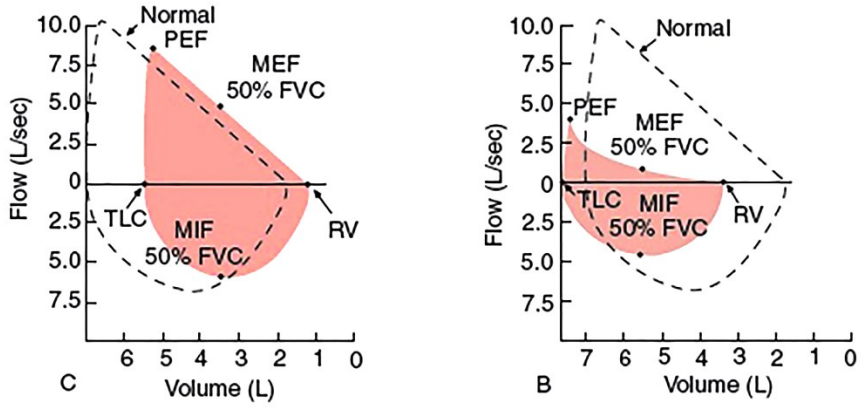
On the other hand, resistance (R) is defined as resistance to gas flow in the respiratory system during inspiration due to frictional forces. R can be calculated as the ratio between the pressure that drives a specific flow and the resulting flow rate (V) with the equation $R = \Delta P/V$ with the resistance dimension being cmH_2O/(l/s). Respiratory system resistance consists of the airway and endotracheal tube resistance because the lung tissue's resistance is low. Resistance can only be calculated during inspiration obtained by Eq $R_{INSP} = (P_{PEAK} - P_{PLAT})/V_{INSP}$ in volume-controlled mode with a constant flow rate. Resistance can be measured continuously using the least squares fitting method to distinguish between inspiratory and expiratory resistance. If expiratory resistance is higher than inspiratory resistance, then it is normal because the shape of the respiratory tract is like a tree. The significant difference between inspiratory and expiratory resistance may cause expiratory flow limitation. Inspiratory resistance (R_{INSP}) in normal lungs with mechanical ventilation is 10-15 cmH_2O/(l/s) (Arnal *et al.,* 2018). A narrow ETT, incorrect position, or use of a heat and moisture exchanger (HME) causes

Table 2. The values of respiratory mechanics are passive mechanical ventilation (Arnal *et al.,* 2018).

	Normal	ARDS	COPD
Compliance (mL/cmH_2O) C_{STAT}	50-60	35-45	50-70
Resistance (cmH_2O/s/l) R_{INS}	10-15	10-15	15-30
Constant Expiratory time (s) RC_{EX}	0.5-0.7	0.4-0.6	0.7-2.1

(a) (b)

Figure 10. (a) Dynamic Lungs Monitoring Panel on a Mechanical Ventilator showing (b) trends for all respiratory mechanics variables (Arnal *et al.,* 2018).



(a) (b)

Figure 11. Flow-Volume Loop on: RLD (a) and OLD (b) (Winter & Dakin, 2020). (RV = residual volume; TLC = total lung capacity; FVC = forced vital capacity; PEF = peak expiratory flow; MEF = maximal expiratory flow; MIF = maximal inspiratory flow).

an increase in RINSP, which increases with flow in an exponential relationship (Arnal *et al.,* 2018). Table 2 compares the respiratory mechanics values of passive mechanical ventilation in normal people, ARDS, and COPD.

The constant expiratory time (RC_{EX}) is defined as the volume change rate after a gradual pressure change. Itis a product of compliance and resistance measured during inspiration or expiration. Its the dimension is expressed in seconds. From the statement above, the equations obtained are $C_{INSP} = C_{STAT} \times R_{INSP}$ and $RC_{EXP} = C_{STAT} \times R_{EXP}$. The dependence of C and R means that RCEXP helps assess the overall respiratory mechanism and its changes. This measurement is accurate in patients who breathe passively and spontaneously, assuming passive expiration. Measurement of R_{CEXP} at 75% of expiratory TV will provide more accurate results with slow compartment time constants in OLD patients who experience expiratory flow limitation (Arnal *et al.,* 2018).

The value of R_{CEXP} in normal lungs is 0.5-0.7 seconds. A prolonged R_{CEXP} value occurs if the resistance increases. Mixed conditions of decreased and increased resistance can lead to pseudo-normal R_{CEXP}. Mechanical ventilators can measure each RC_{EX} breath at approximately 75% of expiratory volume. RC_{EX} results are displayed on a dynamic lung monitoring panel, showing trends for all respiratory mechanics variables (Figure 10). We can also measure CSTAT and RCEXP ourselves using the occlusion method.

2. Flow-Volume Loop

The flow-volume loop displays airflow (L/sec) about lung volume (in L) during maximum residual

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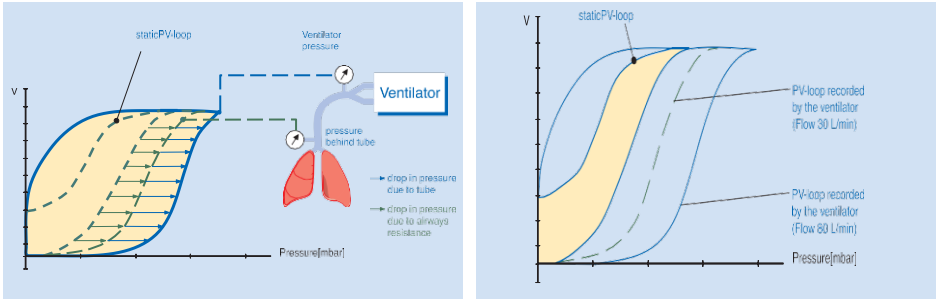


Figure 12. Loop pressure-volume (Rittner & Döring, 2015).

volume inspiration and total lung capacity expiration. The airflow is appropriate for a given lung volume (Figure 11a). The flow-volume loop narrows due to reduced lung volume (Figure 11b). Airflow is more significant than normal lung volume because the increased elasticity of the lungs keeps the airways open (Winter & Dakin, 2020).

The airflow rate is slower at low lung volumes in RLD due to lower compliance. When airflow is viewed as a function of lung volume, it becomes clear that airflow is higher than normal (due to the increased elasticity characteristic of fibrotic lungs). OLD patients experience decreased airflow, prolonged expiration, and MEF < MIF. Peak expiratory flow is occasionally used to estimate the degree of airway obstruction, depending on the patient's respiratory effort (Winter & Dakin, 2020).

3. Pressure-Volume Loop

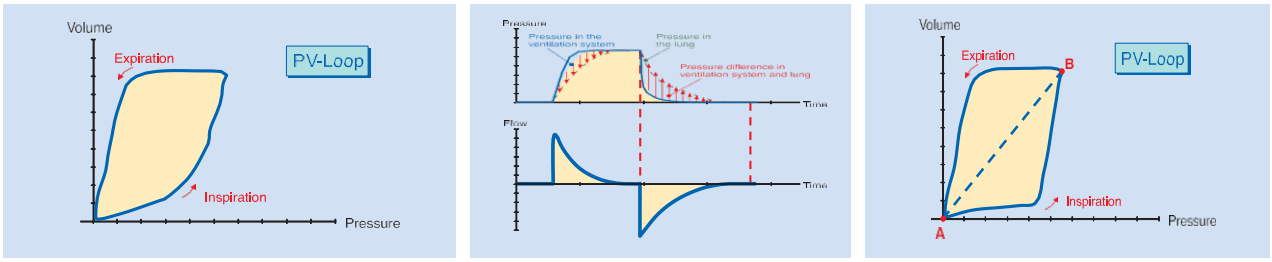
Figure 12 shows that the P-V loop generated during ventilation does not meet the standard that the respiratory gas flow must be equal to zero by the time the individual measured values are recorded. The respiratory gas flow creates an additional pressure gradient (Rittner & Döring, 2015).

The P-V loop does not provide an accurate picture of compliance. The greater the inspiratory flow, the greater the additional pressure gradient and, thus, the degree of inaccuracy. The -V loop obtained in controlled ventilation, in general, can help slow the lung filling and better reflect compliance in the ascending branch (Rittner & Döring, 2015).

Several studies have shown that the P-V loop recorded during ventilation correlates with the loop from the standard procedure during constant inspiratory flow (Hess, 2006). Several studies have shown that the P-V loop recorded during ventilation correlates with the loop from the standard procedure during continuous inspiratory flow. (Hess, 2006) The analysis assumes that the pressure drop due to inspiratory resistance will also remain at constant flow and that the steepness of the inspiratory loop will simply reflect thoracic elastance. This also shows that in ventilation modes with deceleration flow (BIPAP, PCV, etc.), it is impossible to conclude the P-V loop regarding the development of lung compliance (Rittner & Döring, 2015).

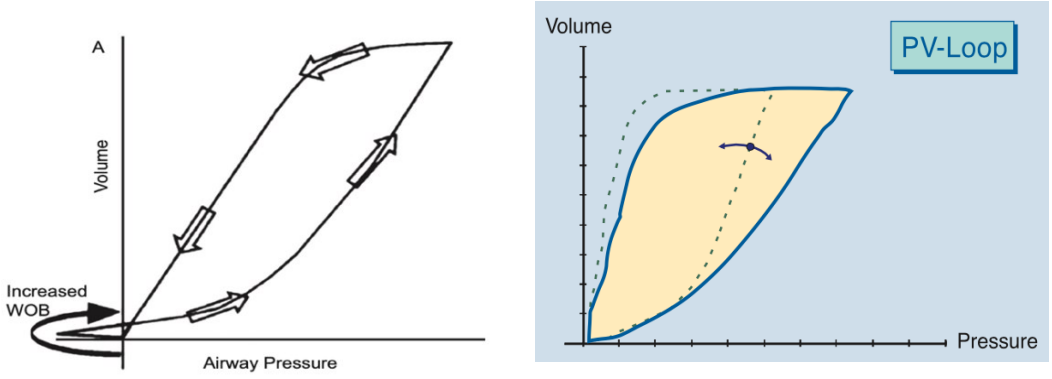
The lungs are filled with a constant flow, and P_{aw} increases gradually during inspiration. Pulmonary pressure rises at the same rate and, at the end of inspiration, reaches the same value as the pressure in the respiratory system ($P_{plateau}$). During expiration, the ventilator opens the exhalation valve wide enough to maintain the set PEEP level. As a result of reversed pressure (the pressure in the lungs is more significant than PEEP), it flows out of the lungs, and lung volume slowly decreases. This is why the P-V loop during controlled ventilation runs counterclockwise (Figure 13a) (Rittner & Döring, 2015). The lungs are filled with a constant flow, and P_{aw} increases gradually during inspiration. Pulmonary pressure rises at the same rate and, at the end of inspiration, reaches the same value as the pressure in the respiratory system ($P_{plateau}$). During expiration, the ventilator opens the exhalation valve wide enough to maintain the set PEEP level. As a result of reversed pressure (the pressure in the lungs is more significant than PEEP), it flows out of the lungs, and lung volume slowly decreases (Figure 13 b and c).

The pressure difference determines the respiratory flow, which decreases during inspiration, thus creating a slowed flow (deceleration). The ventilator constantly maintains the pressure during inspiration, so the P-V loop during pressured-control mode is shaped like a box (Rittner & Döring, 2015). In spontaneous breathing, the P-V loop runs clockwise. The patient's inspiratory effort creates negative pressure in the lungs, which then impacts the respiratory system, the pressure of which is measured by the ventilator. A distinctive feature of synchronized breathing with the patient's inspiratory effort, like assisted spontaneous breathing (ASB), pressure support (PS), and synchronized intermittent mandatory ventilation (SIMV.), is a slight rotation just above the zero point. The patient first generates negative pressure in the lungs. However, once the trigger threshold is exceeded, the ventilator generates positive pressure in the respiratory system (Restrepo & Khusid, 2022). Figure 14a shows an increase in the breathing



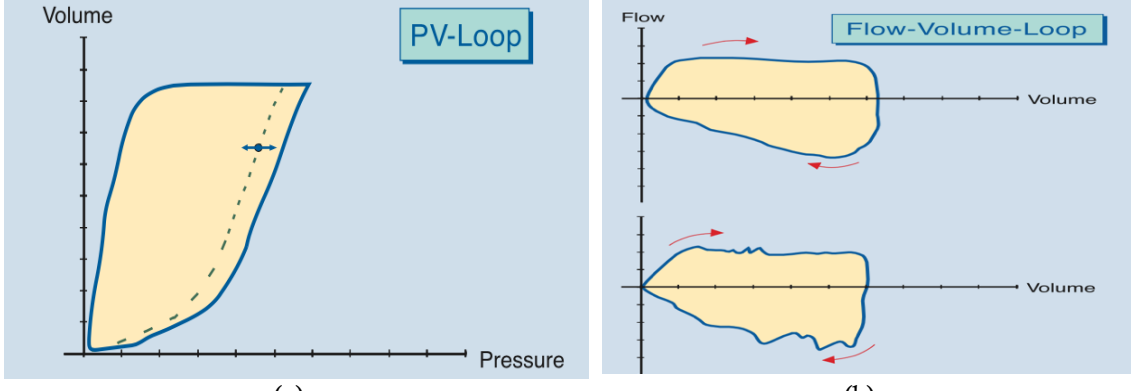
(a) (b) (c)

Figure 13. Loop P-V on volume-control mode (a), the P-V loop in pressure control ventilation mode is shaped like a box (b and c) (Rittner & Döring, 2015).



(a) (b)

Figure 14. Pressure-volume plot showing increased work of breathing (a), P-V loop in changes in lung compliance (b) (Restrepo & Khusid, 2022).



(a) (b)

Figure 15. Loop P-V in changes of airway resistance (a) and Flow-volume loop with airway resistance (b) (Rittner & Döring, 2015).

work on the pressure-volume plot. When there is a decrease in compliance, as seen in RLD, the lungs become less elastic, and the ventilator settings remain constant, making the P-V loop in volume-controlled ventilation flatter, as in Figure 14b. Changes in the steepness of the inspiratory branch of the P-V loop are proportional to changes in lung compliance.

If there is a change in resistance, for example, in OLD, the steepness of the right branch of the loop remains unchanged, but its position changes. If the flow remains constant during ventilation, the loop becomes flatter at the top of the inspiratory branch (Figure 15a). This could indicate overdistension in a particular area of the lung (Rittner & Döring, 2015). A unique pattern of increasing airway resistance will be reflected in the flow-volume loop as a decrease in peak expiratory flow and the pattern captured in the expiratory tracing (Figure 15b). Flow volume plots can be used as diagnostic markers. It can describe the severity of airway obstruction. Weiner *et al.* (2016) found that abnormal flow volume plots can measure disease severity. Karkhanis *et al.* (2013) stated that observing the ventilator flow-volume plot is the most effective way to detect upper airway obstruction, even before symptoms appear (Sarkar *et al.*, 2022).

4. Conclusions

Although RLD and OLD have similar signs and

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symptoms, they have different pathological features. The leading cause of RLD is a pathological condition that causes a decrease in lung compliance. Meanwhile, the primary pathological process of OLD is an increase in airway resistance, which causes typical obstructive symptoms. Addressing this area of interest can help clinicians provide appropriate management of both pharmacotherapy and mechanical ventilation and monitor respiratory mechanisms.

Conflict of interest

All authors have no conflict of interest.

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