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DYSLIPIDEMIA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A METABOLIC COMORBIDITY, SYSTEMIC INFLAMMATION, AND THERAPEUTIC PERSPECTIVES

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Abstract

Dyslipidemia has emerged as a significant and often underappreciated comorbidity in patients with chronic obstructive pulmonary disease (COPD). It is increasingly recognized not merely as a cardiovascular risk factor but as a contributor to systemic inflammation and disease progression in COPD. The mechanisms linking dyslipidemia with COPD are multifactorial, involving oxidative stress, altered adipokine secretion, endothelial dysfunction, and chronic low-grade inflammation. These interactions create a bidirectional relationship that amplifies pulmonary and cardiovascular impairment. Despite accumulating evidence, dyslipidemia remains inadequately addressed in COPD management guidelines. This review synthesizes current knowledge on the pathophysiological interplay between lipid abnormalities and COPD, highlights their clinical consequences, and outlines contemporary and emerging strategies for effective management, including the roles of statins, PCSK9 inhibitors, and targeted metabolic interventions. Emphasis is placed on the need for a comprehensive, multidisciplinary approach in managing COPD patients with metabolic dysfunction.

Keywords

chronic obstructive pulmonary disease, dyslipidemia, systemic inflammation, lipid metabolism, cardiovascular risk, adipokines, PCSK9 inhibitors, metabolic comorbidity, oxidative stress.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder that affects over 250 million people globally and represents the third leading cause of death worldwide (WHO, 2017). While traditionally perceived as a condition limited to the lungs, growing evidence supports its systemic nature, manifesting through skeletal muscle dysfunction, cognitive decline, and, notably,

metabolic syndromes such as insulin resistance and dyslipidemia (Agusti et al., 2012; Buist et al., 2007).

Dyslipidemia, defined by abnormalities in serum lipid concentrations, is increasingly observed in patients with COPD. Typical patterns include elevated triglycerides, increased low-density lipoprotein cholesterol (LDL-C), and reduced high-density lipoprotein cholesterol (HDL-C), which are collectively associated with atherosclerosis, coronary artery disease, and increased mortality (Faner et al., 2015; Kahnert et al., 2017). Yet, despite its prevalence and clinical relevance, dyslipidemia remains insufficiently addressed in COPD therapeutic protocols (GOLD, 2023). This review aims to elucidate the mechanisms connecting lipid abnormalities with pulmonary pathology and to propose integrated therapeutic strategies.

2. Epidemiology and Clinical Burden of Dyslipidemia in COPD

Numerous epidemiological studies have demonstrated a higher prevalence of dyslipidemia in COPD patients than in the general population. According to Tsiligianni et al. (2014), patients with COPD exhibit a 1.5- to 2-fold increased likelihood of presenting with lipid disturbances. The BOLD (Burden of Obstructive Lung Disease) study and subsequent meta-analyses (Xuan et al., 2018; Cebron Lipovec et al., 2016) further confirmed that metabolic syndrome, with dyslipidemia as a core component, is prevalent in up to 45–50% of individuals with moderate to severe COPD.

The presence of dyslipidemia in COPD is associated with a range of clinical consequences:

- **Increased frequency of acute exacerbations** (Agusti et al., 2012; Burge et al., 2003).
- **Worsened lung function parameters**, including accelerated decline in forced expiratory volume (FEV1) (Guo et al., 2016).
- **Greater cardiovascular event rates** (Faner et al., 2015; Matsuo et al., 2014).
- **Reduced exercise capacity and quality of life** (Dahl et al., 2007; Choi et al., 2019).

3. Pathophysiological Mechanisms Linking COPD and Dyslipidemia

3.1 Systemic Inflammation

Chronic low-grade inflammation is a hallmark of COPD. Inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) disrupt lipid metabolism by inhibiting lipoprotein lipase and modulating hepatic lipid synthesis (Zhou et al., 2014; Harrison et al., 2013). These processes result in elevated triglycerides and LDL-C, and reduced HDL-C.

3.2 Oxidative Stress and Lipoprotein Oxidation

Patients with COPD exhibit heightened oxidative stress due to increased production of reactive oxygen species (ROS). These ROS oxidize LDL particles, making them more atherogenic and triggering macrophage activation and endothelial damage (Matsuo et al., 2014). Oxidized lipids also exacerbate airway inflammation and reduce lung elasticity.

3.3 Adipokine Dysregulation

Leptin and adiponectin, hormones secreted by adipose tissue, are dysregulated in COPD. Leptin, a pro-inflammatory cytokine, is elevated and contributes to systemic inflammation and lipid imbalance. Conversely, adiponectin, which exerts anti-inflammatory and lipid-modulating effects, is reduced in COPD patients (Liu et al., 2017; Isago, 2024).

3.4 Endothelial Dysfunction

Endothelial injury, partially driven by oxidized lipids and cytokines, impairs nitric oxide availability, promotes vascular stiffness, and contributes to both pulmonary hypertension and systemic atherosclerosis (Zubiashvili et al., 2023).

4. Clinical Implications

4.1 Cardiovascular Risk

The overlap between COPD and cardiovascular disease (CVD) is well documented. Dyslipidemia significantly amplifies this risk by promoting plaque formation and increasing the likelihood of myocardial infarction, stroke, and peripheral artery disease (Kahnert et al., 2017; Caram et al., 2016).

4.2 Exacerbations and Hospitalizations

Higher triglyceride levels and low HDL-C have been associated with frequent exacerbations and longer hospital stays (Agusti et al., 2012). Lipid-driven inflammation may potentiate the response to respiratory infections, leading to more severe outcomes.

4.3 Lung Function Decline

Longitudinal studies show that COPD patients with untreated dyslipidemia experience a faster decline in FEV1, independent of smoking status (Guo et al., 2016; Jain et al., 2017).

4.4 Quality of Life

Metabolic disturbances, including lipid abnormalities, correlate with reduced physical activity, increased fatigue, and lower scores on standardized quality of life assessments (James et al., 2018; Kytikova et al., 2012).

5. Management Strategies

5.1 Lifestyle Interventions

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Nutritional counseling, weight reduction, and structured exercise programs have demonstrated improvements in lipid profiles and respiratory outcomes (James et al., 2018). Smoking cessation remains paramount.

5.2 Pharmacological Therapies

- **Statins** (e.g., atorvastatin, rosuvastatin) reduce LDL-C and exert anti-inflammatory effects. Some trials suggest improvement in COPD outcomes, though findings remain mixed (Tashkin et al., 2009; Tse et al., 2013).
- **PCSK9 inhibitors** (e.g., alirocumab, evolocumab) offer potent LDL-C reduction and may benefit statin-intolerant patients with COPD.
- **Fibrates** and **omega-3 fatty acids** may aid in lowering triglycerides and improving HDL-C, although their specific role in COPD remains under investigation.
- **Anti-cytokine therapies** targeting IL-6 or TNF-α represent a future direction in modulating systemic inflammation and lipid abnormalities simultaneously.

5.3 Integrated COPD-Metabolic Care

Emerging evidence supports a **multidisciplinary care model** combining pulmonology, cardiology, and endocrinology to optimize metabolic and respiratory health (Stockley et al., 2019; Ospanova et al., 2019).

6. Future Directions

- **Biomarker development** for early identification of high-risk COPD phenotypes with dyslipidemia (Zubiashvili et al., 2023).
- **Randomized clinical trials** examining lipid-lowering therapy in COPD subgroups.
- **Personalized medicine** approaches integrating genomic, metabolic, and environmental data to tailor therapy.

7. Conclusion

Dyslipidemia is a prevalent and clinically impactful comorbidity in COPD, intricately linked to systemic inflammation, oxidative stress, and disease progression. Despite compelling evidence, it remains under-recognized in routine COPD care. Addressing this gap requires a paradigm shift toward integrated management that includes lipid monitoring and targeted therapies. By adopting a multidisciplinary and personalized approach, clinicians can improve outcomes and quality of life in this complex patient population.

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