Chronic obstructive pulmonary disease and aging.

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Abstract

Chronic obstructive pulmonary disease is an obstructive airflow condition in which there is inflammation of the airways. It is one of the chief causes of morbidity and mortality in older age. Age can significantly affect the prognosis and diagnosis of the disease. COPD is mainly being misdiagnosed due to age-related barriers that decrease the sensitivity of the diagnostic tests. Also, the aging group usually has multiple comorbidities to alter the disease and complexity.

Hence, rapidly aging populations' epidemiologic criteria need consideration of aging-related changes. The inadequate age-related scoring would result in increased misidentification of COPD and may, in turn, be a basis of misinformation in public health policy and patient care. Both age and COPD are related to variations in body composition, and therefore, it may be difficult to investigate whether the observed body composition changes are age-related or disease related. Despite increased awareness of COPD, there remains extensive under-recognition and under-diagnosis of the disease. Spirometry, CT scans, and MRI can help determine the disease severity and progression but require age-related adjustment of scales. The first step for COPD betterment is the cessation of smoking. However, bronchodilators, anti-inflammatories, and oxygen therapy are the mainstay treatments.

Keywords Chronic obstructive pulmonary disease, Forced expiratory volume, Forced vital capacity.

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Introduction

Chronic obstructive pulmonary disease is an obstructive airflow condition in which there is inflammation of the airways [1]. It is one of the chief causes of morbidity and mortality in older age around the globe. The disease symptoms and disabilities are partially reflected by the burden of the disease [2].

Fragoso et al., states that as per the World Health Organization, by the year 2025, around 400 million people worldwide will be aged ≥ 80 years [1]. It was highlighted that this aging shift would be noted more in low-and middle-income countries. However, the developed countries will also demonstrate rapidly aging populations. It is predicted that in the United States, the percentage of those aged ≥ 65 years will increase from 12.9% to 20% by 2030[1]. The reason may be various factors, but multiple comorbidities lead to early aging and life loss like in COPD [3].

Third National Health and Nutrition Examination Survey [NHANES III] determined that Americans aged 40 to 80 years had a prevalence of COPD of 12.6% [1]. At the same time, the prevalence rates by using the Global Initiative for Obstructive Lung Disease GOLD-defined COPD were 37.7% in those aged 65-80 years and 22.2% in those aged 40-64 years. With 49% having mild severity (forced expiratory volume in one minute/ forced vital capacity, FEV1/FVC<0.70 and FEV1 ≥ 80%), and 10%-13% having the severe disease (FEV1/FVC<0.70 and FEV1<50%) [1].

Literature Review

Review of Longitudinal Aging Study Amsterdam (LASA) also concluded that the disease is seen more in older age group (50.5% male, mean age 60.5 ± 2.9 years). Compared to non-COPD subjects, COPD subjects had a more impaired disease-specific health status (CAT: 9.5 ± 5.9 vs. 6.7 ± 5.2). It was proposed that patients with COPD had a decreased physical performance, impaired disease-specific health status, and were more socially deprived compared to non-COPD subjects. These impairments need to be contemplated when setting up a management program for patients with COPD [3].

COPD affects one in seven people in the UK, predominantly in the age group above 50 years. A study from Pakistan reflected that around 50% of males and 41% of females were affected by COPD in their sample. The sample showed more cases in the age group 50 years and above [4].

Vaz Fragoso et al., described that more middle-aged and older age groups are susceptible to COPD, and age can significantly affect the prognosis and diagnosis of the disease [5]. COPD is mostly being misdiagnosed due to age-related barriers that decrease the diagnostic tests' sensitivity. Also, the aging group usually has multiple comorbidities to alter the disease course and complexities. Very inadequate insight over age-related changes in the disease diagnosis and management can be found in the literature and hence warrant research.

The current review aims to focus on rapidly aging populations' epidemiologic criteria for diagnosis and management to reduce the misinformation in public health policy and patient care [5].

Impact of aging on development and prognosis

The variations that occur with aging are complex and characterized by deterioration in Forced Expiratory Volume in one minute (FEV1). This is primarily attributed to a reduction in muscular strength and an increase in inflammatory cells. These changes mimic COPD and can cloud the ability to diagnose obstructive disease in addition to exacerbating any pre-existing disease [6].

The aging lung has a progressive reduction in physiologic capacity. The mechanics are mostly impaired. This includes increased rigidity of the chest wall, decreased diameter of the small airways, decreased elastic recoil of the lung, and emphysema. The change in FEV1 is significant and mirrors the increase in obstruction seen in COPD, leading to a hypothesis that COPD represents an acceleration of the aging process. These impairments lead to a decreased FEV1/FVC ratio causing more air to get trapped, which leads to a ventilation-perfusion mismatch. Other age-related physiologic impairments include decreases in pulmonary capillary density, respiratory muscle strength, mucociliary clearance efficiency, and cerebrovascular responsiveness to carbon dioxide [1]. There is a significant overlap in the aging lung's physiologic impairments and the disease pathogenesis leading to misdiagnosis of the severity of the disease in COPD. Hence, Spiro metric measures and chest CT imaging must account for aging-related changes in lung function and structure [1].

Several factors, such as environmental agents, tobacco smoking, or exposure to biomass fuel, and inherited genetic factors cause COPD, while it has been suggested that COPD is a disease of accelerated aging [7]. Cordoba et al., postulated that telomere length is a biomarker of aging and consists of repetitive hexanucleotides (5′-TTAGGG-3') [7]. These hexanucleotides protect the end of chromosomes from being recognized as double-strand breaks and avoid duplication in stress-related conditions. This leads to end replication due to subsequent shortening of the telomeres. Cordoba et al., stated some studies have shown that patients with COPD exhibit shorter telomeres in circulating leukocytes than age-matched smokers without COPD [7]. This highlights an association of aging with the presence of disease. Hence, proposing that telomere shortening might be accelerated in patients with COPD and serve as a disease progression biomarker. The study results by Cordoba et al., revealed that telomeres were shorter in COPD patients ($p=0.003$) [7]. It was hypothesized that this shortening was inversely related to the baseline telomere length ($p<0.001$). Though, no significant association was established between the rate of change in telomere length and change in lung functions in COPD patients ($p>0.05$). This theory has inadequate clinical support in the literature and needs more insight.

Aging increases body fat, mainly in the abdominal region, and a deterioration in lean body mass. According to the European Working Group on sarcopenia in Older People, sarcopenia can occur secondary to an underlying pathology such as COPD, malnutrition, cancer, or organ failure; it is classified as secondary sarcopenia. Hence leading to cachexia and poor prognosis of the disease in individuals from the older age group [7,8].

Respiratory muscle mass decline can lead to incapacity to ventilate in respiratory diseases. The decreased ability to clear mucus from the lungs further adds to problems. A reduction in the respiratory muscles' strength will significantly impact an individual's ability to generate the force required for an effective cough [6].

Literature shows that aging decreases diaphragm peak power by approximately 35% ($P<0.05$) [9]. Such changes in the contractile properties are postulated to be due to decreases in abundance of calsequestrin and sarcoplasmic reticulum Ca^{2+} - ATPase. Kelley et al., stated that aging also increases passive stiffness ($P<0.05$). Both age and COPD are related to variations in body composition, and therefore, it may be difficult to investigate whether the observed body composition changes are age-related or disease-related [9].

Impact of aging on diagnosis

Older individuals often report respiratory symptoms and have a high prevalence of symptomatic lung disease, most commonly obstructive airway disease and lung cancer. It is postulated that there are high chances to misidentify or modify respiratory diagnoses due to other ailments and decreased compliance with diagnostic tests [8]. Literature shows that two-thirds of middle-aged or older individuals who have self-reported pulmonary symptoms do not have spirometry-confirmed COPD [1].

This may be enlightened by age-related rises in factors additional than COPD that contribute to respiratory symptoms, including chronic rhinosinusitis, medications (e.g., angiotensin-converting enzyme inhibitors), and Gastroesophageal reflux disease. Fragoso et al., described that research had shown decreased utilization of spirometry-related diagnostic workup in primary care settings [1]. Moreover, these tests are also not adequately conclusive due to having a generalized scoring system encompassing all ages as a baseline [1].

The Global Initiative for Obstructive Lung Disease (GOLD) is a diagnostic spirometric criterion that includes a reduced ratio of the Forced Expiratory Volume in 1-second (FEV1) to Forced Vital Capacity (FVC), defined by a GOLD threshold of <0.7. The FEV1 percent then stratifies the severity of COPD predicted (%Pred) (Table 1) [1].

Table 1. The Global Initiative for Obstructive Lung Disease (GOLD) criteria for COPD.

Severity for all ages	
Mild	>80% Pred
Moderate	50%-79% Pred
Severe	<50% Pred

However, Fragoso et al., described that GOLD-based spirometric criterion inadequately diagnose COPD. Further, GOLD criteria involve spirometry before and after administration of an inhaled Broncho Dilator (BD) [1].

Among older individuals, this approach has disadvantages. Older individuals have limited capacity to perform multiple FVC maneuvers and may have an adverse response. GOLD defines a reduced FEV1/FVC by a fixed ratio of 0.70 across all ages, thus failing to distinguish between age-related airflow limitation and COPD-related airflow obstruction.

Hence, Fragoso et al., postulated that GLI-based COPD diagnosis shows a higher frequency of severe COPD (GLI-based 89.6%vs. GOLD-based 73.8%) [1]. The misclassification of GLI-based COPD compared with GOLD was only 6.9% [5-10].

Modalities such as Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) can also be used to distinguish COPD cases and their complications. However, assessment of the entire body using CT and MRI is arduous and time-consuming.

Furthermore, CT involves ionizing radiation and is not suggested for older age group or healthy individuals [1].

CT allows one to assess the disease progress and visualize the location and intensity of the lesions. Data shows that the recognition error on CT scan for any lesion is not higher than 7.5% [11].

A pitfall was documented by Fragoso et al., regarding emphysema cases established through a CT-scan, which showed up to > 5% aging-related limitations [1]. The reason being aging is linked with "senile" emphysema and may give falsely high prevalence.

A study with twenty-eight COPD participants and ten control participants were studied for pulmonary function testing, CT, and MRI findings. CT was taken as the reference standard to compare the findings. It was found that MRI and CT were co-relatable. ($P<0.001$) The diagnostic performance and reproducibility were good [95% confidence interval: 0.88] [12].

Despite increased awareness of COPD, there remains extensive under-recognition and under-diagnosis of the disease. It has also been postulated by Vaz Fragoso et al., that not performing spirometry for diagnosing COPD is the strongest predictor for an incorrect diagnosis of COPD [5]. A retrospective analysis showed that COPD had been extensively missed in 85% of 38,859 COPD patients [13]. Hence, this can lead to inappropriate use of COPD pharmacotherapy due to inadequate diagnosis. Which can lead to adverse outcomes and a poor prognosis [5,10].

Dual-energy X-ray Absorptiometry (DXA) can measure the body composition and parameters It can be used along with other baseline tests for airway diseases. DXA can provide insight over the lean, fat, and bone mass due to its high accuracy, and therefore, it is recommended for patients with COPD to rule out cachexia and predict the prognosis [13].

New approaches such as COPD Gene 2019 are also being studied, which include extensions in the definitions of COPD. The Global initiative for chronic Obstructive Lung Disease (GOLD) strategy used only airflow obstruction and exposure to define COPD while also referring to exposure history, respiratory symptoms, and structure without clear delineation. However, COPD Gene 2019 incorporates all features from symptoms, exposure, anatomy, and physiology in redefining COPD. Hence, maybe a good chance in the diagnostic techniques [14].

Impact of aging on the treatment

The first step for COPD betterment is the cessation of smoking. The elderly population is at risk with a higher prevalence of mortality in COPD patients. However, mortality in COPD patients has been documented to be significantly higher among non-quitters than in quitters. During a 5-year follow-up study, in which 113 deaths were included, it was found that the quitting-smoking group (n=92) showed around 40 deaths in the sample, whereas the continuing-smoking group (n=112) showed 73 deaths. The mortality ratio was significantly higher in the continuing-smoking group than the quitting-smoking group ($P=0.0002$). Hence, it is postulated that smokers of any age with COPD benefit significantly from smoking cessation. The reason is that it slows degeneration and decline in the FEV1 [15].

Long-term oxygen therapy is also one of the selected options for COPD patients. Though the failure rate, especially in the elderly, is high. The elderly usually have low compliance and adherence to the treatment. In a study, NIV failure's main reasons were stated as frailty (40%). They documented that the SOFA score was high while the GCS (OR: 1.2, p: 0.042) score was low in the elderly [16].

Literature suggests that the mortality rate of COPD patients undergoing LTOT gets lowered [17]. The maximum exercise power (Wmax), six Minutes Walking Distance (6MWD), maximum oxygen uptake (VO2max), Modified British Medical Research Council (MMRC), quality of life, BODE index, the arterial partial pressure of oxygen (PaO_2), and the arterial partial pressure are also documented to increase with oxygen therapy ($P<0.05$) [18].

Steroids are known to be effective drugs for acute and long-term severe cases. However, the complications in elderly patients cause hindrance in the long term or increased dosage use. Studies show a decline in glucocorticoid receptor expression with age. Hence, if long-term oral steroid treatment is necessary, doctors must consider the NICE guidelines advice that those over 65 years should be prescribed prophylactic osteoporosis management. The risk of diabetes and pneumonia increases with inhaled and oral corticosteroids. A study on the comparison of CHF and COPD patients' health found an

increased risk of pneumonia secondary to inhaled corticosteroids concluded that the elderly and those with more severe disease were at the highest risk of pneumonia [19].

A greater proportion of individuals remain undiagnosed to be sufficiently treated. In the elderly population providing more access to health care facilities and elderly rehabilitation may improve the life's quality in the elderly individuals. Further research is warranted to find the impact of high-dose inhaled corticosteroids in the elderly population and the development of new therapies for COPD [6].

Discussion and Conclusion

Despite an improved awareness of COPD, there remains extensive under-recognition and under-diagnosis of the disease due to the disease association's inadequate information with aging phenomena. Numerous patients with chronic airflow limitation are conscious of symptoms, yet they ignore their disease and report late. Whereas, many health care systems delay diagnosis by avoiding basic diagnostic tests or relying on clinical diagnosis rather than spirometry or CT scan. This discrepancy is further augmented by the inadequate capability of the diagnostic tools in the older age groups. Where the scales do not correctly predict the severity or extent of the disease prevalence, this potentiates the need for research on disease management with respect to age. Since starting treatment early during COPD can significantly slow the disease progression and improve patient-related outcomes. Therefore, it is usually documented that it is valuable for COPD patients to receive an early diagnosis.

References

1. Fragoso CA, Gill TM, Leo-Summers LS, et al. Re-evaluation of combination therapy in chronic obstructive pulmonary disease (COPD). Respir Med. 2019;151(1): 27-34.
2. Franssen FM, Smid DE, Deeg DJ, et al. The physical, mental, and social impact of COPD in a population-based sample: results from the Longitudinal Aging Study Amsterdam. NPJ Prim Care Respir Med. 2018;28(1):1-6.
3. Divo MJ, Celli BR, Poblador-Plou B, et al. Chronic Obstructive Pulmonary Disease (COPD) as a disease of early aging: Evidence from the EpiChron Cohort. PLoS One. 2018;13(2):143.
4. Sultana T, Afzal A, Sultana S, et al. Epidemiological estimates of Respiratory diseases in the hospital population, Faisalabad, Pakistan. Braz Arch Biol Technol. 2017;60.
5. Vaz Fragoso CA, Magnussen H, Miller MR, et al. Spirometry-based diagnostic criteria that are not age-appropriate lack clinical relevance. Am J Respir Crit Care Med. 2018;197(7):963-964.
6. Jayadev A, Gill SK. COPD in the elderly: The ageing lung. GM. 2017.
7. Cordoba-Lanus E, Cazorla-Rivero S, Espinoza-Jimenez A, et al. Telomere shortening and accelerated aging in COPD: findings from the BODE cohort. Respir Res. 2017;18 (1): 59.
8. Fragoso CA. Epidemiology of lung disease in older persons. Clin Geriatr Med. 2017 ;33(4):491-501.
9. Kelley RC, McDonagh B, Ferreira LF. Advanced aging causes diaphragm functional abnormalities, global proteome remodeling, and loss of mitochondrial cysteine redox flexibility in mice. Exp Gerontol. 2018;103(1):69-79.
10. Fragoso CA, Cain HC, Casaburi R, et al. Spirometry, static lung volumes, and diffusing capacity. Respir Care. 2017;62(9):1137-1147.
11. Smelkina NA, Kolsanov AV, Chaplygin SS, et al. Pulmonary emphysema recognition by CT scan. Adv Comput Vis Comput Biol . 2017;41(5):726-31.
12. Benlala I, Berger P, Girodet PO, et al. Automated volumetric quantification of emphysema severity by using ultrashort echo time MRI: validation in participants with chronic obstructive pulmonary disease. Radiology. 2019;292(1):216-225.
13. Ho T, Cusack RP, Chaudhary N, et al. Under-and over-diagnosis of COPD: a global perspective. Breathe. 2019;15(1):24-35.
14. Make BJ. COPD: a new diagnostic paradigm. Chronic Obstructive Pulmonary Diseases. Chronic Obstr Pulm Dis. 2019;6(5):438-443.
15. Bai JW, Mao B, Yang WL et al. Asthma-COPD overlap syndrome showed more exacerbations however lower mortality than COPD. QJM: Int J Med. 2017 ;110(7): 431-436.
16. Kara I, Yildirim F, Zerman A, et al. The impact of frailty on noninvasive mechanical ventilation in elderly medical intensive care unit patients.Aging Clin Exp Res. 2018 ; 30(4):359-366.
17. Pavlov N, Haynes AG, Stucki A, et al. Long-term oxygen therapy in COPD patients: population-based cohort study on mortality. Int J Chron Obstruct Pulmon Dis. 2018;13(1): 979-988.
18. Cui L, Liu H, Sun L. Multidisciplinary respiratory rehabilitation in combination with non-invasive positive pressure ventilation in the treatment of elderly patients with severe chronic obstructive pulmonary disease. Pak J Med Sci. 2019;35(2):500-505.
19. Persson HL, Lyth J, Wiréhn AB, et al. Elderly patients with COPD require more health care than elderly heart failure patients do in a hospital-based home care setting. Int J Chron Obstruct Pulmon Dis. 2019;14(1):1569-1581.

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