

Decaf Score in Acute Exacerbation of COPD.

¹Dr. Radhakrishna R K, 6th floor room no 603 ESIC Medical College, Rajajinagara, Bangalore, Karnataka.

Corresponding Author: Dr. Radhakrishna R K, 6th floor room no 603 ESIC Medical College, Rajajinagara, Bangalore, Karnataka.

How to citation this article: Dr. Radhakrishna R K, “Decaf Score in Acute Exacerbation of COPD”, IJMACR- April - 2023, Volume – 6, Issue - 2, P. No. 473 – 482.

Open Access Article: © 2023, Dr. Radhakrishna R K, et al. This is an open access journal and article distributed under the terms of the creative common’s attribution license (<http://creativecommons.org/licenses/by/4.0>). Which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background

AECOPD is an acute event characterized by the worsening of the patient’s symptoms that is beyond normal day-to-day variations and leads to a change in medication. Exacerbations accelerate the rate of decline of lung function and are associated with significantly high mortality.

Most patients with AECOPD have a severe exacerbation and need hospitalization and may require Intensive care and mechanical ventilation if respiratory failure is present. In such situations, assessing the severity of Exacerbation is mandatory to guide decisions regarding the degree of care.

Objectives

To compare DECAF and CURB 65 in predicting outcomes of acute exacerbation of COPD patients.

Materials and methods

The study will be conducted on all patients with COPD visiting to OPD/ emergency department in the

Department of General Medicine, ESIC MC & PGIMSR, Rajajinagar, Bangalore 560010.

Sample Size

The sample size was calculated based on the previous study by Ahmed et al.

It was found that the sensitivity of DECAF was 67.65% as compared to 64.71% for CURB-65. In the present study sample size was calculated using a sensitivity of 67.65% margin of error of 12% and a prevalence of AECOPD 38.8% for predicting mortality, the minimum required sample size was estimated to be 156 patients with AECOPD.

Results

The study was conducted on 160 patients with Acute exacerbation of COPD. The results showed mid-age and younger age groups at risk and hospitalizations unlike previously thought.

Strengths

This study is concerned with the prediction of prognosis as well as outcomes of AECOPD with comprehensive prognostic indicators using simple investigations that are

easily available at any healthcare facility. Secondly, the study assessed the high-risk groups of AECOPD patients, using DECAF scoring. Thirdly, the data from the study will be useful for other research studies and in Emergency departments for clinical decision-making.

Summary

The prospective cross-sectional study was conducted on all patients with COPD visiting OPD/emergency department in the Department of General Medicine, ESIC MC & PGIMS, Rajajinagar, Bangalore 560010, from March 2021 to August 2022. Sample size was estimated to be 156 patients with AECOPD. The mean DECAF Score was 0.56 ± 0.97 and CURB-65 Score was 2.94 ± 1.00 .

A study of decaf score in predicting the outcomes of acute exacerbation of COPD patients

An acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a clinical diagnosis made when a patient with COPD experiences a sustained (e.g., 24–48 h) increase in cough, sputum production, and/or Dyspnea. Although there is no universal agreement on how to define or diagnose AECOPD, they are commonly defined as acute events with worsening respiratory symptoms beyond normal day-to-day variations.

It is estimated that every year 22%–40% of all patients with COPD experience at least one moderate or severe exacerbation, while 9%–16% experience more than one.[1,2] As a result, exacerbations are responsible for one in eight emergency hospital admissions in the UK; an enormous number, considering that the 3-month mortality rate of a hospitalised exacerbation exceeds 15%.[3-5] Patients experiencing frequent exacerbations have worse quality of life, accelerated lung function decline and are at increased risk of future exacerbations, myocardial infarctions, cerebrovascular events and

mortality.[6] The prevalence ranged between 2 and 22% among the men and 1.2 to 19% among women in different population-based studies across India [7].

AECOPD may be triggered by respiratory viral and bacterial infection; pollution or ambient temperature may also initiate or amplify AECOPD.[8] Characterized by increased systemic inflammatory activity, AECOPD has a negative impact on patients' health status and outcomes [9-11].

The clinical manifestations of exacerbations of COPD are highly variable. Patients with AECOPD may present with symptoms and signs similar to those at baseline except with greater severity. Orthopnoea and paroxysmal nocturnal Dyspnea that are usually not present at baseline may become evident when congestive heart failure coexists. On physical examination, there may be increased expiratory wheezes and rhonchi.

Breath sounds or wheezing may decrease if the airway obstruction is severe. There is usually more prominent use of accessory muscle. Signs of muscle fatigue, such as paradoxical breathing (an inward motion of the upper abdominal wall with inspiration) and respiratory alternans (a cyclic alternation between abdominal and rib cage breathing), may be present and should raise suspicion of impending respiratory failure.

With AECOPD, cough may become more severe and strenuous. Sputum volume may increase, and the color of the sputum may change from whitish to yellow or green. Haemoptysis is not uncommon during AECOPD and may consist of streaks or specks of blood mixed in purulent sputum. Occasionally, hemoptysis may be of larger quantity. In this case, other causes, including lung cancer, pneumonia, bronchiectasis, and heart failure, should be considered.

The severity of AECOPD without respiratory failure can be classified according to several staging systems. The traditional system uses the Winnipeg criteria, which were derived from a double-blind, placebo-controlled trial that evaluated the role of antibiotics in patients with COPD with acute exacerbations.[12] The three-stage system is based on three principal symptoms: increase in sputum volume, increase in sputum purulence, and increase in shortness of breath. This staging system correlates well with the effectiveness of antibiotic treatment for AECOPD.

The Winnipeg criteria

Type of Exacerbations	Criteria
Type 1	All three of the following symptoms: increase in sputum volume, increase in sputum purulence, increase in shortness of breath
Type 2	Any two of the following symptoms: increase in sputum volume, increase in sputum purulence, increase in shortness of breath
Type 3	Any one of the following symptoms: increase in sputum volume, increase in sputum purulence, increase in shortness of breath, plus at least one of the following: upper respiratory tract infection lasting 5 d, fever; increase in wheezes, increase in cough, increase in heart rate $\geq 20\%$

The Canadian Medical Association recently published guidelines for the management of AECOPD based on a five-stage severity system.[13] The system grades the severity based on the classic Winnipeg criteria and some of the factors known to correlate with poorer response to therapy, including age greater than 65 years, significant comorbid illness, FEV1 less than 50% of predicted, and number of exacerbations per year. The antibiotic therapy is adjusted according to the severity of the exacerbation. Another three-level staging system for AECOPD has been proposed that incorporates symptoms criteria and history of the disease and comorbidity.[14]

The CURB-65 score was derived and validated first time by Lim et al. based on 1068 patients from three prospective studies in the UK, New Zealand, and the Netherlands [15]. A 6-point score, one point for each of confusion, urea >7 mmol/l, respiratory rate ≥ 30 /min, low systolic (<90 mm Hg) or diastolic (≤ 60 mm Hg) blood pressure, age ≥ 65 years (CURB-65 score) following initial hospital assessment data, enabled patients to be stratified according to increasing risk of mortality: score 0, 0.7%; score 1, 3.2%; score 2, 3%; score 3, 17%; score 4, 41.5% and score 5, 57%.

Steer et al., in 2010, developed a comprehensive score to predict the risk of in-hospital mortality in AECOPD called the DECAF score [16]. DECAF consists of five parameters: Dyspnea (D), eosinopenia (E), consolidation (C), academia (A), and atrial fibrillation (F). DECAF is a simple tool that can be administered at the bedside using indices routinely available on admission. Administering DECAF in severely ill patients can help to predict mortality. Identified high-risk patients must be closely monitored with efficient and timely medical interventions to help reduce the overall mortality rate. In

their study they compared DECAF and CURB 65 score in predicting in hospital mortality.

Keywords: AECOPD, FEV₁, AF, ICU, AATD

Conclusions

The study was conducted on 160 patients with Acute exacerbation of COPD. The results showed mid age and younger age groups at risk and hospitalizations unlike previously thought. Routine blood tests and chest Xray imaging which are simple, convenient and easy accessible tools are still of diagnostic importance as there were many changes noted through the use of these simple yet effective tools. Higher DECAF scores were noted in older age groups in the study. Guidelines on management of this vulnerable elderly population and patient care would reduce the mortality risk. The DECAF score system was found to have significant association in predicting the outcomes in the AECOPD patients.

Strengths

This study concerns with the prediction of prognosis as well as outcomes of AECOPD with comprehensive prognostic indicators using the routine blood investigations, Chest Xray Imaging, which are easily available at any healthcare facilities. Secondly, the study assessed on the high-risk groups of Acute COPD patients, using the superior mortality risk predictor score system, i.e DECAF scoring. Thirdly, the data from the study will be useful for other research studies and also in emergency departments for clinical decision making and to be prepared with appropriate level of care so as to manage these high-risk population group for a safe discharge and reducing the deaths.

Limitations

In the study, there was a wide age range. The causal and the risk factors may be different for definite age groups.

Considering the wide age range, a larger sample size with equal distribution of the population would create a stronger impact of the study. Also, the study was conducted at a single tertiary centre at a single point of time. So, generalizing the results would not be possible. Long term follow up is required to note the outcome of the discharged patients, as occurrence of re-exacerbations after discharges is not uncommon. Longitudinal study of minimum of two years, with a larger sample size would fill this research gap.

References

1. Gayle A, Dickinson S, Morris K, et al. What is the impact of GOLD 2017 recommendations in primary care? - a descriptive study of patient classifications, treatment burden and costs. *Int J Chron Obstruct Pulmon Dis* 2018; 13:3485–92.
2. Hastie AT, Martinez FJ, Curtis JL, et al. Association of sputum and blood eosinophil concentrations with clinical measures of COPD severity: an analysis of the SPIROMICS cohort. *Lancet Respir Med* 2017; 5:956–67.
3. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: gold executive summary. *Eur Respir J* 2017; 49: 1700214.
4. National Institute for Health and Care Excellence (NICE). Chronic obstructive pulmonary disease in over 16s: diagnosis and management. NICE guideline [NG115]; 2018
5. Wedzicha JA, Seemungal TAR. COPD exacerbations: defining their cause and prevention. *Lancet* 2007; 370:786–96.
6. Kunisaki KM, Dransfield MT, Anderson JA, et al. Exacerbations of Chronic Obstructive Pulmonary

Disease and Cardiac Events. A Post Hoc Cohort Analysis from the SUMMIT Randomized Clinical Trial. *Am J Respir Crit Care Med* 2018; 198:51–7.

7. Jindal SK, Aggarwal AN, Gupta D (2001) A review of population studies from India to estimate national burden of chronic obstructive pulmonary disease and its association with smoking. *Indian J Chest Dis Allied Sci* 43(3): 139-47.

8. White AJ, Gompertz S, Stockley RA. Chronic obstructive pulmonary disease. 6: the aetiology of exacerbations of chronic obstructive pulmonary disease. *Thorax*. 2003; 58:73–80.

9. Hurst JR, Donaldson GC, Perera WR, Wilkinson TM, Bilello JA, Hagan GW, et al. Use of plasma biomarkers at exacerbation of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2006; 174:867–74.

10. Spencer S, Jones PW. Time course of recovery of health status following an infective exacerbation of chronic bronchitis. *Thorax*. 2003;58(7):589–93.

11. Suissa S, Dell’Aniello S, Ernst P. Long-term natural history of chronic obstructive pulmonary disease: severe exacerbations and mortality. *Thorax*. 2012;67(11):957–63.

12. Anthonisen NR, Manfreda J, Warren CP, Hershfield ES, Harding GK, Nelson NA. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 1987; 106:196–204.

13. Balter MS, La Forge J, Low DE, Mandell L, Grossman RF. Canadian guidelines for the management of acute exacerbations of chronic bronchitis: executive summary. *Can Respir J* 2003; 10:248–258.

14. Ball P, Make B. Acute exacerbations of chronic bronchitis: an international comparison. *Chest* 1998; 113:199S–204S.

15. Lim WS, van der Eerden MM, Laing R, et al.: Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*. 2003, 58:377-382.

16. The DECAF score: predicting hospital mortality in exacerbations of chronic obstructive pulmonary disease. Steer J, Gibson GJ, Bourke SC. *Thorax*. 2012; 67:970–976.

17. The body-mass index, airflow obstruction, Dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. Celli BR, Cote CG, Marin JM, et al. *N Engl J Med*. 2004;350:1005–1012.

18. Exacerbations of COPD. Viniol C, Vogel Meier CF. *Eu Respir Rev*. 2018;27:170103.

19. Predicting outcomes following hospitalization for acute exacerbations of COPD. Steer J, Gibson GJ, Bourke SC. *Int J Med*. 2010;103:817–829.

20. Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbations. *Chest* 2000; 117:398S–401.

21. Yang IA, Brown JL, George J, et al. COPD-X Australian and New Zealand guidelines for the diagnosis and management of chronic obstructive pulmonary disease: 2017 update. *Med J Aust* 2017; 207:436–42.

22. Trappeburg JCA, van Deventer AC, Troosters T, et al. The impact of using different symptom-based exacerbation algorithms in patients with COPD. *Eur Respir J* 2011; 37:1260–8.

23. Leidy NK, Wilcox TK, Jones PW, et al. Standardizing measurement of chronic obstructive pulmonary disease exacerbations. reliability and validity of a patient reported diary. *Am J Respir Crit Care Med* 2011; 183:323–9.

24. Pauwels R, Calverly P, Buist AS, Rennard S, Fukuchi Y, Stahl E, et al. COPD exacerbations: The

importance of a standard definition. *Respir Med.* 2004; 98: 99–107.

25. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet.* 2007; 370: 765–773

26. Awopeju O, Erhabor G, Awosusi B, Awopeju O, Adewole O, Irabor I. Smoking prevalence and attitudes regarding its control among health professional students in South-Western Nigeria. *Ann Med Health Sci Res.* 2013; 3: 355–360.

27. Chang JT, Meza R, Levy DT, Arenberg D, Jeon J. Prediction of COPD risk accounting for timevarying smoking exposures. *PLoS One.* 2021; 16: 1–16.

28. Laniado-Laborin R. Smoking and chronic obstructive pulmonary disease (COPD). Parallel Epidemics of the 21st century. *Int J Environ Res Public Health.* 2009; 6: 209–224.

29. Hou W, Hu S, Li C, Ma H, Wang Q, Meng G, et al. Cigarette Smoke Induced Lung Barrier Dysfunction, EMT, and Tissue Remodelling: A Possible Link between COPD and Lung Cancer. *Biomed Res Int.* 2019; 2019: 2025636

30. Willemsse BWM, Postma DS, Timmermans W, Ten Hacken NHT. The impact of smoking cessation on respiratory symptoms, lung function, airway hyperresponsiveness and inflammation. *Eur Respir J.* 2004; 23: 464–476.

31. Cho J, Lee CH, Hwang SS, Kim KU, Lee SH, Park HY, et al. Risk of acute exacerbations in chronic obstructive pulmonary disease associated with biomass smoke compared with tobacco smoke. *BMC Pulm Med.* 2019; 19: 1–10.

32. Zhu B, Wang Y, Ming J, Chen W, Zhang L. Disease burden of COPD in China: A systematic review. *Int J COPD.* 2018; 13: 1353–1364.

33. Li J, Sun S, Tang R, Qiu H, Huang Q, Mason TG, et al. Major air pollutants and risk of COPD exacerbations: a systematic review and meta-analysis. *Curr Environ Heal reports.* 2018; 5: 70–76.

34. Stockley RA, O'Brien C, Pye A, Hill SL. Relationship of sputum color to nature and outpatient management of acute exacerbations of COPD. *Chest.* 2000; 117: 1638–1645.

35. McCrory DC, Brown C, Gelfand SE, Bach PB. Management of acute exacerbations of COPD: A summary and appraisal of published evidence. *Chest.* 2001; 119: 1190–209.

36. Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, Tal-Singer R, et al. Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease. *N Engl J Med.* 2010; 363: 1128–1138.

37. Sjøgaard M, Madsen M, Løkke A, Heilberg O, Sorensen HT, Thomsen RW. Incidence and outcomes of patients hospitalized with COPD exacerbation with and without pneumonia. *Int J COPD.* 2016; 11: 455–465.

38. Shimizu K, Yoshii Y, Morozumi M, Chiba N, Ubukata K, Uruga H, et al. Pathogens in COPD exacerbations identified by comprehensive real-time PCR plus older methods. *Int J COPD.* 2015; 10: 2009–2016.

39. Mathioudakis, Alexander & Janssens, Wim & Sivapalan, Pradeesh & Singanayagam, Aran & Dransfield, Mark & Jensen, Jens Ulrik & Vestbo, Jorgen. (2020). Acute exacerbations of chronic obstructive pulmonary disease: In search of diagnostic biomarkers and treatable traits. *Thorax.* 75. thoraxjnl-2019.

40. Viniol C, Vogel Meier CF. Exacerbations of COPD. *Eur Respir Rev.* 2018; 27: 170103.

41. Han MLK, Kazerooni EA, Lynch DA, Liu LX, Murray S, Curtis JL, et al. Chronic obstructive

pulmonary disease exacerbations in the COPD Gene study: Associated radiologic phenotypes. *Radiology*. 2011; 261: 274–282.

42. Celli BR, Barnes PJ. Exacerbations of chronic obstructive pulmonary disease. *Eur Respir J*. 2007; 29: 1224–1238.

43. Ari A, Fink JB. Guidelines for aerosol devices in infants, children and adults: Which to choose, why and how to achieve effective aerosol therapy. *Expert Rev Respir Med*. 2011; 5: 561–572.

44. Davies L, Angus R, P. Calverley. Oral corticosteroids in patients admitted to hospital with exacerbations of chronic obstructive pulmonary disease: A prospective randomised controlled trial. *Lancet*. 1999; 354: 456–460.

45. Bafadhel M, McKenna S, Terry S, Mistry V, Pancholi M, Venge P, et al. Blood eosinophils to direct corticosteroid treatment of exacerbations of chronic obstructive pulmonary disease: A randomized placebo-controlled trial. *Am J Respir Crit Care Med*. 2012; 186: 48–55.

46. Vollenweider D, Frei A, Steurer-Stey C, Garcia-Aymerich J, Puhan M. Antibiotics for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2018; (10): CD010257.

47. Evenson AE. Management of COPD exacerbations. *Am Fam Physician*. 2010; 81: 607–613.

48. NICE Guidelines (NG115) – Chronic obstructive pulmonary disease in over 16s: Diagnosis and management. 2018. www.nice.org.uk/guidance/ng115.

49. Obaseki DO, Erhabor GE, Gnatiuc L, Adewole OO, Buist SA, Burney PG. Chronic Airflow Obstruction in a Black African Population: Results of BOLD Study, Ile-Ife, Nigeria. *COPD J Chronic Obstr Pulm Dis*. 2016; 13: 42–49.

50. Steer J, Gibson J, Bourke SC. The DECAF Score: predicting hospital mortality in exacerbations of chronic obstructive pulmonary disease. *Thorax* 2012;67:970-976.

51. Son JH, Lee JY, Yang YM, Sung WY, Seo SW, Kim JC, Lee W. Utility of the DECAF Score in Patients Admitted to Emergency Department with Acute Exacerbation of Chronic Obstructive Pulmonary Disease. *Korean J Crit Care Med*. 2013;28(4):255-265.

52. R Nafae, S Embarak, D M Gad. Value of the DECAF score in predicting hospital mortality in patients with acute exacerbation of chronic obstructive pulmonary disease admitted to Zagazig University Hospitals, Egypt, *Egyptian Journal of Chest Diseases and Tuberculosis*, 2015;64(1):35-40.

53. R K Yadavilli, N Shah, C Craig, L Collier. Does higher DECAF score increase length of hospital stay in acute exacerbation of COPD? *European Respiratory Journal* Sep 2016, 48 (Suppl 60) PA3437.

54. Echevarria C, Steer J, Heslop-Marshall K, Stanton SC, Hickey PM, Hughes R, Wijesinghe M, Harrison RN, Steen N, Simpson AJ, Gibson GJ, Bourke SC. Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD. *Thorax*. 2016 Feb;71(2):133-40.

55. Shi, Qi-fang & sheng, Ying & Zhu, Nian & Tan, Yan & Xie, Xiao-Hong & Wang, Shu-yun & Cai, Jin-fang. (2019). The v-DECAF score can predict 90-day all-cause mortality in patients with COPD exacerbation requiring invasive mechanical ventilation. *The Clinical Respiratory Journal*. 13. 10.1111/crj.13028.

56. Memon MA, Faryal S, Brohi N, Kumar B. Role of the DECAF Score in Predicting In-hospital Mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. *Cureus*. 2019;11(6): e4826. Published 2019 Jun 4. doi:10.7759/cureus.4826

57. Sharma S, Khan K, Yadav GS, Kool Wal S. A study of modified DECAF score in predicting hospital outcomes in patients of acute exacerbation of chronic obstructive pulmonary disease at SMS Medical College, Jaipur. *Adv Hum Biol* 2020; 10:171-5
58. Huang Q, He C, Xiong H, et al. DECAF score as a mortality predictor for acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *BMJ Open*. 2020; 10(10): e037923. Published 2020 Oct 30. doi:10.1136/bmjopen-2020-037923
59. Shen MH, Qiu GQ, Wu XM, Dong MJ. Utility of the DECAF score for predicting survival of patients with COPD: a meta-analysis of diagnostic accuracy studies. *Eur Rev Med Pharmacol Sci*. 2021 Jun;25(11):4037-4050.
60. GBD 2015 Chronic Respiratory Disease Collaborators Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir Med*. 2017; 5:691–706.
61. Colak Y, Afzal S, Nordestgaard BG, Lange P, Vestbo J. Importance of early COPD in young adults for development of clinical COPD. Findings from the Copenhagen General Population Study. *American journal of respiratory and critical care medicine*. 2021 May 15;203(10):1245-56.
62. Stoller JK, Smith P, Yang P, Spray J. Physical and social impact of alpha 1-antitrypsin deficiency: results of a survey. *C level and Clinic Journal of Medicine*. 1994; 61 (6):461–467.
63. Gaude GS, Rajesh BP, Chaudhury A, Hattiholi J. Outcomes associated with acute exacerbations of chronic obstructive pulmonary disorder requiring hospitalization. *Lung India: Official Organ of Indian Chest Society*. 2015 Sep;32(5):465.
64. Kshatriya RM, Paliwal RP, Khara NV, Patel SN. Acute exacerbation of chronic obstructive pulmonary disease in rural area: Why, how, and what next? *Indian Journal of Respiratory Care*. 2019 Jul 1;8(2):92.
65. Rennard SI, Drummond MB. Early chronic obstructive pulmonary disease: definition, assessment, and prevention. *Lancet*. 2015; 385:1778–1788.
66. Agustí A, Edwards LD, Rennard SI, McNee W, Tal-Singer R, Miller BE, Vestbo J, Lomas DA, Calverley PM, Wouters E, Crim C. Persistent systemic inflammation is associated with poor clinical outcomes in COPD: a novel phenotype. *PloS one*. 2012 May 18;7(5):e37483.
67. Fattouh M, Alkady O. Inflammatory biomarkers in chronic obstructive pulmonary disease. *Egypt J Chest Dis Tuberc*. 2014; 63:799–804.
68. Koo HK, Kang HK, Song P, Park HK, Lee SS, Jung H. Systemic white blood cell count as a biomarker associated with severity of chronic obstructive lung disease. *Tuberculosis and respiratory diseases*. 2017 Jul 3;80(3):304-10.
69. Lonergan M, Dicker AJ, Crichton ML, Keir HR, Van Dyke MK, Muller ova H, Miller BE, Tal-Singer R, Chalmers JD. Blood neutrophil counts are associated with exacerbation frequency and mortality in COPD. *Respiratory research*. 2020 Dec;21(1):1-0.
70. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogel Meier C, Anzueto A, Barnes PJ, Fabbri LM, Martinez FJ, Nishimura M, Stockley RA. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive

summary. American journal of respiratory and critical care medicine. 2013 Feb 15;187(4):347-65.

71. Xiong, W., Xu, M., Zhao, Y., Wu, X., Pudasaini, B., & Liu, J. M. (2017). Can we predict the prognosis of COPD with a routine blood test? International journal of chronic obstructive pulmonary disease, 12, 615–625.

72. Sorensen AK, Holmgaard DB, Mygind LH, Johansen J. Neutrophil-to-lymphocyte ratio, calprotectin and YKL-40 in patients with chronic obstructive pulmonary disease: correlations and 5-year mortality—a cohort study. Journal of Inflammation. 2015 Dec;12(1):1-2.

73. Lee H, Um SJ, Kim YS, Kim DK, Jang AS, Choi HS, Kim YH, Kim TE, Yoo KH, Jung KS. Association of the neutrophil-to-lymphocyte ratio with lung function and exacerbations in patients with chronic obstructive pulmonary disease. PloS one. 2016 Jun 3;11(6): e015 6511.

74. Singh D, Kolsum U, Bright ling CE, Locant ore N, Agusti A, Tal-Singer R. Eosinophilic inflammation in COPD: prevalence and clinical characteristics. European Respiratory Journal. 2014 Dec 1;44(6):1697-700.

75. Weir M, Zhao H, Han MK, Kanner R, Pirozzi CS, Scholand M, Hoffman EA, Martinez FJ, Criner GJ. D41 copd: biomarkers in stable disease and exacerbations: Eosinophils In Chronic Obstructive Pulmonary Disease, The Spiromics Cohort. American Journal of Respiratory and Critical Care Medicine. 2014; 189:1.

76. Liu M, Hu R, Jiang X, Mei X. Coagulation dysfunction in patients with AECOPD and its relation to infection and hypercapnia. Journal of Clinical Laboratory Analysis. 2021 Apr;35(4):e23733.

77. White H, Bird R, Sosnowski K, Jones M. An in vitro analysis of the effect of acidosis on coagulation in

chronic disease states - a thromboelastographic study. Clin Med. 2016;16(3):230-234.

78. Leem, A., Kim, Y., Lee, JH. et al. Serum bilirubin level is associated with exercise capacity and quality of life in chronic obstructive pulmonary disease. Respir Res 20, 279 (2019).

79. Schunemann HJ, Muti P, Freudenheim JL, Armstrong D, Browne R, Klocke RA, Trevisan M. Oxidative stress and lung function. Am J Epidemiol. 1997; 146:939–48.

80. Komatsu S. Radiological diagnosis--diagnosis and evaluation by chest X ray, chest CT and chest MRI. Nihon rinsho. Japanese Journal of Clinical Medicine. 2007 Apr 1;65(4):670-4.

81. Feldman C, Richards GA, Smilg J. The Findings on Initial Admission Chest Radiograph of Patients Presenting with an Acute Exacerbation of COPD—A South African Study. Southern African Journal of Infectious Diseases. 2015 Jul 3;30(2):57-60

82. Özgen Niksarlıoğlu EY, Aktürk ÜA. Chest X-ray: Is it still important in determining mortality in patients hospitalized due to chronic obstructive pulmonary diseases exacerbation in intensive care unit? Eurasian J Pulmonol 2018; 20:133-7.

83. Jain P, Misra A. Routine chest x-ray in chronic obstructive airways disease: a myth. The New Zealand medical journal. 1990 Apr 11;103(887):163

84. Huerta A., Crisafulli E., Menéndez R., Martínez R., Soler N., Guerrero M., Montull B., Torres A. Pneumonic and non-pneumonic exacerbations of COPD: Inflammatory response and clinical characteristics. Chest. 2013; 144:1134–1142.

85. Sayami M, Baral S, Shrestha R, Karki DB. Prevalence of Chronic Cor Pulmonale in Chronic Obstructive Pulmonary Disease Patients in a Teaching

Hospital in Nepal. Journal of Institute of Medicine Nepal. 2019 Apr 30;41(1):15-9.

86. Mac Nee W. Pathophysiology of cor pulmonale in chronic obstructive pulmonary disease. Part One. Am J Respir Crit Care Med 1994 Sep; 150(3):833-52.

87. Gupta NK, Agrawal RK, Srivastav AB, Ved ML. Echocardiographic evaluation of heart in chronic obstructive pulmonary disease patient and its co-relation with the severity of disease. Lung India. 2011 Jun 28(2).
Ciaglia P, Fersching R, Syniec C. Elective percutaneous dilatational tracheostomy: a new simple bedside procedure— preliminary report. Chest 1985; 87:715–7.

88. Thabut G, Dauriat G, Stern JB, et al. Pulmonary hemo dynamic in advanced COPD candidates for lung volume reduction surgery or lung transplantation. Chest. 2005; 127:1531–6.

89. Weitzenblum E, Loiseau A, Hirth C, et al. Course of pulmonary hemodynamics in patients with chronic obstructive pulmonary disease. Chest. 1979; 75:656–62.

90. Agarwal RL, Kumar D, Agarwal DK, Chabra GS. Diagnostic values of electrocardiogram in chronic obstructive pulmonary disease (COPD). Lung India: Official Organ of Indian Chest Society. 2008 Apr; 25 (2):78.

91. Spodick DH, Hauger - Kelvene JH, Tyler JM, Muesch H, Dorr CA. The electrocardiogram in pulmonary emphysema. Relationship of characteristic electrocardiographic findings to severity of disease as measured by degree of airway obstruction. Am Rev Resp Dis. 1963; 88:14

92. Carid FI, Wilcken DEL. ECG in chronic bronchitis with generalised obstructive lung diseases - Its relation to ventilatory junction. Am J Card. 1962; 10:5.

93. Scott RC, Kaplan S, Fowler O, Helm RA, Westcott RN, Walker IC, et al. The electrocardiographic pattern of

right ventricular hypertrophy in chronic cor pulmonale Circulation. 1955; 11:927.

94. Pinto, Hansoti RC. The ECG changes in chronic cor pulmonale. J Assoc Phy India. 1960; 8:213.

95. Chappell AG. The electrocardiogram in chronic bronchitis and emphysema. Brit Heart J. 1996; 28:517.

96. Yousif M, El Wahsh RA. Predicting in-hospital mortality in acute exacerbation of COPD: Is there a golden score? Egyptian Journal of Chest Diseases and Tuberculosis. 2016 Jul 1;65(3):579-84.

97. Kumar H, Choubey S. Predictors of mortality in patients of acute exacerbation of chronic obstructive pulmonary disease: A prospective observational study. Indian Journal of Respiratory Care. 2018 Jul 1;7(2):77.

98. Stone RA, Lowe D, Potter JM, Buckingham RJ, Roberts CM, Pursey NJ. Managing patients with COPD exacerbation: does age matter? Age and ageing. 2012 Jul 1;41(4):461-8.

99. Parras AM, Bautista CL, Chica GP, López ML. Evaluation of DECAF, CURB-65 and BAP-65 scales as predictor of mortality risk in acute exacerbation of COPD in a retrospective cohort.