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ORIGINAL RESEARCH

# The D-Dimer to Albumin Ratio Could Predict Hospital Readmission Within One Year in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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**Purpose:** To explore the association of D-dimer-to-albumin ratio (DAR) with hospital readmission within one year in patients with acute exacerbation chronic obstructive pulmonary disease (AECOPD).

**Patients and Methods:** From January 2019 to October 2022, 509 patients with COPD were enrolled in Baise People's Hospital for this retrospective cohort study. Baseline data and blood samples were collected, and patients were followed up for one year after inclusion. The AECOPD hospital readmission within one year was the outcome. Receiver operating characteristics (ROC) curves were conducted to determine the prognostic performance of DAR for predicting readmission within one year. The relationships between DAR, neutrophil-to-lymphocyte ratio (NLR), and AECOPD hospital readmission were conducted using univariate and multivariate logistic regression models, with odds ratios (ORs) and 95% confidence intervals (CIs). The relationship was further explored in different modified Medical Research Council (mMRC), COPD assessment test (CAT), COPD course, pneumonia, glucocorticoid, antibiotic subgroups.

**Results:** Totally, 117 (22.99%) COPD patients were hospital readmission due to AECOPD. The area under the curve (AUC) for the DAR was 0.726. DAR ≥2.21 (OR=1.80, 95% CI: 1.05–3.17) was associated with elevated odds of AECOPD hospital readmission within one year. DAR ≥2.21 was related to increased odds of AECOPD hospital readmission in patients of those mMRC ≥2, CAT >20, COPD course <10 years, and pneumonia. NLR ≥3.69 was associated with higher odds of AECOPD hospital readmission in patients of those mMRC ≥2 and COPD course ≥10 years.

**Conclusion:** In patients with AECOPD, DAR showed a better predictive value in predicting the risk of hospital readmission in patients with AECOPD within one year. The findings of our study might help identify patients with a high risk of readmission within one year and provide timely treatment to prevent the reoccurrence of AECOPD.

**Keywords:** acute exacerbation, chronic obstructive pulmonary disease, readmission, D-dimer to albumin ratio

## Introduction

Chronic obstructive pulmonary disease (COPD) is a prevalent and debilitating respiratory condition, characterized by persistent airflow restriction and frequent exacerbations.[1] COPD ranks as the third leading cause of mortality globally, resulting in over 3 million deaths annually.[2,3] In China, COPD affects approximately 13.6% of adults aged over 40 years, imposing a significant disease burden.[4] Acute exacerbation of COPD (AECOPD), a condition in which respiratory symptoms increase beyond the level of daily variation and necessitate changes in treatment, is a major contributor to hospitalizations and increased healthcare costs.[5] The incidence of acute exacerbation could hasten disease progression, diminish quality of life, and increase mortality risk.[6] Approximately 20% of patients undergo hospital readmission for AECOCP within 30 days after admission.[7,8] And more than 50% of patients experience at least one readmission for acute exacerbation within 1 year after discharge, with frequent exacerbation correlating with progressive COPD severity and

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increased mortality risk.[9,10] Despite advancements in COPD management, the prediction and prevention of AECOPD hospital readmissions remain a challenge. Identifying indicators that can predict AECOPD exacerbation and subsequent hospital readmission is crucial for improving patient prognosis.

The D-dimer-to-albumin ratio (DAR) is a sensitive indicator of hypercoagulability, inflammation, and nutritional status, and has been shown to have prognostic value in COVID-19 and gastric cancer.[11,12] DAR may also be linked to disease severity and prognosis in patients with COPD. COPD is a chronic inflammatory disease characterized by a hypercoagulable state.[13] And an interactive relationship exists between coagulation and inflammation.[14,15] D-dimer not only reflects the activation of the coagulation system, but also promotes the release of inflammatory factors and contributes to the inflammatory response.[16,17] In stable COPD, elevated D-dimer levels are associated with increased disease severity and mortality risk.[18,19] During acute exacerbations, high D-dimer levels are linked to an increased risk of hospitalized and one-year mortality in patients with AECOPD.[20] Low levels of albumin, an acute phase response protein, may signify persistent inflammation in AECOPD.[21] Malnutrition, as indicated by albumin levels, is related to more frequent acute exacerbations in COPD patients.[22] Additionally, low serum albumin levels are associated with prolonged hospitalization in patients with AECOPD.[23]

Our study aimed to explore the association between DAR and hospital readmission within one year in patients with AECOPD. The findings would contribute to risk stratification of COPD patients, enabling the timely identification of high-risk patients and the implementation of targeted interventions to slow disease progression and improve prognosis.

# Methods

## Study Design, Setting and Participants

All patients with COPD during the period from January 2019 to October 2022 in Baise People's Hospital, Guangxi, were included in this retrospective cohort study. Cases were included if the patients were older than 18 years, in hospitalization for more than 24 hours,[24] have a complete electronic patient documents, and had a confirmed diagnosis of AECOPD. AECOPD was defined as an acute worsening of respiratory symptoms that results in additional therapy.[5] The exclusion criteria were (1) have died during hospitalization, (2) receiving glucocorticoid therapy before blood sampling, and (3) missing data on D-dimer, albumin, high sensitivity C-reactive protein (hsCRP), and blood urea nitrogen. The study was conducted according to the Declaration of Helsinki, and the procedures were approved by the Ethics Committee of the Baise People's Hospital (approval number: LW2024060401). The need for written informed consent was waived by the Ethics Committee of the Baise People's Hospital due to retrospective nature of the study.

## Data Collection

Patient data were recorded from the electronic patient records and managed using the hospital information system. The collection was performed by two doctors and a nurse. Demographic and clinical values, including age, sex, drug used, smoking, body mass index (BMI), heart failure, type 2 diabetes mellitus, hypertension, asthma, pneumonia, hemoglobin, DAR, neutrophil-to-lymphocyte ratio (NLR), D-dimer, albumin, red blood cell, white blood cell, platelet, monocyte, eosinophils, red blood cell distribution width (RDW-CV), alanine transaminase, aspartate transaminase, glutamyltransferase, blood urea nitrogen, creatinine, prothrombin time, activated partial thromboplastin time, thrombin time, fibrinogen, hsCRP, the forced expiratory volume in one second/the forced vital capacity (FEV1/FVC), treat with glucocorticoid/antibiotic/mechanical ventilation, inpatient time, uric acid, $PaO_2$, $PaCO_2$, $SaO_2$, PH, BMI, comorbidity, times of acute exacerbation in previous one year, modified Medical Research Council (mMRC), COPD assessment test (CAT), COPD course, were recorded at admission. If a patient has two or more of the five comorbidities of heart failure, diabetes, hypertension, asthma and pneumonia, the individual was considered multimorbidity, otherwise the individual was non-multimorbidity. The mMRC scale was used to assess the dyspnea of patients, with higher grade indicating more severe dyspnea of patients.[25,26] The CAT was to supplement information obtained from lung function measurement and assessment of exacerbation risk.[27] The CAT consists of eight items, including cough, expectoration, dyspnea, chest tightness, confidence, limitation of daily activities, quality of sleep, and levels of energy with scores ranging from 0 to 5 (0 = no impairment, 5 = greatest impairment), with higher score indicating more severe symptoms.[26]

## Calculation of the DAR and NLR

DAR= D-dimer level (mg/L)/albumin level (g/dL).

NLR= Neutrophil level/lymphocyte level.

## Sample Size

The sample size was calculated by using PASS 11.0 version, yielding an optimal size of 310, considering 5% of confidence interval width (two-sided), a 95% confidence level, and odds ratio (OR)=2.8 for numbers of one-year hospital readmission ≥2. Considering a proportional distribution of 7/3, a shedding rate of 10%, a total sample size of 500 was needed for the study. Finally, the sample was acquired 567.

## Statistical Analysis

Continuous data were presented as mean and standard deviation (SD) for normally distributed data and median (25%–75% quarters) for abnormally distributed data. The comparison between two groups were detected using Student's *t* tests, Satterthwaite *t* tests, and Wilcoxon rank sum tests. Categorical data were presented as a frequency (percentage), with compared according the Chi-square tests between two groups. Potential covariates were selected according to the univariate logistic regression model and previous researches. Univariate and multivariate logistic regression models were conducted to explore the relationship between DAR, NLR and hospital readmission within one year in patients with AECOPD. The relationship was further investigated in different mMRC, CAT, COPD course, pneumonia, glucocorticoid, and antibiotic subgroups. All results were presented with ORs and 95% confidence intervals (CIs). Receiver operating characteristic (ROC) analysis was performed to determine predictive power of the DAR for the hospital readmission within one year in patients with AECOPD. Net reclassification improvement (NRI) and integrated discrimination improvement (IDI) are 2 indexes that assess improvement in model performance accomplished by adding new markers. We added mMRC, pulmonary function, and CAT to compare the predictive capability with DRA on AECOPD hospital readmission (Table S1-3 in supplementary material). All analyses were performed based on the R version 4.2.3 (2023–03-15 ucrt), and statistical significance was set at $P<0.05$.

# Results

In total, 509 patients were included for further analysis. Patients were excluded of those without diagnosis of AECOPD (n=8), missing data on D-dimer (n=15), albumin (n=17), hsCRP (n=16), and blood urea nitrogen (n=2). The patient selection process is shown in Figure 1. With a mean age of 65.07 (10.32) years, and the majority of patients (84.68%) were males. The main clinical events for hospital readmission occurred in 117 (22.99%) patients with AECOPD. Statistical significances were found between the two groups on DAR, NLR, D-dimer, albumin, drug used, heart failure, RDW-CV, FEV1/FVC, treat with glucocorticoid, treat with antibiotic, inpatient time, $PaCO_2$, comorbidity, times of acute exacerbation in previous one year, mMRC, CAT, and COPD course. Table 1 shows the characteristics between the two groups.

Figure 2 illustrates the predictive power of DAR on the hospital readmission in patients with AECOPD. The area under the curve (AUC) value of the DAR was found to be 0.726, and 71.8% sensitivity, 66.3% specificity, 38.9% positive predictive value and 88.7% negative predictive value were reached with a DAR cut-off value of 2.21. For NLR, the cut-off value was 3.69.

Then, the relationship between DAR, NLR, and AECOPD hospital readmission was explored (Table 2), stratified based on the optimal cut-off value of DAR and NLR. After adjusting age, sex, mMRC, FEV1/FVC, and COPD course, DAR ≥2.21 was associated with higher odds of AECOPD hospital readmission (OR=1.80, 95% CI: 1.05–3.17). No relationship was found between NLR and odds of AECOPD hospital readmission (OR=1.57, 95% CI: 0.99–2.50).

Table 3 shows the associations of DAR, NLR, with AECOPD hospital readmission were further explored in different mMRC, CAT, COPD course, and pneumonia populations. After adjusting covariates, DAR ≥2.21 was related to increased odds of AECOPD hospital readmission in patients of those mMRC ≥2 (OR=2.15, 95% CI: 1.18–4.10), CAT >20 (OR=2.70, 95% CI: 1.38–5.66), COPD course <10 years (OR=2.44, 95% CI: 1.14–5.71), and pneumonia (OR=2.44, 95% CI: 1.29–4.92). NLR ≥3.69 was associated with higher odds of AECOPD hospital readmission in patients of those mMRC ≥2 (OR=1.75, 95% CI: 1.07–2.90) and COPD course ≥10 years (OR=2.72, 95% CI: 1.38–5.57).

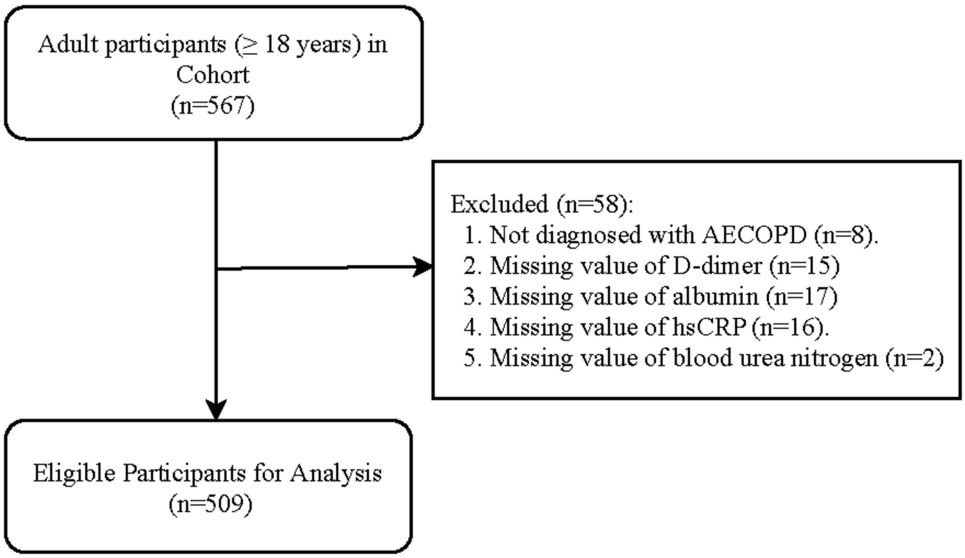


**Figure 1** Selection process of included AECOPD patients.

## Discussion

Our study suggested that high DAR was associated with increased odds of AECOPD hospital readmission within one year. Moreover, the findings indicated DAR may have superior predictive value for AECOPD hospital readmission compared to the NLR in patients with AECOPD. The relationships between DAR or NLR and AECOPD readmission

**Table 1** Characteristics of Patients with AECOPD

| Variables | Total (N=509) | No AECOPD Hospital Readmission (N=392) | AECOPD Hospital Readmission (N=117) | Statistics | *P* |
|---|---|---|---|---|---|
| DAR, n (%) | | | | $\chi^2$ = 8.473 | 0.004 |
| <2.21 | 153 (30.06) | 131 (33.42) | 22 (18.8) | | |
| ≥2.21 | 356 (69.94) | 261 (66.58) | 95 (81.2) | | |
| NLR, n (%) | | | | $\chi^2$ = 11.978 | 0.001 |
| <3.69 | 252 (49.51) | 211 (53.83) | 41 (35.04) | | |
| ≥3.69 | 257 (50.49) | 181 (46.17) | 76 (64.96) | | |
| D-dimer, ng/mL, M ($Q_1$, $Q_3$) | 153 (73–320) | 138 (68–315) | 184 (95–348) | W = 19,682.5 | 0.020 |
| ALB, g/L, Mean (±SD) | 37.43 (±5.15) | 37.81 (±5.08) | 36.16 (±5.20) | t = 3.067 | 0.002 |
| Age, years, Mean (±SD) | 65.07 (±10.32) | 64.66 (±10.16) | 66.46 (±10.73) | t = −1.660 | 0.098 |
| Age, years, n (%) | | | | $\chi^2$ = 0.317 | 0.574 |
| <65 | 240 (47.15) | 188 (47.96) | 52 (44.44) | | |
| ≥65 | 269 (52.85) | 204 (52.04) | 65 (55.56) | | |
| Sex, n (%) | | | | $\chi^2$ = 0.505 | 0.477 |
| Male | 431 (84.68) | 329 (83.93) | 102 (87.18) | | |
| Female | 78 (15.32) | 63 (16.07) | 15 (12.82) | | |
| Drug used, n (%) | | | | $\chi^2$ = 14.228 | 0.003 |
| Single | 49 (9.63) | 42 (10.71) | 7 (5.98) | | |
| Other | 199 (39.1) | 164 (41.84) | 35 (29.91) | | |
| Double combination | 81 (15.91) | 64 (16.33) | 17 (14.53) | | |
| Triple combination | 180 (35.36) | 122 (31.12) | 58 (49.57) | | |

(*Continued*)

**Table 1** (Continued).

| Variables | Total (N=509) | No AECOPD Hospital Readmission (N=392) | AECOPD Hospital Readmission (N=117) | Statistics | *P* |
|---|---|---|---|---|---|
| Smoking, n (%) | | | | $\chi^2$ = 1.785 | 0.410 |
| Nonsmoker | 133 (26.13) | 108 (27.55) | 25 (21.37) | | |
| Light smoker | 131 (25.74) | 99 (25.26) | 32 (27.35) | | |
| Heavy smoker | 245 (48.13) | 185 (47.19) | 60 (51.28) | | |
| BMI, $kg/m^2$, Mean (±SD) | 21.10 (±3.47) | 21.08 (±3.54) | 21.17 (±3.27) | t = −0.252 | 0.801 |
| Heart failure, n (%) | | | | $\chi^2$ = 8.463 | 0.004 |
| No | 407 (79.96) | 325 (82.91) | 82 (70.09) | | |
| Yes | 102 (20.04) | 67 (17.09) | 35 (29.91) | | |
| T2DM, n (%) | | | | $\chi^2$ = 2.290 | 0.130 |
| No | 460 (90.37) | 359 (91.58) | 101 (86.32) | | |
| Yes | 49 (9.63) | 33 (8.42) | 16 (13.68) | | |
| Hypertension, n (%) | | | | $\chi^2$ = 2.949 | 0.086 |
| No | 385 (75.64) | 304 (77.55) | 81 (69.23) | | |
| Yes | 124 (24.36) | 88 (22.45) | 36 (30.77) | | |
| Asthma, n (%) | | | | $\chi^2$ = 1.622 | 0.203 |
| No | 446 (87.62) | 339 (86.48) | 107 (91.45) | | |
| Yes | 63 (12.38) | 53 (13.52) | 10 (8.55) | | |
| Pneumonia, n (%) | | | | $\chi^2$ = 0.264 | 0.607 |
| No | 111 (21.81) | 88 (22.45) | 23 (19.66) | | |
| Yes | 398 (78.19) | 304 (77.55) | 94 (80.34) | | |
| Hemoglobin, g/L, Mean (±SD) | 134.27 (±22.42) | 134.23 (±20.68) | 134.38 (±27.59) | t' = −0.052 | 0.958 |
| RBC, $10^{12}$/L, Mean (±SD) | 4.78 (±0.87) | 4.77 (±0.85) | 4.81 (±0.93) | t = −0.493 | 0.622 |
| WBC, $10^9$/L, Mean (±SD) | 8.87 (±4.15) | 8.74 (±4.03) | 9.33 (±4.50) | t = −1.354 | 0.176 |
| PLT, $10^9$/L, Mean (±SD) | 241.97 (±92.12) | 239.18 (±88.94) | 251.32 (±101.93) | t = −1.252 | 0.211 |
| MONO, $10^9$/L, M ($Q_1$, $Q_3$) | 0.65 (0.48–0.88) | 0.65 (0.48–0.88) | 0.65 (0.49–0.87) | W = 22,956.5 | 0.986 |
| EOS, $10^9$/L, M ($Q_1$, $Q_3$) | 0.12 (0.05–0.27) | 0.13 (0.05–0.27) | 0.11 (0.04–0.26) | W = 24,188 | 0.368 |
| RDW-CV, %, M ($Q_1$, $Q_3$) | 13.6 (12.8–15.2) | 13.5 (12.8–14.93) | 13.9 (13.1–15.9) | W = 19,673.5 | 0.020 |
| ALT, U/L, M ($Q_1$, $Q_3$) | 18 (13–27) | 19 (13–27) | 18 (13–27) | W = 24,304 | 0.326 |
| AST, U/L, M ($Q_1$, $Q_3$) | 22 (18–31) | 23 (18–31) | 22 (17–29) | W = 24,570 | 0.240 |
| GGT, μmol/L, M ($Q_1$, $Q_3$) | 30 (18–52) | 30 (18–51) | 30 (18–56) | W = 22,560.5 | 0.790 |
| BUN, μmol/L, Mean (±SD) | 6.12 (±2.63) | 5.99 (±2.56) | 6.53 (±2.83) | t = −1.959 | 0.051 |
| Cr, μmol/L, M ($Q_1$, $Q_3$) | 78 (67–95) | 77 (67–92.25) | 82 (68–100) | W = 20,598 | 0.095 |
| PT, s, M ($Q_1$, $Q_3$) | 11.5 (10.9–12.5) | 11.45 (10.9–12.4) | 11.8 (11–12.6) | W = 20,454 | 0.076 |
| APTT, s, Mean (±SD) | 30.96 (±3.71) | 30.89 (±3.60) | 31.17 (±4.08) | t = −0.707 | 0.480 |
| TT, s, Mean (±SD) | 14.57 (±1.52) | 14.59 (±1.50) | 14.51 (±1.58) | t = 0.529 | 0.597 |
| FIB, g/L, Mean (±SD) | 3.61 (±1.19) | 3.58 (±1.20) | 3.70 (±1.16) | t = −0.921 | 0.358 |
| hsCRP, mg/L, Mean (±SD) | 25.63 (±42.57) | 24.55 (±42.03) | 29.24 (±44.33) | t = −1.045 | 0.296 |
| FEV1/FVC, %, Mean (±SD) | 50.22 (±12.77) | 51.70 (±12.49) | 45.28 (±12.47) | t = 4.872 | <0.001 |
| Treat with Glucocorticoid, n (%) | | | | $\chi^2$ = 6.449 | 0.011 |
| No | 246 (48.33) | 202 (51.53) | 44 (37.61) | | |
| Yes | 263 (51.67) | 190 (48.47) | 73 (62.39) | | |
| Treat with antibiotic, n (%) | | | | $\chi^2$ = 10.494 | 0.001 |
| No | 70 (13.75) | 65 (16.58) | 5 (4.27) | | |
| Yes | 439 (86.25) | 327 (83.42) | 112 (95.73) | | |
| Treat with mechanical ventilation, n (%) | | | | $\chi^2$ = 2.417 | 0.120 |
| No | 475 (93.32) | 370 (94.39) | 105 (89.74) | | |
| Yes | 34 (6.68) | 22 (5.61) | 12 (10.26) | | |

(*Continued*)

**Table 1** (Continued).

| Variables | Total (N=509) | No AECOPD Hospital Readmission (N=392) | AECOPD Hospital Readmission (N=117) | Statistics | *P* |
|---|---|---|---|---|---|
| Inpatient Time, days, Mean (±SD) | 8.82 (±4.38) | 8.50 (±3.94) | 9.88 (±5.51) | t' = −2.519 | 0.013 |
| UA, μmol/L, Mean (±SD) | 339.50 (±153.51) | 341.79 (±157.65) | 331.82 (±139.13) | t = 0.616 | 0.538 |
| $PaO_2$, mmHg, Mean (±SD) | 82.70 (±28.70) | 81.67 (±26.64) | 86.18 (±34.65) | t' = −1.300 | 0.195 |
| $PaCO_2$, mmHg, Mean (±SD) | 48.02 (±11.32) | 47.15 (±10.91) | 50.94 (±12.18) | t' = −3.026 | 0.003 |
| $SaO_2$, %, M ($Q_1$, $Q_3$) | 95 (92–97) | 95 (92–97) | 95 (91–98) | W = 22,781.5 | 0.914 |
| PH, Mean (±SD) | 7.40 (±0.05) | 7.40 (±0.05) | 7.39 (±0.06) | t' = 1.414 | 0.159 |
| BMI, $kg/m^2$, n (%) | | | | $\chi^2$ = 0.262 | 0.609 |
| Normal weight | 416 (81.73) | 318 (81.12) | 98 (83.76) | | |
| Unhealthy Weight | 93 (18.27) | 74 (18.88) | 19 (16.24) | | |
| Comorbidity, n (%) | | | | $\chi^2$ = 8.605 | 0.003 |
| Non-multimorbidity | 301 (59.14) | 246 (62.76) | 55 (47.01) | | |
| Multimorbidity | 208 (40.86) | 146 (37.24) | 62 (52.99) | | |
| Times of acute exacerbation in previous 1 year, n (%) | | | | $\chi^2$ = 10.850 | 0.004 |
| 0 | 139 (27.31) | 119 (30.36) | 20 (17.09) | | |
| 1 | 171 (33.6) | 133 (33.93) | 38 (32.48) | | |
| ≥2 | 199 (39.1) | 140 (35.71) | 59 (50.43) | | |
| MMRC, n (%) | | | | $\chi^2$ = 18.169 | <0.001 |
| <2 | 126 (24.75) | 115 (29.34) | 11 (9.4) | | |
| ≥2 | 383 (75.25) | 277 (70.66) | 106 (90.6) | | |
| CAT, n (%) | | | | $\chi^2$ = 8.985 | 0.003 |
| ≤20 | 174 (34.18) | 148 (37.76) | 26 (22.22) | | |
| >20 | 335 (65.82) | 244 (62.24) | 91 (77.78) | | |
| COPD course, years, n (%) | | | | $\chi^2$ = 16.426 | <0.001 |
| <10 | 306 (60.12) | 255 (65.05) | 51 (43.59) | | |
| ≥10 | 203 (39.88) | 137 (34.95) | 66 (56.41) | | |

**Abbreviations**: SD, standard deviation; M, median; $Q_1$, 1st quartile; $Q_3$, 3st quartile; *t*, Student's *t* test; *t'*, Satterthwaite *t* test; *W*, Wilcoxon rank sum test; $\chi^2$, Chi-square test; AECOPD, acute exacerbation of chronic obstructive pulmonary disease; DAR, D-dimer to albumin ratio; NLR, neutrophil to lymphocyte ratio; ALB, albumin; BMI, body mass index; T2DM, type 2 diabetes mellitus; RBC, red blood cell; WBC, white blood cell; PLT, platelet; MONO, monocyte; EOS, eosinophils; RDW-CV, red blood cell distribution width; ALT, alanine transaminase; AST, aspartate transaminase; GGT, glutamyltransferase; BUN, blood urea nitrogen; Cr, creatinine; PT, prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; FIB, fibrinogen; hsCRP, high sensitivity C-reactive protein; FEV1/FVC, the forced expiratory volume in one second/the forced vital capacity; UA, uric acid; PH, pondus hydrogenii; mMRC, the modified Medical Research Council; CAT, the COPD assessment test; COPD, chronic obstructive pulmonary disease.

risk were influenced by the duration of COPD. Higher DAR was related to higher odds of AECOPD readmission within one year in patients with CODP <10 years, while NLR was the opposite.

DAR is a novel indicator for patients with AECOPD, while it has been established that D-dimer and albumin alone can serve as predictive factors for prognosis in patients with AECOPD. D-dimer was an independent risk factor for in-hospital and 1-year death for AECOPD patients.[20] Low serum albumin level was associated with prolonged lengths of stay.[23] Kamstrup et al also reported in patients with moderate-to-severe COPD, a high level of D-dimer was more likely to die.[28] NLR could be as biomarkers in patients with AECOPD.[29] Our findings indicated that DAR may be a more robust predictor of AECOPD hospital readmission within one year compared to NLR, underscoring the importance of considering multiple biomarkers in assessing disease prognosis. Furthermore, future studies are needed to detect the predictive value of DAR combined with other biomarkers.

The mechanism underlying the relationship between DAR and AECOPD hospital readmission is likely multifactorial. Elevated DAR levels reflect a state of systemic inflammation and fibrinolysis, which are integral processes in the pathogenesis of COPD exacerbations.[13] Heightened fibrinolytic activity, as indicated by elevated D-dimer levels, may exacerbate airway obstruction and impair gas exchange, thereby exacerbating respiratory symptoms and necessitating

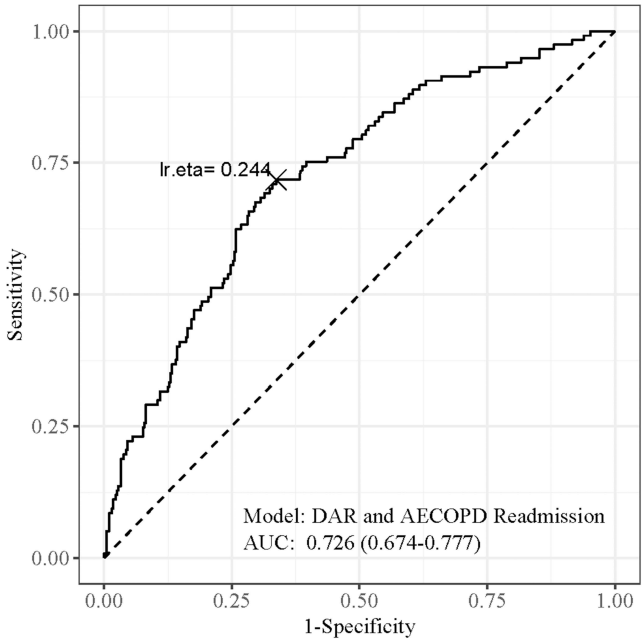


**Figure 2** The ROC plot of DAR and AECOPD hospital readmission.

hospitalization.[30] Additionally, impaired albumin synthesis in patients with COPD may contribute to increased DAR levels, as albumin plays a crucial role in regulating inflammation and maintaining vascular integrity.[31] Finally, the association between DAR and AECODP hospital readmission may be attributed to the systemic consequence s of COPD exacerbations. Acute exacerbations elicit a cascade of pro-inflammatory cytokines and acute phase reactants, including fibrinogen and D-dimer, which perpetuate systemic inflammation and endothelial dysfunction.[32] This systemic inflammation not only exacerbates respiratory symptoms but also contributes to multi-organ dysfunction, increasing the risk of subsequent exacerbations and hospital readmission.

The differing associations between DAR and NLR with AECOPD hospital readmission according to COPD duration suggest potential variations in disease pathophysiology over time. In patients with shorter COPD durations, elevated DAR may be as a more sensitive marker of disease severity and exacerbation risk, reflecting early inflammatory and coagulation and abnormalities. Conversely, in individuals with long-standing COPD, NLR may become a more prominent predictor of exacerbation outcomes, reflecting chronic inflammation and immune dysregulation.[33,34] These divergent associations underscore the dynamic nature of considering disease duration in biomarker interpretation.

The findings underscore the potential of the DAR as a valuable adjunctive tool in assessing readmission risk for patients experiencing AECOPD. While DAR demonstrated an association with increased odds of readmission, it is essential to

**Table 2** The Associations Between DAR, NLR and AECOPD Hospital Readmission

| Variables | Unadjusted Model | | Adjusted Model | |
|---|---|---|---|---|
| | OR (95% CI) | *P* | OR (95% CI) | *P* |
| DAR, % | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 2.17 (1.32–3.68) | 0.003 | 1.80 (1.05–3.17) | 0.036 |
| NLR, % | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 2.16 (1.41–3.34) | <0.001 | 1.57 (0.99–2.50) | 0.057 |

**Notes**: Adjusted Model adjusting age, sex, mMRC, FEV1/FVC, and COPD course.
**Abbreviations**: OR, odds ratio; CI, confidence interval.

**Table 3** The Associations Between DAR, NLR and AECOPD Hospital Readmission in Subgroups

| Subgroups (Outcome/Total) | Unadjusted Model | | Adjusted Model | |
|---|---|---|---|---|
| | OR (95% CI) | *P* | OR (95% CI) | *P* |
| MMRC, <2, (11/126) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 0.89 (0.25–3.25) | 0.855 | 0.88 (0.23–3.41) | 0.845 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 0.86 (0.21–3.01) | 0.814 | 0.96 (0.23–3.54) | 0.955 |
| mMRC, ≥2, (106/383) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 2.20 (1.26–4.04) | 0.008 | 2.15 (1.18–4.10) | 0.016 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 2.23 (1.40–3.60) | 0.001 | 1.75 (1.07–2.90) | 0.027 |
| CAT, ≤20, (26/174) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 1.03 (0.44–2.50) | 0.944 | 0.76 (0.28–2.10) | 0.586 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 2.63 (1.13–6.38) | 0.027 | 1.68 (0.63–4.56) | 0.298 |
| CAT, >20, (91/335) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 2.81 (1.49–5.71) | 0.002 | 2.70 (1.38–5.66) | 0.005 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 1.84 (1.12–3.07) | 0.017 | 1.53 (0.90–2.61) | 0.115 |
| COPD course, <10 years, (51/306) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 2.96 (1.44–6.73) | 0.005 | 2.44 (1.14–5.71) | 0.028 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 1.33 (0.73–2.43) | 0.356 | 0.94 (0.49–1.79) | 0.848 |
| COPD course, ≥10 years, (66/203) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 1.24 (0.61–2.63) | 0.557 | 1.34 (0.61–3.08) | 0.471 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 3.08 (1.63–6.07) | 0.001 | 2.72 (1.38–5.57) | 0.005 |
| Pneumonia, No, (23/111) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 1.13 (0.44–3.06) | 0.810 | 0.84 (0.29–2.51) | 0.757 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 2.84 (1.11–7.72) | 0.033 | 2.49 (0.92–7.16) | 0.078 |

(*Continued*)

**Table 3** (Continued).

| Subgroups (Outcome/Total) | Unadjusted Model | | Adjusted Model | |
|---|---|---|---|---|
| | OR (95% CI) | *P* | OR (95% CI) | *P* |
| Pneumonia, Yes, (94/398) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 2.72 (1.51–5.22) | 0.001 | 2.44 (1.29–4.92) | 0.009 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 2.00 (1.25–3.26) | 0.005 | 1.43 (0.85–2.42) | 0.179 |
| Treat with glucocorticoid, No (44/246) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 2.50 (1.18–5.79) | 0.022 | 2.01 (0.90–4.83) | 0.101 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 1.87 (0.97–3.63) | 0.062 | 1.45 (0.71–2.98) | 0.302 |
| Treat with glucocorticoid, Yes (73/263) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 1.74 (0.90–3.55) | 0.110 | 1.54 (0.74–3.34) | 0.259 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 2.14 (1.21–3.88) | 0.011 | 1.72 (0.94–3.22) | 0.083 |
| Treat with antibiotic, No (5/70) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 3.43 (0.48–69.03) | 0.282 | 4.48 (0.52–98.29) | 0.218 |
| NLR | | | | |
| <3.69 | Insufficient Sample size | | Insufficient Sample size | |
| ≥3.69 | | | | |
| Treat with antibiotic, Yes (112/439) | | | | |
| DAR | | | | |
| <2.21 | Ref | | Ref | |
| ≥2.21 | 1.94 (1.16–3.36) | 0.014 | 1.70 (0.98–3.07) | 0.068 |
| NLR | | | | |
| <3.69 | Ref | | Ref | |
| ≥3.69 | 2.15 (1.38–3.41) | 0.001 | 1.61 (1.00–2.63) | 0.053 |

**Notes**: Adjusted Model adjusting age, sex, mMRC, FEV1/FVC, and COPD course.
**Abbreviations**: OR, odds ratio; CI, confidence interval.

contextualize these results within the broader scope of COPD management. Clinicians should be aware that while high DAR levels could signify a higher risk of subsequent hospitalization, this biomarker does not replace clinical judgment or established management protocols. Therefore, unnecessary routine laboratory testing solely for DAR measurement is not recommended. Instead, our findings may inform clinicians in refining risk stratification and optimizing follow-up care for high-risk patients, ultimately enhancing patient outcomes through tailored post-discharge strategies.

Several limitations should be acknowledged for our study. First, this is a retrospective and single-center study which limited the number of cases. Prospective studies and random control trails are required for further evaluation of our findings. Second, although some covariates were adjusted, other possible confounders such as changes in treatment regimens after discharge were not available. Finally, no data on respiratory rehabilitation, nutritional therapy, and differences in economic or educational level, which limited the exploration of their relationship with readmission.

## Conclusion

Higher DAR was associated with elevated odds of AECOPD hospital admission within one year. DAR may be a helpful biomarker for identifying AECOPD patients at higher risk of hospital readmission within one-year. Future investigations should be untaken to apply this prediction tool in order to improve patient care to reduce the need for AECOPD readmissions.

## Ethics Approval and Informed Consent

The study was conducted according to the Declaration of Helsinki, and the procedures were approved by the Ethics Committee of the Baise People's Hospital (approval number: LW2024060401). The need for written informed consent was waived by the Ethics Committee of the Baise People's Hospital due to retrospective nature of the study. We ensured the confidentiality of all patient data by anonymizing records and limiting access to authorized personnel only. Patient information was handled in compliance with applicable privacy regulations throughout the research process.

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## Disclosure

The author reports no conflicts of interest in this work.

## References

1. Mirza S, Clay RD, Koslow MA, Scanlon PD. COPD Guidelines: a Review of the 2018 GOLD Report. *Mayo Clin Proc*. 2018;93(10):1488–1502. doi:10.1016/j.mayocp.2018.05.026
2. Celli BR, Wedzicha JA. Update on Clinical Aspects of Chronic Obstructive Pulmonary Disease. *N Engl J Med*. 2019;381(13):1257–1266. doi:10.1056/NEJMra1900500
3. Rabe KF, Watz H. Chronic obstructive pulmonary disease. *Lancet*. 2017;389(10082):1931–1940. doi:10.1016/S0140-6736(17)31222-9
4. Fang L, Gao P, Bao H, et al. Chronic obstructive pulmonary disease in China: a nationwide prevalence study. *Lancet Respir Med*. 2018;6(6):421–430. doi:10.1016/S2213-2600(18)30103-6
5. 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. *Am J Respir Crit Care Med*. 2017;195(5):557–582. doi:10.1164/rccm.201701-0218PP
6. MacLeod M, Papi A, Contoli M, et al. Chronic obstructive pulmonary disease exacerbation fundamentals: diagnosis, treatment, prevention and disease impact. *Respirology*. 2021;26(6):532–551. doi:10.1111/resp.14041
7. Crisafulli E, Torres A, Huerta A, et al. C-Reactive Protein at Discharge, Diabetes Mellitus and ≥ 1 hospitalization During Previous Year Predict Early Readmission in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease. *COPD*. 2015;12(3):306–314. doi:10.3109/15412555.2014.933954
8. Fernández-García S, Represas-Represas C, Ruano-Raviña A, et al. Social and clinical predictors of short- and long-term readmission after a severe exacerbation of COPD. *PLoS One*. 2020;15(2):e0229257. doi:10.1371/journal.pone.0229257
9. Guerrero M, Crisafulli E, Liapikou A, et al. Readmission for Acute Exacerbation within 30 Days of Discharge Is Associated with a Subsequent Progressive Increase in Mortality Risk in COPD Patients: a Long-Term Observational Study. *PLoS One*. 2016;11(3):e0150737. doi:10.1371/journal.pone.0150737
10. Jing Z, Chun C, Ning S, Hong Z, Bei H, Wan-Zhen Y. Systemic Inflammatory Marker CRP Was Better Predictor of Readmission for AECOPD Than Sputum Inflammatory Markers. *Arch Bronconeumol*. 2016;52(3):138–144. doi:10.1016/j.arbres.2015.01.011
11. Küçükceran K, Ayranci MK, Girişgin AS, Koçak S. Predictive value of D-dimer/albumin ratio and fibrinogen/albumin ratio for in-hospital mortality in patients with COVID-19. *Int J Clin Pract*. 2021;75(7):e14263. doi:10.1111/ijcp.14263
12. Zhang L, Wang Z, Xiao J, et al. Prognostic Value of Albumin to D-Dimer Ratio in Advanced Gastric Cancer. *J Oncol*. 2021;2021:9973743. doi:10.1155/2021/9973743
13. Kyriakopoulos C, Gogali A, Kostikas K, Konstantinidis A. Hypercoagulable State in COPD-A Comprehensive Literature Review. *Diagnostics*. 2021;11(8). doi:10.3390/diagnostics11081447
14. Burzynski LC, Clarke MCH. Death Is Coming and the Clot Thickens, as Pyroptosis Feeds the Fire. *Immunity*. 2019;50(6):1339–1341. doi:10.1016/j.immuni.2019.05.015
15. Luyendyk JP, Schoenecker JG, Flick MJ. The multifaceted role of fibrinogen in tissue injury and inflammation. *Blood*. 2019;133(6):511–520. doi:10.1182/blood-2018-07-818211
16. Abou-Ismail MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: incidence, pathophysiology, and management. *Thromb Res*. 2020;194:101–115. doi:10.1016/j.thromres.2020.06.029
17. Shorr AF, Thomas SJ, Alkins SA, Fitzpatrick TM, Ling GS. D-dimer correlates with proinflammatory cytokine levels and outcomes in critically ill patients. *Chest*. 2002;121(4):1262–1268. doi:10.1378/chest.121.4.1262
18. Zhang M, Zhang J, Zhang Q, et al. D-dimer as a potential biomarker for the progression of COPD. *Clin Chim Acta*. 2016;455:55–59. doi:10.1016/j.cca.2016.01.024

19. Husebø GR, Gabazza EC, D'Alessandro Gabazza C, et al. Coagulation markers as predictors for clinical events in COPD. *Respirology*. 2021;26(4):342–351. doi:10.1111/resp.13971
20. Hu G, Wu Y, Zhou Y, et al. Prognostic role of D-dimer for in-hospital and 1-year mortality in exacerbations of COPD. *Int J Chron Obstruct Pulmon Dis*. 2016;11:2729–2736. doi:10.2147/COPD.S112882
21. Gunen H, Hacievliyagil SS, Kosar F, et al. Factors affecting survival of hospitalised patients with COPD. *Eur Respir J*. 2005;26(2):234–241. doi:10.1183/09031936.05.00024804
22. Yoshikawa M, Fujita Y, Yamamoto Y, et al. Mini Nutritional Assessment Short-Form predicts exacerbation frequency in patients with chronic obstructive pulmonary disease. *Respirology*. 2014;19(8):1198–1203. doi:10.1111/resp.12380
23. Wang Y, Stavem K, Dahl FA, Humerfelt S, Haugen T. Factors associated with a prolonged length of stay after acute exacerbation of chronic obstructive pulmonary disease (AECOPD). *Int J Chron Obstruct Pulmon Dis*. 2014;9:99–105. doi:10.2147/COPD.S51467
24. Bernabeu-Mora R, García-Guillamón G, Valera-Novella E, Giménez-Giménez LM, Escolar-Reina P, Medina-Mirapeix F. Frailty is a predictive factor of readmission within 90 days of hospitalization for acute exacerbations of chronic obstructive pulmonary disease: a longitudinal study. *Ther Adv Respir Dis*. 2017;11(10):383–392. doi:10.1177/1753465817726314
25. Rong B, Liu Y, Li M, Fu T, Gao W, Liu H. Correlation of serum levels of HIF-1α and IL-19 with the disease progression of COPD: a retrospective study. *Int J Chron Obstruct Pulmon Dis*. 2018;13:3791–3803. doi:10.2147/COPD.S177034
26. Cheng W, Li X, Duan J, et al. Prevalence and Characteristics of Pain in Patients of Chronic Obstructive Pulmonary Disease: a Cross-Sectional Study in China. *COPD*. 2020;17(1):90–100. doi:10.1080/15412555.2020.1713076
27. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. *Eur Respir J*. 2009;34(3):648–654. doi:10.1183/09031936.00102509
28. Kamstrup P, Sivapalan P, Rønn C, et al. Fibrin degradation products and survival in patients with chronic obstructive pulmonary disease: a protocolized prospective observational study. *Respir Res*. 2023;24(1):172. doi:10.1186/s12931-023-02472-9
29. Liao QQ, Mo YJ, Zhu KW, et al. Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Lymphocyte Ratio (NLR), Monocyte-to-Lymphocyte Ratio (MLR), and Eosinophil-to-Lymphocyte Ratio (ELR) as Biomarkers in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD). *Int J Chron Obstruct Pulmon Dis*. 2024;19:501–518. doi:10.2147/COPD.S447519
30. Cheng Z, Yang M, Zhang Z, et al. Predictive value of Wells Score, Revised Geneva Score combined with D-dimer for Pulmonary Embolism in patients with acute exacerbation of chronic obstructive pulmonary disease. *Zhonghua Yi Xue Za Zhi*. 2018;98(48):3925–3929. doi:10.3760/cma.j.issn.0376-2491.2019.48.004
31. Zinellu E, Fois AG, Sotgiu E, et al. Serum Albumin Concentrations in Stable Chronic Obstructive Pulmonary Disease: a Systematic Review and Meta-Analysis. *J Clin Med*. 2021;10(2):269. doi:10.3390/jcm10020269
32. Polosa R, Malerba M, Cacciola RR, et al. Effect of acute exacerbations on circulating endothelial, clotting and fibrinolytic markers in COPD patients. *Intern Emerg Med*. 2013;8(7):567–574. doi:10.1007/s11739-011-0636-1
33. Günay E, Sarınç Ulaşlı S, Akar O, et al. Neutrophil-to-lymphocyte ratio in chronic obstructive pulmonary disease: a retrospective study. *Inflammation*. 2014;37(2):374–380. doi:10.1007/s10753-013-9749-1
34. Furutate R, Ishii T, Motegi T, et al. The Neutrophil to Lymphocyte Ratio Is Related to Disease Severity and Exacerbation in Patients with Chronic Obstructive Pulmonary Disease. *Intern Med*. 2016;55(3):223–229. doi:10.2169/internalmedicine.55.5772