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Monocyte distribution width (MDW) and DECAF: two simple tools to determine the prognosis of severe COPD exacerbation

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Abstract

Monocyte distribution width (MDW) has been associated with inflammation and poor prognosis in various acute diseases. Chronic obstructive pulmonary disease (COPD) exacerbations (ECOPD) are associated with mortality. The objective of this study was to evaluate the utility of the MDW as a predictor of ECOPD prognosis. This retrospective study included patient admissions for ECOPD. Demographic, clinical and biochemical information; intensive care unit (ICU) admissions; and mortality during admission were recorded. A total of 474 admissions were included. MDW was positively correlated with the DECAF score ($r = 0.184$, $p < 0.001$) and C-reactive protein (mg/dL) ($r = 0.571$, $p < 0.001$), and positively associated with C-RP (OR 1.115 95% CI 1.076–1.155, $p < 0.001$), death (OR 9.831 95% CI 2.981– 32.417, $p < 0.001$) and ICU admission (OR 11.204 95% CI 3.173–39.562, $p < 0.001$). High MDW values were independent risk factors for mortality (HR 3.647, CI 95% 1.313–10.136, $p = 0.013$), ICU admission (HR 2.550, CI 95% 1.131–5.753, $p = 0.024$), or either mortality or ICU admission (HR 3.084, CI 95% 1.624–5.858, $p = 0.001$). In ROC analysis, a combined MDW–DECAF score had better diagnostic power (AUC 0.777 95% IC 0.708–0.845, $p < 0.001$) than DECAF ($p = 0.023$), MDW ($p = 0.026$) or C-RP ($p = 0.002$) alone. MDW is associated with ECOPD severity and predicts mortality and ICU admission with a diagnostic accuracy similar to that of DECAF and C-RP. The MDW– DECAF score has better diagnostic accuracy than MDW or DECAF alone in identifying mortality or ICU admission.

Keywords COPD · MDW · DECAF · Exacerbation · Prognosis

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide [1]. COPD exacerbation (ECOPD) is a major outcome of this disease and ECOPD severity is associated with future mortality risk [2], a decline in FEV1 [3], diminished quality of life [4] and future ECOPD [5, 6]. Moreover, ECOPD hospitalizations are associated with high mortality rates [7, 8]. Nonetheless, few tools are available to help clinicians to determine ECOPD prognosis in hospitalized patients. These tools include C-reactive protein (C-RP), the only biomarker recommended by GOLD [9] to evaluate ECOPD severity, and the dyspnea–eosinopenia–consolidation–acidemia–atrial fibrillation (DECAF) prognostic score, which uses several clinical variables (dyspnea, eosinopenia, consolidation, acidemia and atrial fibrillation) to establish the prognosis of severe ECOPD [10]. Therefore, new parameters must be

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investigated in clinical practice to determine prognosis in patients with severe ECOPD.

The inflammatory response during ECOPD is mediated by the activation of neutrophilic and lymphocytic inflammation [11]. Circulating neutrophils and monocytes are involved in the initial response to pathogenic organisms that cause ECOPD [12]. Monocyte distribution width (MDW) reflects the degree of change in circulating monocyte volume ("heterogeneity") in response to proinflammatory signals elicited by infectious organisms. MDW determination is easily automated, inexpensive and quickly obtained as part of routine blood counts. Recent data have suggested that an increase in MDW may be useful in early detection of all-cause sepsis [13–21]. However, few studies have been performed in acute respiratory conditions; one example is a study in a limited number of patients with COVID-19 [22–24]. Some studies have suggested that MDW may be associated with the neutrophil/lymphocyte ratio, a biomarker associated with ECOPD prognosis [11].

We hypothesized that high MDW at hospital admission might serve as a prognostic inflammatory biomarker in patients with ECOPD and that combining the MDW with the DECAF score might further increase the prognostic value. To our knowledge, this aspect has not previously been studied in this setting.

Methods

This was a multicenter observational retrospective study in which clinical records from patients admitted for ECOPD between March 1st, 2020, and March 1st, 2023, to three public hospitals of the Servicio Cántabro de Salud network in the Cantabria community in northern Spain were reviewed. The ethics committee of our institution (2023.061) approved the study.

Participants

We recruited patients hospitalized for ECOPD between March 2020 and March 2023.

The inclusion criteria were as follows: (1) Patients older than 40 years previously diagnosed with COPD according to the GesEPOC guidelines [25] and (2) Patients hospitalized because of ECOPD. ECOPD was defined by an increase in more than one of the following respiratory symptoms: dyspnea, sputum purulence, increased sputum, cough or wheezing; symptoms persisting for at least 2 consecutive days; and symptoms requiring treatment with antibiotics and/or systemic steroids [9].

The exclusion criteria were as follows: (1) Patients with a diagnosis other than ECOPD at discharge; (2) Patients without clinical, biochemical or microbiological data consistent with ECOPD; (3) Patients with active cancer, leukemia, lymphoma, lymphoproliferative disorders, bone marrow diseases or AIDS; (4) Patients with vitamin B12 or folic acid deficiency; and (5) Patients treated with immunosuppressants (including systemic corticosteroids) or drugs causing macrocytosis.

Measurements

Stable spirometry was performed according to the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) protocol [26] less than 1 year before admission. Patient age; sex; smoking status; number of moderate and severe ECOPD events 1 year before admission; comorbidities included in the Charlson index [27]; basal mMRC dyspnea score; and dates of hospital admission, ICU admission and/or death during hospitalization were retrospectively recorded. The DECAF score [25] was calculated for all patients. The MDW and results of routine blood tests performed after arrival at the emergency department of each center were retrospectively collected.

Routine hematological and biochemical analytes were measured with automated assays. Specifically, C-RP was measured with Siemens traceable enzymatic method assays (Atellica Analyzer, Siemens, Germany).

MDW was measured in the emergency laboratory of each center with the same DxH 900 analyzer (Beckman Coulter. Inc., Brea, California, USA), according to the manufacturer´s instructions.

Statistical analysis

Data are presented as mean ± SD for normally distributed data or median (interquartile range) for nonparametric data. We calculated sample sizes in *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC.), with an α level of 0.05 and a β level of 0.2. Differences between groups were analyzed with unpaired *t* tests for parametric data or Mann–Whitney tests for nonparametric data. Normality of distribution was evaluated with the Kolmogorov–Smirnov test. We evaluated the correlation between MDW and other variables with Spearman tests. Evaluation of MDW as a dichotomized variable was established with a cutoff at 21.5 units, according to previous studies [28–30] performed in the same setting and using similar laboratory protocols as our study. We evaluated cross-sectional associations with high versus low MDW through univariate and multivariate logistic regression, with outcome variables of mortality; ICU admission; and a composite end point including in-hospital all-cause mortality and escalation to ICU admission. We used Kaplan–Meier estimates to calculate the proportion of participants experiencing mortality; ICU admission; and a composite end point including in-hospital all-cause

mortality and escalation to ICU admission due to ECOPD over time. We performed univariate and multivariate Cox proportional risk analysis in SPSS version 25.00. A receiver operating characteristic (ROC) curve and the area under the ROC curve (AUC) were used to assess the diagnostic value of MDW for a composite end point including in-hospital all-cause mortality and escalation to ICU admission as the outcome variables. ROC curve analysis was performed in MEDCALC version 11.6.1.0 (MedCalc Software, Mariakerke, Belgium). Differences with p values < 0.05 were considered significant. All reported p values were two sided.

Results

Patient characteristics

A total of 474 pw ECOPD were ultimately included in the study (flowchart for patient selection in Fig. 1; demographic, clinical and biochemical data in Table 1). The median patient age was 75 (67–82) years, and most patients were men (67.7%). The prevalence of current smokers (32.9%) was high. Most patients had a previous admission for ECOPD [178 (37.6%)] and moderate or severe obstruction, on the basis of FEV1 (%) 50 (35–67). A total of 26 patients died (5.5%); although ICU admission was not frequent [31 (6.5)], a composite end point including mortality or ICU admission reached 11% (52 patients). The blood MDW levels were 19.2 (17.2–21.2) units, the blood leucocyte levels were 9900 (7300–13525) cells/μL and the serum C-RP levels were 4.4 (1.5–11.7) mg/dL.

The group of patients with ECOPD and high MDW tended to have high ECOPD severity, on the basis of the DECAF score, mortality, ICU admission rate and elevated inflammatory parameters, such as C-RP and the neutrophil to lymphocyte ratio. Notably, the group with high MDW had slightly higher FEV1 values. However, the two groups had similar age, sex distribution, smoking habits, basal mMRC scores and ECOPD history.

MDW correlations

MDW was positively correlated with the DECAF score ($r = 0.184$, $p < 0.001$), FEV1 (L) ($r = 0.153$, $p = 0.001$), FEV1 (% predicted) ($r = 0.149$, $p = 0.001$), FEV1/FVC ($r = 0.106$, $p = 0.022$), C-RP (mg/dL) ($r = 0.571$, $p < 0.001$) and neutrophil to lymphocyte ratio ($r = 0.135$, $p = 0.003$).

MDW was negatively correlated with basophil count ($r = -0.111$, $p = 0.016$) and eosinophil count ($r = -0.288$, $p < 0.001$).

MDW did not correlate with age ($r = 0.025$, $p = 0.588$), Charlson score ($r = 0.056$, $p = 0.291$), BMI ($r = -0.02$, $p = 0.978$), FVC (L) ($r = 0.069$, $p = 0.145$), FVC FEV1 (% predicted) ($r = 0.077$, $p = 0.099$), paO_2 ($r = -0.084$, $p = 0.069$), $paCO_2$ ($r = -0.088$, $p = 0.056$), HCO_3 ($r = -0.065$, $p = 0.173$), pH ($r = 0.088$, $p = 0.056$), leucocyte count ($r = 0.024$, $p = 0.597$), neutrophil count ($r = 0.063$, $p = 0.172$), monocyte count ($r = 0.050$, $p = 0.274$) or lymphocyte count ($r = -0.080$, $p = 0.081$).

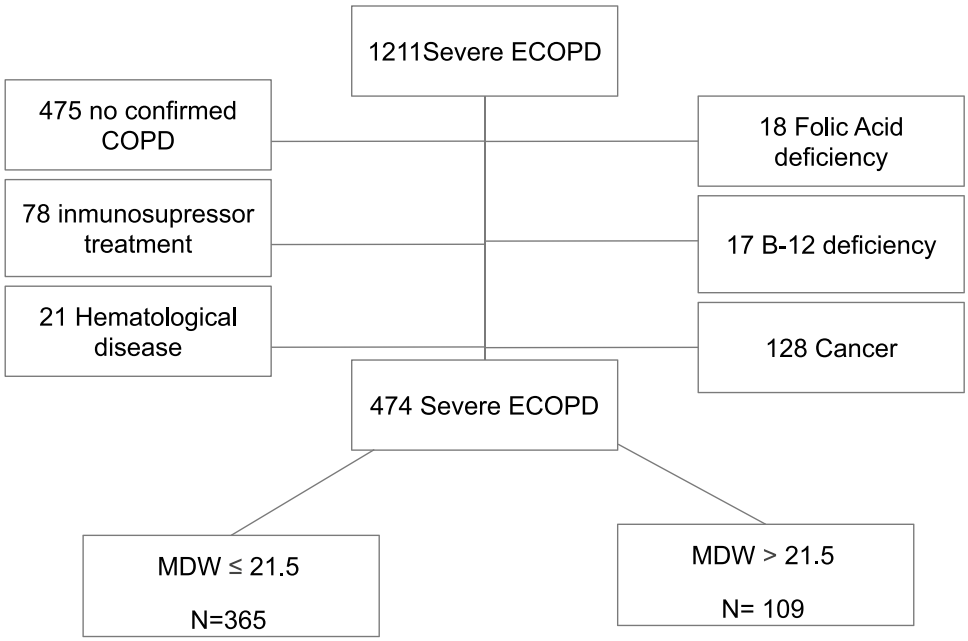

Fig. 1 Flowchart for patient selection

Table 1 Demographic, clinical and biochemical characteristics of all patients and patients with MDW ≤ 21.5 units vs MDW > 21.5 units

Variable	Total ($n=474$)	MDW ≤ 21.5 ($n=365$)	MDW > 21.5 ($n=109$)	p*
Age (years)	75 (67–82)	74(67–82)	76(66–84)	0.338
Sex male *n* (%)	321(67.7)	248(67.9)	73(67)	0.849
Current smokers *n* (%)	156 (32,9)	127(34.8)	29(26.6)	0.110
Charlson index	2(1–4)	2(1–4)	2(2–4)	0.742
Previous admission *n* (%)	178(37.6)	135(37.1)	43(39.4)	0.655
2 or more exacerbations during the previous year *n* (%)	151(31.9)	117(32.1)	34(31.2)	0.865
Basal mMRC score 0/I/II/III/IV n (%)	35/116/137/139/47	27(7.4)/84(23)/108(29.6)/108(29.6)/38(10.4)	8(7.3)/32(29.4)/29(26.6)/31(28.4)/9(8.3)	0.723
DECAF score	**2(1–3)**	**2(1–2.5)**	**2(2–3)**	**< 0.001**
Mortality during hospitalization *n* (%)	**26(5.5)**	**8(2.2)**	**18(16.5)**	**< 0.001**
ICU admission during hospitalization *n* (%)	**31(6.5)**	**14(3.8)**	**17(15.6)**	**< 0.001**
Composite end point (mortality or ICU admission) *n* (%)	**52(11)**	**22(6)**	**30(27)**	**< 0.001**
BMI (kg/m^2)	28(24–32)	28(24–32)	28(23–32)	0.448
FVC (L)	2.45 ± 0.86	2.43 ± 0.83	2.529 ± 0.99	0.155
FVC (% predicted)	78(65–93)	78(64–92)	79(70–95)	0.119
FEV_1 (L)	**1.10(0.84–1.63)**	**1.09(0.82–1.55)**	**1.23(0.92–1.73)**	**0.018**
FEV_1 (% predicted)	**50(35–67)**	**50(33–64)**	**57(43–69)**	**0.004**
FEV_1/FVC	**50(41–59)**	**49(40–59)**	**54(43–60)**	**0.04**
MDW (units)	**19.2(17.2–21.2)**	**18.3(16.7–19.8)**	**23.4(22.4–24.6)**	**< 0.001**
C-reactive protein (mg/dl)	**4.4(1.5–11.7)**	**2.9(1–7.9)**	**12.6(5.0–20.8)**	**< 0.001**
pH	7.40(7.36–7.42)	7.40(7.36–7.41)	7.40(7.35–7.43)	0.414
paO_2 (mmHg)	67(58.5–82)	68(58–82)	63(58–82)	0.159
$paCO_2$ (mmHg)	44(36–54)	43(36–55)	44(38–49)	0.587
HCO_3 (mmol/L)	27(22–31)	27(22–31)	27(23–29)	0.817
Leucocytes (cells/μL)	9900(7300–13525)	10,000(7500–13500)	9500(6800–14350)	0.828
Neutrophils (cells/μL)	7700(5400–11025)	7700(5500–10750)	7400(5000–11500)	0.773
Monocytes (cells/μL)	800(500–1100)	800(500–1100)	800(500–1200)	0.945
Lymphocytes (cells/μL)	**1000(600–1600)**	**1000(600–1600)**	**800(500–1400)**	**0.049**
Basophils (cells/μL)	**0(0–100)**	**0(0–100)**	**0(0–50)**	**0.015**
Eosinophils (cells/μL)	**100(0–125)**	**100(0–200)**	**0(0–100)**	**< 0.001**
Netrophils/lymphocytes	**7.23(4.68–14.00)**	**6.91(4.58–12.18)**	**9.60(5.20–17.83)**	**0.008**

Bold font indicates statistical significance

MDW monocyte distribution width, *mMRC* modified Medical Research Council dyspnea score, *FVC* forced vital capacity, *FEV1* forced expiratory volume in the first second, *DECAF* dyspnea, eosinopenia, consolidation, acidemia and atrial fibrillation score, *BMI* body mass index

*p value for patients with MDW ≤ 21.5 vs upper MDW

Association of MDW with ECOPD characteristics

Table 2 highlights the associations of MDW with baseline ECOPD characteristics. Multivariate logistic regression analysis showed that high MDW was positively associated with C-RP (OR 1.115 95% CI 1.076–1.155, $p < 0.001$), death (OR 9.831 95% CI 2.981–32.417, $p < 0.001$) and ICU admission (OR 11.204 95% CI 3.173–39.562, $p < 0.001$); however, no associations with other ECOPD characteristics were observed.

MDW as a predictor of mortality, ICU admission or both

Among 474 patients with ECOPD included in the study, 109 had a high MDW. Table 1 shows the clinical characteristics of both groups. A total of 26 patients died during hospitalization (18 in the high MDW group), 31 patients were admitted to the ICU (17 in the high MDW group) and 52 patients met the composite end point including mortality or ICU admission (30 in the high MDW group).

Table 2 Univariate and multivariate logistic regression analysis of the associations between ECOPD characteristics and high MDW

		MDW > 21.5 units			
		Univariate		Multivariate	
		OR (95% CI)	*p*	OR (95% CI)	**p*
Age (years)		1.009 (0.988–1.030)	0.880	1.007 (0.976–1.039)	0.657
Sex					
	Male	1		1	
	Female	0.957 (0.607–1.509)	0.185	0.880(0.477–1.623)	0.682
Smoking status					
	Former smoker	1		1	
	Current smoker	0.679 (0.422–1.094)	0.112	1.228 (0.608–2.480)	0.566
Previous exacerbations					
	0–1	1		1	
	≥ 2	0.961 (0.606–1.524)	0.865	1.163 (0.566–2.389)	0.682
Previous hospitalization					
	0	1		1	
	≥ 1	1.105 (0.712–1.714)	0.655	0.728 (0.370–1.431)	0.357
Basal mMRC		0.909 (0.749–1.103)	0.333	0.931 (0.706–1.229)	0.614
Charlson		0.993 (0.878–1.124)	0.915	0.997 (0.851–1.169)	0.972
FEV1 (%)		1.001 (0.999–1.003)	0.324	1.002 (0.999–1.004)	0.145
C-RP (mg/dL)		**1.120 (1.089–1.151)**	**< 0.001**	**1.115 (1.076–1.155)**	**< 0.001**
DECAF score		**1.518 (1.249–1.845)**	**0.001**	1.172 (0.905–1.517)	0.230
Leucocytes (cells/microL)		1.000 (1.000–1.000)	0.826	1.000 (0.999–1.000)	0.437
Neutrophils (cells/microL)		1.000 (1.000–1.000)	0.164	1.000 (1.000–1.001)	0.495
Monocytes (cells/microL)		1.000 (1.000–1.000)	0.947	1.000 (0.999–1.001)	0.743
Lymphocytes (cells/microL)		1.000 (1.000–1.000)	0.122	1.000 (1.000–1.001)	0.362
Basophils (cells/microL)		0.997 (0.993–1.001)	0.107	1.000 (0.995–1.005)	0.960
Eosinophils (cells/microL)		**0.997 (0.995–0.999)**	**0.002**	0.998 (0.996–1.000)	0.102
Netrophils/lymphocytes		1.000 (1.000–1.000)	0.412	1.000 (1.000–1.000)	0.373
pH		0.853 (0.040–18.117)	0.919	369.808 (0.837–163,329.086)	0.057
$paCO_2$ (mmHg)		1.000 (0.986–1.013)	0.968	0.996 (0.969–1.023)	0.748
HCO_3 (mmHg		0.998 (0.982–1.014)	0.809	1.001 (0.987–1.016)	0.852
paO_2 (mmHg)		0.998 (0.987–1.010)	0.787	1.000 (0.986–1.015)	0.965
Death					
	Survivors	1		1	
	Death	**3.720 (3.720–20.944)**	**< 0.001**	**9.831 (2.981–32.417)**	**< 0.001**
ICU admittance					
	Not admitted to ICU	1		1	
	Admitted to ICU	**4.633 (2.202–9.746)**	**< 0.001**	**11.204 (3.173–39.562)**	**< 0.001**

Bold font indicates statistical significance

MDW monocyte distribution width, *mMRC* modified Medical Research Council dyspnea score, *FEV1* forced expiratory volume in the first second, *DECAF* dyspnea, eosinopenia, consolidation, acidemia and atrial fibrillation score

**p* value for patients with MDW ≤ 21.5 vs upper MDW

Predictors of mortality

Univariate Cox proportional risk analysis indicated that age ($p = 0.04$), sex (women) ($p = 0.292$), MDW ($p = 0.001$) and high MDW (higher than 21.5) ($p = 0.002$), but not smoking status ($p = 0.064$), FEV1 ($p = 0.626$), Charlson index ($p = 0.101$), DECAF score ($p = 0.069$), C-RP ($p = 0.127$) or neutrophil to lymphocyte ratio ($p = 0.416$) were predictors of mortality during hospitalization due to ECOPD. Multivariate Cox proportional risk analysis revealed that the absolute values of MDW (HR 1.171, CI 95% 1.073–1.277, $p < 0.001$) (Table 3) and high MDW (HR 3.647, CI 95% 1.313–10.136, $p = 0.013$) (Table 3, Fig. 2) were independent risk factors for mortality during hospitalization for ECOPD.

Table 3 Cox regression analysis showing absolute and dichotomized values of MDW as a predictor of death, ICU admission and the composite end point (mortality or ICU admission)

Variable	B	Wald	*p*	HR	95% CI HR	
					Lower	Upper
MDW (absolute value in units)						
Mortality	**0.158**	**12.648**	**< 0.001**	**1.171**	**1.073**	**1.277**
ICU admittance	**0.083**	**4.866**	**0.027**	**1.086**	**1.009**	**1.169**
Composite end point	**0.115**	**18.839**	**< 0.001**	**1.122**	**1.065**	**1.182**
Dichotomized MDW (> 21.5 units vs rest of patients)						
Mortality	**1.294**	**6.158**	**0.013**	**3.647**	**1.313**	**10.136**
ICU admittance	**0.936**	**5.088**	**0.024**	**2.550**	**1.131**	**5.753**
Composite end point	**1.126**	**11.840**	**0.001**	**3.084**	**1.624**	**5.858**

Bold font indicates statistical significance

MDW monocyte distribution width, *DECAF* dyspnea, eosinopenia, consolidation, acidemia and atrial fibrillation score, *composite end point* mortality or ICU admission

*All variables adjusted by age, sex, Charlson index, forced expiratory volume in the first second, smoking status, DECAF score, C-reactive protein, neutrophil to lymphocyte ratio

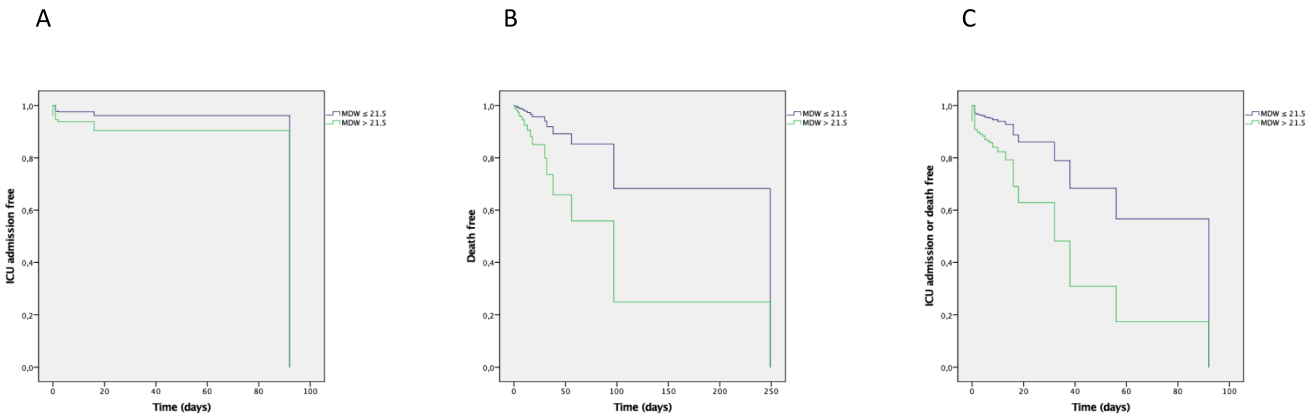

Fig. 2 High MDW (> 21.5 units) as a predictor of **A** ICU admission, **B** mortality and **C** ICU admission or mortality. *MDW* monocyte distribution width

Predictors of ICU admission

Univariate Cox proportional risk analysis indicated that age ($p < 0.001$), smoking status ($p = 0.007$), DECAF score ($p < 0.001$), C-RP ($p = 0.002$), MDW ($p < 0.001$) and high MDW (higher than 21.5) ($p < 0.001$), but not sex ($p = 0.292$), FEV1 ($p = 0.802$), Charlson index ($p = 0.995$) or neutrophil to lymphocyte ratio ($p = 0.654$) were predictors of ICU admission. Multivariate Cox proportional risk analysis revealed that absolute values of MDW (HR 1.086, CI 95% 1.009–1.169, $p = 0.027$) (Table 3) and high MDW (HR 2.550, CI 95% 1.131–5.753, $p = 0.024$) (Table 3, Fig. 2) were independent risk factors for ICU admission.

Predictors of the composite end point (mortality or ICU admission)

Univariate Cox proportional risk analysis indicated that age ($p = 0.047$), DECAF score ($p < 0.001$), C-RP ($p < 0.001$), MDW ($p < 0.001$) and high MDW (higher than 21.5) ($p < 0.001$), but not smoking status ($p = 0.072$), sex ($p = 0.767$), FEV1 ($p = 0.786$), Charlson index ($p = 0.100$) or neutrophil to lymphocyte ratio ($p = 0.754$) were predictors of the composite end point (mortality or ICU admission). Multivariate Cox proportional risk analysis revealed that absolute values of MDW (HR 1.122, CI 95% 1.065–1.182, $p < 0.001$) (Table 3) and high MDW (HR

3.084, CI 95% 1.624–5.858, $p = 0.001$) (Table 3, Fig. 2) were independent risk factors for the composite end point (mortality or ICU admission).

Potential utility of the MDW and DECAF–MDW score in predicting the composite end point

According to our findings, we created a new tool, the MDW–DECAF score, based on the DECAF score and including the same variables as DECAF and the MDW, with a relative weight assigned according to the regression coefficient for the composite end point (3 points). In ROC analysis (Fig. 3), the MDW–DECAF score's AUC for differentiating patients who died or were admitted to the ICU from the rest of the patients (AUC 0.777 95% IC 0.708–0.845, $p < 0.001$) had the best diagnostic power and was followed by the DECAF score (AUC 0.710 95% IC 0.639–0.782, $p < 0.001$) and MDW (AUC 0.705 95% IC 0.618–0.791, $p < 0.001$) (Fig. 3, Supplementary file 1). Youden's index for MDW was > 21.7, with a sensitivity of 57.69 and a specificity of 81.95. Youden's index for the MDW–DECAF score was > 2, with a sensitivity of 84.62 and a specificity of 63.01. MDW–DECAF had a statistically significantly higher AUC than the DECAF score ($p = 0.023$), MDW ($p = 0.026$), C-RP ($p = 0.002$) and neutrophil to lymphocyte ratio. No statistically significant differences were found among the AUC values of the remaining variables.

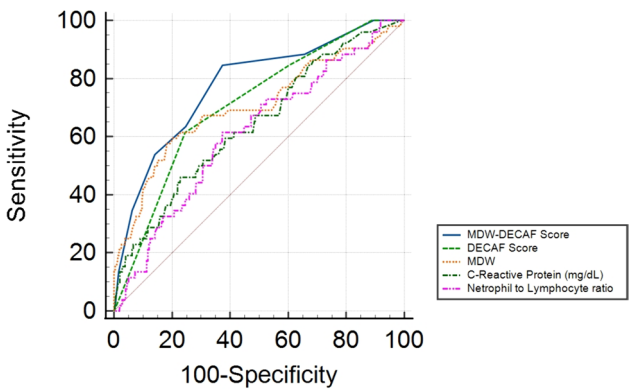

Fig. 3 Receiver operator characteristic curve showing the discrimination ability of MDW, C-reactive protein, neutrophil to lymphocyte ratio, the DECAF score and the MDW–DECAF score for in-hospital mortality or ICU admission. *MDW* monocyte distribution width, *DECAF* dyspnea, eosinopenia, consolidation, acidemia and atrial fibrillation score

Discussion

This study provides the first demonstration that MDW is associated with the severity of severe ECOPD and can be used as a predictor of mortality and ICU admission. Moreover, it introduces the new MDW–DECAF score.

Patients with high MDW, as reported by previous studies in patients with systemic inflammatory response syndrome [28, 29] or COVID-19 [30], had elevated C-RP, DECAF scores and neutrophil to lymphocyte ratios, and lower blood eosinophils; these prognostic factors are well known to be associated with both ECOPD inflammatory response and severity [10, 11, 31–33]. We also evaluated variables associated with higher MDW values in a multivariate logistic regression analysis, which indicated that C-RP, mortality and ICU admission were associated with high MDW values. Our findings indicate the importance of inflammation in MDW levels, as discussed in other clinical contexts, such as sepsis [16, 19, 20, 24, 28, 29], COVID-19 [22–24], influenza [34] and complicated diverticulitis [35].

Our findings provide the first evidence that the MDW values according to blood tests performed after emergency department arrival predict death and ICU admission for ECOPD. This novel finding has not previously been described in the context of COPD, but has been reported in other settings, such as COVID-19 [23] and sepsis [28]. Furthermore, our results were obtained by using Cox regression analysis considering the time to the event, whereas other studies have evaluated ECOPD prognosis by using only logistic regression analysis [10, 11]. Additionally, the cutoff point of the test was determined on the basis of previous studies [28–30]. This was similar to Youden's index in our study.

The AUC of MDW for predicting the prognosis of severe ECOPD in terms of mortality or ICU admission was comparable to that of other well-known inflammatory markers of COPD, such as C-RP [9] or the neutrophil to lymphocyte ratio [11]. MDW is biomarker that can be routinely measured rapidly, easily and inexpensively in emergency departments. Further studies are necessary to evaluate the limitations and benefits of each biomarker in COPD. The DECAF score [10] is a well-known risk stratification tool for patients with severe ECOPD, but its AUC can be improved by using novel biomarkers. Because MDW is a different predictor from the DECAF score for mortality or ICU admission, we created a new score, the MDW–DECAF score, which had a better AUC than the other biomarkers or the DECAF score alone. Further studies are required to evaluate the potential roles of these scores in assessing specific etiologies of ECOPD or inflammatory conditions.

This study has several strengths. First, it is a novel study reporting the first evaluation of MDW in ECOPD in

real-world circumstances. Second, this was a multicenter study in patients from three hospitals. Finally, the patients included in this study were carefully selected and well characterized, and patients with diseases or therapies that might have influenced the results were excluded.

However, our study also has several limitations. First, this was a retrospective study and therefore was subject to a risk of information bias. Although all routine blood tests were performed minutes after arrival at the emergency department, the retrospective nature of this study could imply different timing for analysis from whole blood venous sample collection. Furthermore, our results cannot be extrapolated to all patients with COPD since we excluded patients with hematological and nutritional conditions. Our findings should be replicated in other settings, in a larger number of patients, with standardized therapy and multiple samples, to evaluate the time course of the responses of MDW. Future specifically designed prospective studies should be performed to evaluate the utility of MDW and externally validate MDW–DECAF.

Conclusion

Our study provides the first evidence that MDW is associated with ECOPD severity and predicts mortality and ICU admission with a diagnostic accuracy similar to that of DECAF and C-RP. Furthermore, on the basis of our results, we created a new tool, the MDW–DECAF score, which has better diagnostic accuracy than the DECAF score in identifying mortality or ICU admission.

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Data availability The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Conflict of interest Carlos Amado has received speaker or consulting fees from Boehringer Ingelheim, Pfizer, AstraZeneca, Novartis, Chiesi, Faes Farma, Esteve and GSK. Guido Andretta has received speaker fees from AstraZeneca. Javier Zuazaga has received speaker fees from Boehringer Ingelheim. The rest of the authors do not have any conflict of interest.

Ethical statement This study complies with internationally accepted standards for research practice and reporting. The ethics committee of our Institution approved the study (2023.061).

Consent for publication Not applicable.

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