DOI: 10.1002/jmv.27764

LETTER TO THE EDITOR

JOURNAL OF MEDICAL VIROLOGY WILEY

RDW shows prognostic potential in hospitalized patients with COVID-19

To the Editor,

A recent meta-analysis published in the Journal of Medical Virology identified a potential association between red cell distribution width (RDW) and mortality risk in patients with coronavirus disease 2019 (COVID-19).[1] This follows similar reports elsewhere.[2,3] COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[4] which has been associated with over 5 million deaths worldwide since December 2019.[5] RDW is a routine full blood count (FBC) parameter that reflects the level of change in size between red cells (anisocytosis)[6] and has been widely researched as an independent predictor of mortality in different hospital settings, including critically ill patients with sepsis.[7] Identifying patients with a higher risk of in-hospital mortality may enable prioritization of resources and targeted treatments directed at those at increased risk of death which could ultimately improve outcomes.

This retrospective study included all laboratory-confirmed cases of SARS-CoV-2 infection in patients presenting at the General Hospital in Jersey (Channel Islands, UK) between March and December 2020. Laboratory confirmation for SARS-CoV-2 was defined as a positive result of real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay using a nasopharyngeal/oropharyngeal swab as per World Health Organization guidance.[8] Specimens were initially tested at Public Health England, Porton Down (UK), and in-house testing commenced in April 2020, using qualitative Gene Xpert SARS-CoV-2 RT-PCR test kits (Cepheid). FBC tests were locally performed on venous blood samples collected into a 4-ml anticoagulated BD Vacutainer tube containing K2 ethylenediaminetetraacetic acid (0.184 mol/L; BD), and analysis performed in Sysmex XN-2000 analyzers (Sysmex corporation). Biochemistry tests were performed on a venous blood sample collected into a 3.5-ml BD Vacutainer SST II gel tube (BD), centrifuged at 3500 rpm for 10 min before analysis, and then analyzed using Ortho Vitros 5600 analyzers (Ortho-Clinical Diagnostics) by MicroSlide technology. Statistical analysis was performed in the IBM SPSS software (version 26).

Differences between groups were calculated using the *t* test if data were normally distributed; otherwise, the Mann–Whitney test was used. Categorical variables were compared using the χ^2 or Fisher exact test, as appropriate. Probability (p) <0.05 was considered significant for all tests. Receiver operating characteristic (ROC) curves were calculated for continuous variables showing statistically significant differences between the survivors and non-survivors. The area under the curve (AUC) and the 95% confidence interval (CI) were determined to establish the optimal cut-off point that maximized sensitivity and specificity to predict death by the Youden's index. These cut-offs were used to transform the continuous variables into binary variables, and univariate and multivariate logistic regression models were applied to calculate the estimated odds ratio and the 95% CI.

A total of 139 patients were identified as having had a positive SARS-CoV-2 RT-PCR test on admission or during hospitalization: 27 patients presented with minor symptoms and only required a short hospitalization (<2 days), and 29 were hospital-acquired cases. 77 patients (55.4%) were male, and 62 were female (44.6%). Nonsurvivors were found to be significantly older (median age: 82 vs. 69 years; $p = 0.001$) and presented with higher RDW results when compared with survivors (14.1 vs. 13.2 in survivors; $p = 0.004$) (Table 1). Men accounted for most deaths in this cohort (males: 18 deaths, 58.1% vs. females: 13 deaths, 41.9%). Like other studies, no statistically significant difference was found in gender distribution between survivors and nonsurvivors ($p = 0.735$).[2,9]

ROC curve analysis determined RDW >14% as the optimal cut-off point for logistic regression analysis (AUC = 0.668 [95% CI: 0.572–0.764]; $p = 0.004$), and univariate analysis confirmed this cut-off was significantly associated with death ($p = 0.008$). Cut-offs determined for the other parameters showing statistically significant differences between survivors and nonsurvivors are shown in Table 2. The multivariate logistic analysis demonstrated that RDW > 14% on admission was associated with a 3.7-fold increased mortality risk in hospitalized patients with COVID-19 ($p = 0.015$), and this association was independent of the effects of age, WBC, neutrophils, lymphocytes, creatinine, or CRP. Age >70 years, neutrophils $\geq 10.2 \times 10^9$/L, and lymphocytes $< 0.88 \times 10^9$/L were also shown to be important risk factors associated with death in this patient group (Table 2).

This study showed nonsurvivors presented with higher RDW ($p = 0.004$), which is comparable with other studies,[2,3] although the author reports more modest differences between sub-groups. Regression analysis identified a significantly higher mortality risk in hospitalized patients with COVID-19 presenting with RDW greater than 14% on admission, confirming its prognostic potential. RDW has been widely researched as an independent predictor of mortality in other settings,[7] suggesting RDW may act as a generic predictor of mortality, not directly linked to specific pathological changes arising from SARS-CoV-2 infection. Despite this, RDW may play a role in the risk-stratification of hospitalized patients with COVID-19.

TABLE 1 Demographics and laboratory features in COVID-19 patients

Parameter	Survivors (n = 108) Median (IQR) or mean ± SD	Non-Survivors (n = 31) Median (IQR) or mean ± SD	p value
Age (years)	69 (53–80)	82 (75–87)	0.001[a,b]
Hemoglobin (g/dl)	13.09 ± 1.91	12.54 ± 2.40	0.190[c]
WBC (10^9/L)	6.9 (5.5–9.4)	9.5 (6.1–13.6)	0.012[a,b]
Platelets (10^9/L)	228.5 (183.0–292.0)	255.0 (173.2–337.5)	0.556[a]
RDW (%)	13.2 (12.3–14.3)	14.1 (13.0–15.0)	0.004[a,b]
Neutrophils (10^9/L)	4.8 (3.5–6.9)	7.3 (4.2–12.2)	0.008[a,b]
Lymphocytes (10^9/L)	1.1 (0.7–1.7)	0.7 (0.5–0.9)	<0.001[a,b]
Monocytes (10^9/L)	0.6 (0.4–0.8)	0.6 (0.4–1.0)	0.680[a]
Eosinophils (10^9/L)	0.04 (0.01–0.12)	0.03 (0.01–0.08)	0.422[a]
Basophils (10^9/L)	0.02 (0.01–0.04)	0.02 (0.01–0.06)	0.478[a]
Creatinine (μmol/L)	72.0 (55.0–90.0)	102 (63.0–123.0)	0.004[a,b]
CRP (mg/L)	34.0 (11.0–69.0)	62.0 (33.0–174.0)	0.003[a,b]

Note: ♂ male; ♀ female.

Abbreviations: IQR: Interquartile range (Q1, Q3); SD, standard deviation.

[a]Mann-Whitney U test.

[b]Statistically significant ($p < 0.05$).

[c]t Test.

TABLE 2 Mortality risk associated with RDW results

Variable	Univariate analysis OR	95% CI	p value	Multivariate analysis OR	95% CI	p value
Age >70 years	10.431	2.991–36.378	<0.001	12.076	2.601–56.059	0.001
WBC >8.3 × 10^9/L	3.636	1.574–8.402	0.003			
RDW >14%	3.048	1.335–6.958	0.008	3.744	1.292–10.852	0.015
Neutrophils ≥10.2 × 10^9/L	7.078	2.695–18.588	<0.001	10.187	2.761–37.582	<0.001
Lymphocytes <0.88 × 10^9/L	7.151	2.812–18.186	<0.001	5.592	1.848–16.916	0.002
Creatinine ≥100 μmol/L	5.624	2.371–13.341	<0.001			
CRP >44 mg/L	3.500	1.472–8.320	0.005			

Abbreviations: CI, confidence interval; OR, odds ratio.

CONFLICT OF INTEREST

The author declares no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1002/jmv.27764

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