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RESEARCH ARTICLE

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Red blood cell distribution width-to-albumin ratio is associated with all-cause mortality in cancer patients

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Abstract

Background: Cancer causes a serious health burden on patients worldwide. Chronic low-level inflammation plays a key role in tumorigenesis and prognosis. However, the role of the red blood cell distribution width (RDW)-to-albumin (RA) ratio in cancer mortality remains unclear.

Methods: In this retrospective cohort study, we collected clinical information from cancer patients from the Medical Information Mart for Intensive Care III (MIMIC-III) version 1.4 database and then calculated RA by dividing RDW by albumin concentration. The primary outcome was 30 days mortality, while secondary outcomes were 90 days and 1 year mortality. Next, we adopted Cox regression models to calculate hazard ratios (HR) together with 95% confidence intervals (CI) for all-cause mortalities associated with the RA ratio.

Results: For 30 days mortality, the HR (95% CI) for the high RA ratio (≥5.51) was 2.17 [95CI% (1.87–2.51); $p = <0.0001$], compared with the low RA ratio (<5.51). In Model 2, we adjusted sex and age and obtained HR (95% CI) of 2.17 [95CI% (1.87–2.52); $p = <0.0001$] for the high RA ratio (≥5.51) group, compared to that in the low RA ratio (<5.51). In Model 3, adjusting for age, sex, anion gap, hematocrit, white blood cell count, congestive heart failure, SOFA, liver disease, and renal failure resulted in HR (95% CI) of 1.74 [95CI% (1.48–2.04); $p = <0.0001$] for the high RA ratio (≥5.51) relative to the low RA ratio (<5.51). We also analyzed common diseases in cancer patients but found no significant association.

Conclusion: To the best of our knowledge, this is the first study demonstrating that increased RA ratio is independently associated with increased all-cause mortality in cancer patients.

KEYWORDS
albumin, cancer, medical information mart for intensive care-III, RDW

Chengdong Lu and Jianyun Long contributed equally to this work.

1 | INTRODUCTION

Cancer causes a serious health burden on patients worldwide.[1,2] Previous estimates have shown that the global incidence of cancer will increase from 12.7 to 22.2 million cases by 2030.[3] Overall cancer mortality has declined owing to advancement in techniques used for the early detection of tumors and the emergence of new treatment strategies.[4–6] However, the number of patients admitted to the intensive care unit (ICU) has increased.[7] Results from a previous epidemiological study revealed an ICU admission rate of 5.2% within 2 years of a definite diagnosis of cancer.[8] Currently, identification of biomarkers for predicting the prognosis of cancer patients in the ICU is a hot research topic.[9]

Previous studies have shown that chronic low-level inflammation plays a significant role in both tumorigenesis and prognosis.[10,11] The red blood cell distribution width (RDW), which can be obtained by evaluating complete blood count, is used to represent variability in the size of circulating erythrocytes and differentiate different types of anemia in clinical settings. Recent studies have demonstrated the ability of RDW to reflect inflammation and nutritional dysregulation in lung cancer patients with cardiovascular disease,[12–14] sepsis,[15] and chronic obstructive pulmonary disease (COPD).[16] Additional studies have shown that RDW is a new and effective indicator of the general condition and mortality of patients with lung cancer. In patients with breast cancer, elevated RDW exhibited a significant positive correlation with the size of primary tumors, degree of axillary lymphatic spread, and levels of *HER2* expression, but was negatively correlated with tumor grade.[17] Some scholars believe that RDW can be used as a novel indicator of tumor metastasis in breast and other solid tumors, owing to its advantages of convenience and cost-effectiveness.[18,19] To date, however, RDW's prognostic value in patients with tumors admitted to the ICU remains unknown. A recent study proposed analyzed the use of RDW in combination with other identified biomarkers, such as serum albumin level, and found that it was associated with mortality of patients with various diseases including tumors.[20] Albumin not only exerts anti-inflammatory effects but also reduces oxidative stress and inhibits apoptosis of endothelial cells.[21,22] The RDW-to-albumin (RA) ratio is a novel inflammatory biomarker,[23] which has previously been used to assess the prognosis of patients with stroke[22] and aortic aneurysms.[23,24] We hypothesized that the use of RDW in combination with albumin may be a potential predictor of cancer mortality. In the present study, we assessed the prognostic value RA ratio in predicting cancer mortality.

2 | MATERIALS AND METHODS

2.1 | Study population

Clinical data for 50,000 critically ill patients, who were admitted to the Beth Israel Deaconess Medical Center between 2001 and 2012,[25] were obtained from a free accessible critical care Medical Information Mart for Intensive Care III database version 1.4 (MIMIC-III, v1.4). To access the database, we completed the Protecting Human Research Participants, an online course developed by the National Institutes of Health. The database was recognized by the institutional review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. All personal information was removed to protect the privacy of patients. Patients were included in the study if they: (1) were diagnosed with cancer based on the International Classification of Diseases, Ninth Revision (ICD-9); (2) were aged ≥16 years; and (3) only had one ICU admission during the study period. Conversely, subjects who had more than 10% of the data missing and those with a length of hospital stay <24 h were excluded from the study.

2.2 | Study variables

Study variables included demographic characteristics (age, gender, race), vital signs, laboratory indices, and comorbidities. Vital signs included heart rate, oxygen saturation (S_PO_2), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate, and body temperature. Comorbidities included acute coronary artery disease (CAD), kidney disease, and liver disease, whereas laboratory indices included neutrophil count, monocyte count, lymphocyte count, white blood cell (WBC) count, hemoglobin, platelet count, RDW, glucose level, serum creatinine level, blood urea nitrogen (BUN), and anion gap within 24 h of ICU admission. Sequential Organ Failure Assessment (SOFA) was also included. Primary outcome was all-cause 30 days mortality, whereas secondary outcomes were all-cause 90 days and 1 year mortality, and the length of ICU stay.

2.3 | Statistical analysis

Continuous variables that conformed to normal distribution were presented as means ± standard deviations (SD), non-normally distributed data were presented using medians (interquartile range). Between-group differences were determined using the Wilcoxon W or Kruskal-Wallis tests. Categorical variables were expressed as numbers and percentages and then compared between groups using the chi-squared or Fisher's exact tests. The RA ratio was evaluated in the tertile and dichotomized groups, with that in the former group considered the reference value. Multivariate analysis was performed using Cox regression models and used to investigate the prognostic value of the RA ratio in predicting cancer mortality. Confounding factors, with estimated effects >10%, were selected for adjustment.[26] These included age, sex, anion gap, hematocrit, white blood cell count, congestive heart failure, SOFA scores, liver disease, and renal failure. In addition, we performed a stratified analysis based on each variable and comorbidity to examine the stability of RA in predicting disease survival outcomes across various subgroups. Moreover, propensity score matching was performed because of

the differences in baseline characteristics. Propensity score matching, at a ratio of 1:1, was performed using a caliper width of 0.01 of the SD of the logit of the propensity score.[27] All statistical analyses were performed using packages implemented in R software version 4.01 (https://www.r-project.org/), and statistical significance was defined by a two-tailed *p*-value <0.05.

TABLE 1 Baseline characteristics of the study population

		RA Ratio		
Characteristics	**Total**	**<5.51**	**≥5.51**	***p* value**
N	3381	1686	1695	
Age, years	65.78 ± 14.44	65.85 ± 14.72	65.73 ± 14.18	0.803
Sex, *n* (%)				0.407
Female	1356 (40.11)	688 (40.81)	668 (39.41)	
Male	2025 (59.89)	998 (59.19)	1027 (60.59)	
Vital signs				
SBP, mmHg	116.48 ± 17.19	120.11 ± 17.07	112.87 ± 16.54	<0.001
DBP, mmHg	60.82 ± 10.90	62.50 ± 10.83	59.16 ± 10.72	<0.001
MAP, mmHg	77.01 ± 11.47	78.98 ± 11.30	75.05 ± 11.31	<0.001
Heart rate, beats/min	89.89 ± 17.17	87.09 ± 16.89	92.69 ± 17.00	<0.001
SpO2, %	96.92 ± 2.69	96.95 ± 2.24	96.90 ± 3.08	0.622
Laboratory parameters				
RA	5.87 ± 1.97	4.42 ± 0.69	7.32 ± 1.76	<0.001
RDW, %	16.36 ± 2.64	14.99 ± 1.71	17.73 ± 2.69	<0.001
Albumin, g/dL	2.97 ± 0.68	3.45 ± 0.49	2.50 ± 0.48	<0.001
WBC count, 10^9/L	11.58 ± 16.15	10.96 ± 14.88	12.20 ± 17.29	0.026
Hemoglobin, g/dl	11.17 ± 2.03	11.75 ± 2.05	10.59 ± 1.84	<0.001
Hematocrit, %	28.11 ± 6.12	29.89 ± 6.22	26.33 ± 5.47	<0.001
Platelet, 10^9/L	201.01 ± 147.36	210.18 ± 136.92	191.89 ± 156.56	<0.001
Anion gap, mg/dl	13.11 ± 3.78	13.11 ± 3.32	13.11 ± 4.18	0.979
Bicarbonate, mg/dl	24.52 ± 4.69	25.34 ± 4.24	23.71 ± 4.97	<0.001
Glucose, mmol/L	140.50 ± 48.52	142.53 ± 45.72	138.48 ± 51.08	0.016
Blood lactic acid, mmol/L	3.46 ± 3.09	3.14 ± 2.83	3.73 ± 3.27	<0.001
Serum creatinine, mg/dl	1.29 ± 1.32	1.24 ± 1.37	1.34 ± 1.27	0.019
Serum urea nitrogen, mg/dl	27.16 ± 22.25	24.13 ± 20.60	30.18 ± 23.40	<0.001
Serum sodium, mg/dl	135.68 ± 5.59	135.97 ± 5.43	135.39 ± 5.73	0.003
Serum potassium, mg/dl	4.65 ± 0.93	4.60 ± 0.91	4.70 ± 0.94	<0.001
Severity of illness				
SOFA score	5.18 ± 3.59	4.25 ± 3.06	6.10 ± 3.83	<0.001
Comorbidities				
CHF, *n* (%)	442 (13.07)	222 (13.17)	220 (12.98)	0.871
CAD, *n* (%)	501 (14.81)	284 (16.84)	217 (12.80)	<0.001
Renal failure, *n* (%)	440 (13.01)	201 (11.92)	239 (14.10)	<0.001
Liver disease, *n* (%)	388 (11.48)	154 (9.13)	234 (13.81)	<0.001
Mortality, n (%)				
30 days	787 (23.28)	265 (15.72)	522 (30.80)	<0.001
90 days	1131 (33.45)	390 (23.13)	741 (43.72)	<0.001
1 year	1564 (46.26)	608 (36.06)	956 (56.40)	<0.001
Length of ICU stay, day	4.43 ± 6.14	3.90 ± 5.01	4.98 ± 7.07	<0.001

Abbreviations: DBP—diastolic blood pressure; MAP—mean arterial pressure; RA—red blood cell distribution width-to-albumin; RDW—red cell distribution width; SBP—systolic blood pressure; SOFA—Sequential Organ Failure Assessment; WBC—white blood cell.

TABLE 2 HR (95% CIs) for all-cause mortality of RA level

	Model 1[a]		Model 2[b]		Model 3[c]	
	HR (95% CIs)	*p value*	HR (95% CIs)	*p value*	HR (95% CIs)	*p value*
30-Day all-cause mortality						
Dichotomized groups						
<5.51	1		1		1	
≥5.51	2.17 (1.87, 2.51)	<0.0001	2.17 (1.87, 2.52)	<0.0001	1.74 (1.48, 2.04)	<0.0001
Tertile						
<4.84	1		1		1	
4.84–6.29	1.73 (1.41, 2.12)	<0.0001	1.70 (1.39, 2.08)	<0.0001	1.52 (1.23, 1.87)	<0.0001
≥6.29	2.99 (2.47, 3.61)	<0.0001	2.97 (2.46, 3.59)	<0.0001	2.18 (1.77, 2.69)	<0.0001
90-Day all-cause mortality						
Dichotomized groups						
<5.51	1		1		1	
≥5.51	2.19 (1.93, 2.47)	<0.0001	2.19 (1.94, 2.48)	<0.0001	1.84 (1.61, 2.10)	<0.0001
Tertile						
<4.84	1		1		1	
4.84–6.29	1.83 (1.55, 2.17)	<0.0001	1.81 (1.53, 2.14)	<0.0001	1.65 (1.39, 1.96)	<0.0001
≥6.29	3.03 (2.59, 3.55)	<0.0001	3.02 (2.58, 3.54)	<0.0001	2.40 (2.02, 2.85)	<0.0001
One-Year all-cause mortality						
Dichotomized groups						
<5.51	1		1		1	
≥5.51	1.92 (1.73, 2.12)	<0.0001	1.93 (1.74, 2.13)	<0.0001	1.65 (1.48, 1.84)	<0.0001
Tertile						
<4.84	1		1		1	
4.84–6.29	1.64 (1.43, 1.87)	<0.0001	1.62 (1.42, 1.85)	<0.0001	1.47 (1.28, 1.69)	<0.0001
≥6.29	2.49 (2.19, 2.83)	<0.0001	2.48 (2.18, 2.82)	<0.0001	2.02 (1.75, 2.33)	<0.0001

Abbreviations: CI—confidence interval; HR—hazard ratio; RA—the ratio of RDW to albumin.

Models 1, 2, and 3 were derived from Cox proportional hazard regression models:

[a]Model 1 covariates were adjusted for nothing.

[b]Model 2 covariates were adjusted for age and sex.

[c]Model 3 covariates were adjusted for age, sex, anion gap, hematocrit, white blood cell count, congestive heart failure, SOFA, liver disease, and renal failure.

3 | RESULTS

3.1 | Subject characteristics

A total of 3381 cancer patients were enrolled in this study. Details on their demographic characteristics, vital signs, laboratory indices, and comorbidities at baseline are outlined in Table 1. Summarily, patients with higher RA ratios had higher 30 days, 90 days, and one year mortality, but lower SBP, DBP, and MAP. In addition, this patient population had a history of renal failure and liver disease.

3.2 | RA ratio is an independent risk factor for mortality in cancer patients

The relationship between RA ratio and patient mortality at 30 days, 90 days, and 1 year is outlined in Table 2. For 30 days mortality, the HR (95% CI) for the high RA ratio (≥5.51) was 2.17 [95CI% (1.87–2.51); p = <0.0001], compared with the low RA ratio (<5.51). In Model 2, sex and age were adjusted, and the HR (95% CI) for the high RA ratio (≥5.51) was 2.17 [95CI% (1.87–2.52); $p < 0.0001$], compared with the low RA ratio (<5.51). In Model 3, age, sex, anion gap, hematocrit, white blood cell count, congestive heart failure, SOFA, liver disease, and renal failure were adjusted, revealing HR (95% CI) for the high RA ratio (≥5.51) was 1.74 [95CI% (1.48–2.04); $p < 0.0001$], compared with the low RA ratio (<5.51). In the tertile groups, we found a significant association between higher RA ratios and 30 days all-cause mortality (compared with the first dichotomized groups, <5.51) in model 1. The HR (95% CIs) for the three models for 30 days all-cause mortality were 1.52 (1.23–1.87), and 2.18 (1.77–2.69), respectively (all $p < 0.001$). A similar relationship was also observed for 90 days and 1 year all-cause mortalities.

Furthermore, linear regression was used to evaluate the association between RA ratio and length of stay, and obtained results were expressed as β (95% CIs). Results are outlined in Table 3. Results

TABLE 3 β (95% CIs) for length of ICU stay of RA ratio

	Model 1[a]		Model 2[b]		Model 3[c]	
	β (95% CIs)	*p value*	β (95% CIs)	*p value*	β (95% CIs)	*p value*
Length of ICU stay						
Dichotomized groups						
<5.51	1		1		1	
≥5.51	1.08 (0.67, 1.50)	<0.0001	1.08 (0.67, 1.50)	<0.0001	0.67 (0.23, 1.12)	0.0032
p for trend	<0.0001		<0.0001		0.0032	
Tertile						
<4.84	1		1		1	
4.84–6.29	0.72 (0.21, 1.22)	0.0054	0.73 (0.22, 1.24)	<0.0001	0.44 (−0.08, 0.97)	0.0987
≥6.29	1.40 (0.90, 1.91)	<0.0001	1.41 (0.90, 1.91)	<0.0001	0.83 (0.26, 1.39)	0.0042
p for trend	<0.0001		<0.0001		0.0047	

Abbreviations: CI—confidence interval; RA—the ratio of RDW to albumin.

Models 1, 2, and 3 were derived from linear regression and used to evaluate the relationship between RA ratio and length of stay. Results were expressed as β (95% CIs).

[a]Model 1 covariates were adjusted for nothing.

[b]Model 2 covariates were adjusted for age and sex.

[c]Model 3 covariates were adjusted for age, sex, anion gap, hematocrit, white blood cell count, congestive heart failure, SOFA, liver disease, and renal failure.

TABLE 4 Results from subgroup analysis showing the relationship between 30-day all-cause mortality and RA

		RA Ratio		
	N	<5.51	≥5.51	*p value*
Clinical parameters				
Age, years				
≤59	1127	1	2.59 (1.91, 3.51)	<0.0001
59–73	1125	1	2.46 (1.89, 3.19)	<0.0001
≥73	1129	1	1.78 (1.43, 2.23)	<0.0001
Sex				
Female	1356	1	2.17 (1.72, 2.73)	<0.0001
Male	2025	1	2.16 (1.79, 2.62)	<0.0001
Vital signs				
Heart rate, beats/min				
≤66	1074	1	2.80 (2.12, 3.69)	<0.0001
67–81	1167	1	2.08 (1.59, 2.71)	<0.0001
≥82	1134	1	1.66 (1.32, 2.10)	<0.0001
SBP, mmHg				
≤106	1125	1	2.38 (1.86, 3.04)	<0.0001
107–121	1123	1	1.73 (1.34, 2.25)	<0.0001
≥122	1126	1	1.59 (1.18, 2.14)	0.0022
MAP, mmHg				
≤71	1127	1	2.45 (1.92, 3.13)	<0.0001
72–80	1123	1	1.95 (1.50, 2.53)	<0.0001
≥81	1124	1	1.45 (1.08, 1.94)	0.0133
Respiratory rate, bate/min				
≤19	1680	1	2.53 (1.99, 3.22)	<0.0001
≥20	1686	1	1.84 (1.53, 2.22)	<0.0001

(Continues)

TABLE 4 (Continued)

		RA Ratio		
	N	<5.51	≥5.51	*p value*
SPO_2, %				
≤96.36	1126	1	2.22 (1.77, 2.79)	<0.0001
96.37–98.23	1120	1	2.60 (1.95, 3.47)	<0.0001
≥98.24	1125	1	1.87 (1.44, 2.45)	<0.0001
Laboratory parameters				
WBC count, $10^9/L$				
≤6.5	1101	1	2.32 (1.75, 3.08)	<0.0001
6.6–11.5	1150	1	2.13 (1.63, 2.77)	<0.0001
≥11.6	1130	1	2.02 (1.60, 2.55)	<0.0001
Hematocrit, %				
≤25.2	1117	1	1.87 (1.40, 2.49)	<0.0001
25.3–30.2	1131	1	2.73 (2.10, 3.55)	<0.0001
≥30.3	1133	1	2.14 (1.66, 2.75)	<0.0001
Hemoglobin, g/dL				
≤8.4	1066	1	1.98 (1.46, 2.67)	<0.0001
8.5–10.1	1166	1	2.34 (1.81, 3.02)	<0.0001
≥ 10.2	1149	1	2.31 (1.79, 2.99)	<0.0001
Platelet count, $10^9/L$				
≤120	1126	1	2.18 (1.69, 2.81)	<0.0001
121–233	1125	1	2.33 (1.78, 3.06)	<0.0001
≥234	1130	1	1.79 (1.39, 2.31)	<0.0001
BUN, mg/dL				
≤17	1002	1	2.03 (1.44, 2.87)	<0.0001
18–33	1248	1	1.88 (1.48, 2.41)	<0.0001
≥34	1131	1	1.97 (1.57, 2.46)	<0.0001
Serum creatinine, mg/dL				
≤0.6	828	1	1.83 (1.33, 2.52)	0.0002
0.7–1.1	1419	1	2.37 (1.85, 3.04)	<0.0001
≥1.2	1134	1	1.97 (1.57, 2.47)	<0.0001
Anion gap				
≤10	753	1	2.43 (1.60, 3.69)	<0.0001
11–13	1333	1	2.02 (1.57, 2.59)	<0.0001
≥14	1291	1	2.37 (1.93, 2.91)	<0.0001
Serum bicarbonate, mmol/L				
≤19	1036	1	2.16 (1.66, 2.80)	<0.0001
20–23	1136	1	1.72 (1.32, 2.24)	<0.0001
≥24	1208	1	2.17 (1.68, 2.81)	<0.0001
Direct bilirubin, μmol/L				
≤0.4	814	1	2.63 (1.95, 3.55)	<0.0001
0.5–1.1	1094	1	1.99 (1.53, 2.57)	<0.0001
≥1.2	976	1	1.62 (1.23, 2.13)	0.0006
Serum chloride, mmol/L				
≤99	1102	1	1.96 (1.58, 2.44)	<0.0001
100–104	1145	1	2.32 (1.76, 3.05)	<0.0001

TABLE 4 (Continued)

		RA Ratio		
	N	<5.51	≥5.51	*p value*
≥105	1134	1	2.66 (1.96, 3.60)	<0.0001
Serum glucose, mg/dL (min)				
≤94	1126	1	1.99 (1.54, 2.58)	<0.0001
95–117	1089	1	2.15 (1.63, 2.82)	<0.0001
≥118	1166	1	2.29 (1.80, 2.92)	<0.0001
Serum potassium, mmol/L				
≤3.4	941	1	1.94 (1.45, 2.59)	<0.0001
3.5–3.9	1158	1	1.97 (1.52, 2.56)	<0.0001
≥4.0	1282	1	2.48 (1.97, 3.12)	<0.0001
Serum sodium, mmol/L				
≤133	947	1	1.73 (1.34, 2.23)	<0.0001
134–137	1170	1	2.07 (1.58, 2.70)	<0.0001
≥138	1264	1	2.50 (1.95, 3.21)	<0.0001

Note: HRs (95% CIs) were derived from Cox proportional hazards regression models. Covariates were adjusted as in model 1 (Table 2).

showed that the β (95% CIs) for the length of stay 1.08 (0.67, 1.50) 1.08 (0.67, 1.50), and 0.67 (0.23, 1.12) across the three models, respectively (all $p < 0.001$). Similar results were obtained in the tertile groups.

3.3 | Subgroup analyses

Results from subgroup analyses are illustrated in Table 4. Summarily, we found no statistically significant association among factors in cancer patients.

3.4 | Propensity score matching

Next, we performed propensity score matching to assess the relationship between RA ratio and cancer prognosis. Results are outlined in Table 5. We found no statistically significant differences among RA ratios of patients at baseline (Table 5). On the other hand, results from Cox regression analysis revealed that a high RA ratio was independently correlated to 30 days mortality (HR =1.33; 95% CI, 1.04–1.70; $p = 0.0247$).

4 | DISCUSSION

Systemic inflammation plays an important role in cancer progression.[28,29] Here, we provide the first report describing the RA ratio as an independent risk factor of all-cause mortality in cancer patients with cancer. RDW is a classical indicator used to evaluate the size of circulating erythrocytes and assess the size variability, mainly in hematological, infectious, and cardiovascular diseases.[30] Although RDW significance in the early diagnosis of tumors has been revealed in recent years, its ability as a novel biomarker in early screening and prognostic evaluation remains unclear. RDW-coefficient of variation is an independent indicator of colorectal cancer prognosis that can efficiently predict adverse recurrence and poor survival outcomes when combined with carcinoma embryonic antigen. Some studies have shown that high RDW may result from the overproduction of cytokines, such as TNF-a and IL-6, in the tumor microenvironment.[31] However, whether it is caused by systemic inflammatory response or poor chemotherapeutic effects remains unknown, necessitating further clarification. Elevated RDW, due to chronic inflammation, has been closely associated with erythrocyte deficiency, which is a part of the natural aging process in patients with cancer. In addition, elevated RDW in patients with cancer can result in anemia and poor nutrition status.

Albumin, a product of liver parenchymal cells that constitutes 40%–60% of the total plasma proteins,[32] is abundant in plasma where it is strongly associated with the nutritional status of the body. Previous studies have associated persistent systemic inflammatory responses with reduced albumin concentration in patients with advanced lung cancer or gastrointestinal tumors. In addition, inflammatory responses are reportedly stronger in youngers than middle-aged and elderly patients. Notably, the occurrence of inflammation in the tumor microenvironment may not only initiate tumor development but also promote its progression.

The RA ratio may be a superior tool to other single identified markers in evaluating inflammatory response. In addition, it can serve as a prognostic marker owing to its ability to reflect tumor activities, thus can be used to identify high-risk patients and as a therapeutic target to alleviate tumor progression. Since the RA ratio is rapidly and easily evaluated using laboratory examinations, it can function as a simple but relatively reliable index for the stratification of cancer patients at risk, even before ICU admission. To the best of our knowledge, this is the first report describing the relationship between the RA ratio and

TABLE 5 Characteristics of the study population after propensity score matching

Characteristics	RA Ratio		*p* value
	<5.51	≥5.51	
N	555	555	
Age, years	65.70 ± 14.35	66.37 ± 13.69	0.4230
Sex, *n* (%)			0.8034
Female	207 (37.3)	202 (36.4)	
Male	348 (62.7)	353 (63.6)	
Vital signs			
SBP, mmHg	116.40 ± 16.75	115.73 ± 17.26	0.5560
DBP, mmHg	61.17 ± 10.39	60.79 ± 11.27	0.5560
MAP, mmHg	77.08 ± 11.12	76.72 ± 11.89	0.6031
Heart rate, beats/min	91.53 ± 16.32	91.52 ± 16.39	0.9963
SpO_2, %	97.07 ± 2.28	96.99 ± 2.51	0.5605
Laboratory parameters			
RA	4.65 ± 0.61	7.01 ± 1.47	<0.001
RDW, %	15.32 ± 1.75	17.39 ± 2.51	<0.001
Albumin, g/dL	3.34 ± 0.49	2.54 ± 0.46	<0.001
WBC count, 10^9/L	11.56 ± 18.80	11.85 ± 14.16	0.7256
Hemoglobin, g/dl	9.21 ± 1.76	9.25 ± 1.70	0.7552
Hematocrit, %	27.42 ± 5.44	27.51 ± 5.26	0.7791
Platelet, 10^9/L	192.11 ± 154.68	189.99 ± 149.62	0.8162
Anion gap, mg/dl	13.25 ± 3.87	12.91 ± 4.08	0.1579
Bicarbonate, mg/dl	20.96 ± 4.89	21.11 ± 5.35	0.4208
Glucose, mmol/L	144.37 ± 46.57	143.92 ± 58.28	0.8855
Blood lactic acid, mmol/L	1.85 ± 1.43	1.95 ± 1.50	0.2435
Serum creatinine, mg/dl	1.39 ± 1.22	1.39 ± 1.54	0.9588
Serum urea nitrogen, mg/dl	28.49 ± 24.27	28.98 ± 21.83	0.7256
Serum sodium, mg/dl	135.58 ± 5.49	135.58 ± 5.39	0.9340
Serum potassium, mg/dl	3.77 ± 0.60	3.77 ± 0.61	0.8741
Severity of illness			
SOFA score	5.72 ± 3.34	5.89 ± 3.44	0.4208
Comorbidities			
CHF, *n* (%)	89 (16)	90 (16.2)	1.0000
CAD, *n* (%)	96 (17.3)	95 (17.1)	1.0000
Renal failure, *n* (%)	86 (15.5)	86 (15.5)	1.0000
Liver disease, *n* (%)	82 (14.8)	75 (13.5)	0.6053
Mortality, *n* (%)			
30 days	113 (20.4)	144 (25.9)	0.0328
90 days	163 (29.4)	222 (40)	0.0003
1 year	228 (41.1)	287 (51.7)	0.0005
Length of stay in ICU	4.28 ± 4.84	5.02 ± 7.09	0.0420

Abbreviations: DBP—diastolic blood pressure; MAP—mean arterial pressure; RA—red blood cell distribution width-to-albumin; RDW—red cell distribution width; SBP—systolic blood pressure; SOFA—sequential organ failure assessment; WBC—white blood cell.

cancer survival outcomes. Notably, we used a large sample size, which increased the reliability of our findings.

This study had several limitations. Firstly, being a single-center retrospective study, it may have been affected by selection bias, which potentially affected the accuracy of our results. Therefore, multicenter studies are needed to validate these findings. Secondly, we did not have a dynamic RA ratio in this study, and RDW was evaluated after ICU admission, which may have caused inevitable bias. Furthermore, the inclusion of more significant variables increases the predictive accuracy of a model. However, this study did not include some variables owing to missing data, which may have compromised model accuracy.

5 | CONCLUSION

In summary, we provide the first evidence showing that increased RA is an independent predictor of increased all-cause mortality in cancer patients. Additional prospective cohort studies are required to validate our findings.

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CONFLICTS OF INTEREST

None.

DATA AVAILABILITY STATEMENT

All the data used to support this study are available from the corresponding author upon request.

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