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ORIGINAL RESEARCH

The Red Blood Cell Distribution Width to Albumin Ratio Is Associated with in Hospital Mortality and Adverse Outcome in Elderly Chinese Patients with Gastrointestinal Bleeding

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Background: Gastrointestinal bleeding (GIB) in elderly patients is a common and life-threatening condition, often complicated by comorbidities. The ratio of red blood cell distribution width to albumin (RAR) has recently been proposed as a prognostic marker in various diseases, but its role in predicting adverse outcomes in GIB patients remains unclear.

Methods: A total of 51,824 aged 65 years or older patients were initially screened for inclusion in the study. After excluding those lost to follow-up, with missing vital information during the screening period (n = 50,423), 1401 hospitalized patients with GIB in Beijing Hospital (2013–2019) were included. Restricted cubic spline modeling and logistic regression analyses assessed the relationships between RAR, adverse outcomes, and in hospital mortality.

Results: Among the 1, 401 patients, 648 experienced adverse outcomes, and 427 patients died during hospitalization. Higher RAR was significantly associated with an increased risk of both in-hospital mortality and adverse outcomes, even after adjusting for age, sex, education level, body mass index (BMI), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), cancer, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), white blood cell count (WBC), estimated glomerular filtration rate (eGFR), hemoglobin, heart failure, blood urea nitrogen (BUN), and heart rate.

Conclusion: RAR is a novel and independent predictor of mortality and adverse outcomes in elderly patients with GIB. Its simplicity and cost-effectiveness make it a valuable tool for identifying high-risk patients. Further studies in larger, multicenter cohorts are needed to confirm these findings and evaluate the clinical benefits of RAR-based interventions.

Keywords: gastrointestinal bleeding, elderly, RAR, mortality, adverse outcomes

Introduction

With the progression of population aging, it is estimated that by 2050, individuals aged 65 years and older will constitute 26% of China's total population.[1] Among the elderly, gastrointestinal bleeding (GIB) is a common and life-threatening condition. Compared with younger patients, the impact of GIB in older adults extends beyond the primary disease to include the significant influence of comorbidities such as cardiovascular and cerebrovascular diseases, chronic pulmonary conditions, and mental health disorders.[2] Moreover, older adults often experience issues like polypharmacy, the need for surgical procedures, disabilities, and diminished physiological capacity, which collectively heighten their susceptibility to negative outcomes, such as mortality, ICU admission, and other serious complications.[3]

Platelet count and red blood cell distribution width (RDW) offer valuable information regarding hemostatic function and the variability in red blood cell size in peripheral blood. Platelets are critical for clot formation, immune defense, and

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tissue repair.[4,5] RDW indicates the variation in red blood cell volume, and several diseases can affect red blood cell production or survival, leading to an increase in RDW.[6,7] Human serum albumin, the most abundant plasma protein, serves as a key marker for assessing inflammation and nutritional status.[8] Many studies have demonstrated a positive correlation between RDW and both age and poor prognosis,[9,10] whereas albumin levels are negatively correlated with age. Both markers play significant roles in the aging process.[11,12]

Given their roles in inflammation, oxidative stress, and nutrition, RDW and albumin are considered potential biomarkers for evaluating organ function.[13,14] Since they reflect these pathological processes from different angles, combining both may yield more informative insights than using them independently. Recently, the ratio of RDW to albumin (RAR) has been proposed as an indicator of adverse outcomes in various diseases, including acute myocardial infarction, diabetes, and stroke.[15–17] However, the association between RAR and mortality or adverse outcomes in patients with gastrointestinal bleeding still remains unclear.

The objective of this study was to investigate the association between the RAR and adverse outcomes as well as mortality in patients with GIB. Adverse outcomes were defined as the occurrence of any of the following events during hospitalization: in-hospital death, the requirement for one or more blood transfusions, or transfer to the intensive care unit (ICU). Additionally, the study aimed to evaluate whether RAR could serve as an additional predictive factor, potentially offering valuable insights for identifying high-risk GIB elderly patients with poor prognosis.

Materials and Methods

Study Design and Participants

The study was a retrospective cohort analysis conducted on patients aged 65 years and older who received care at Beijing Hospital, China, between July 2013 and September 2019. Participants were excluded from the analysis if they had experienced two or more hospitalizations, had hospital stays of less than one day or more than 66 days, had missing data on RDW, albumin or other covariates, or lacked a diagnosis of gastrointestinal hemorrhage or bleeding (Figure 1). When hospitalized, any patient who presented with hematemesis, melena, or was identified with gastrointestinal bleeding based on endoscopic or imaging findings—such as upper or lower gastrointestinal bleeding confirmed by gastroscopy, colonoscopy, or other radiologic examinations, including capsule endoscopy suggesting small bowel bleeding during hospitalization—was diagnosed with gastrointestinal hemorrhage or bleeding.

Study Outcome and Definitions

The duration of hospital stay was calculated as the number of days between the admission and discharge dates. Hospital charges encompassed costs related to nursing care, medications, laboratory tests, imaging studies (eg, CT or MRI), surgical procedures, and blood transfusions when applicable. Mortality status during hospitalization was determined through a review of hospital records. Adverse outcomes were defined as previously mentioned.

Baseline Assessment

Demographic factors included age, sex, body mass index (BMI), and educational attainment. Clinical variables encompassed diabetes mellitus status, hypertension status, estimated glomerular filtration rate (eGFR), liver function tests, complete blood count, lipids and glucose levels. The RAR was calculated as RDW divided by albumin. Hypertension was defined as self-reported hypertension, a systolic blood pressure (SBP) of $\geq$ 140 mmHg, a diastolic blood pressure (DBP) of $\geq$ 90 mmHg, or the use of antihypertensive medications.[18] Educational levels were categorized into three groups: less than high school, high school, and more than high school. Additionally, stroke, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), diabetes and cancer were documented based on the participants' medical history. All laboratory values, including albumin, cholesterol, and other relevant biomarkers, were obtained under fasting conditions on the morning following hospital admission. Blood pressure measurements and medical history, such as a history of stroke or heart failure, were recorded at the time of admission.

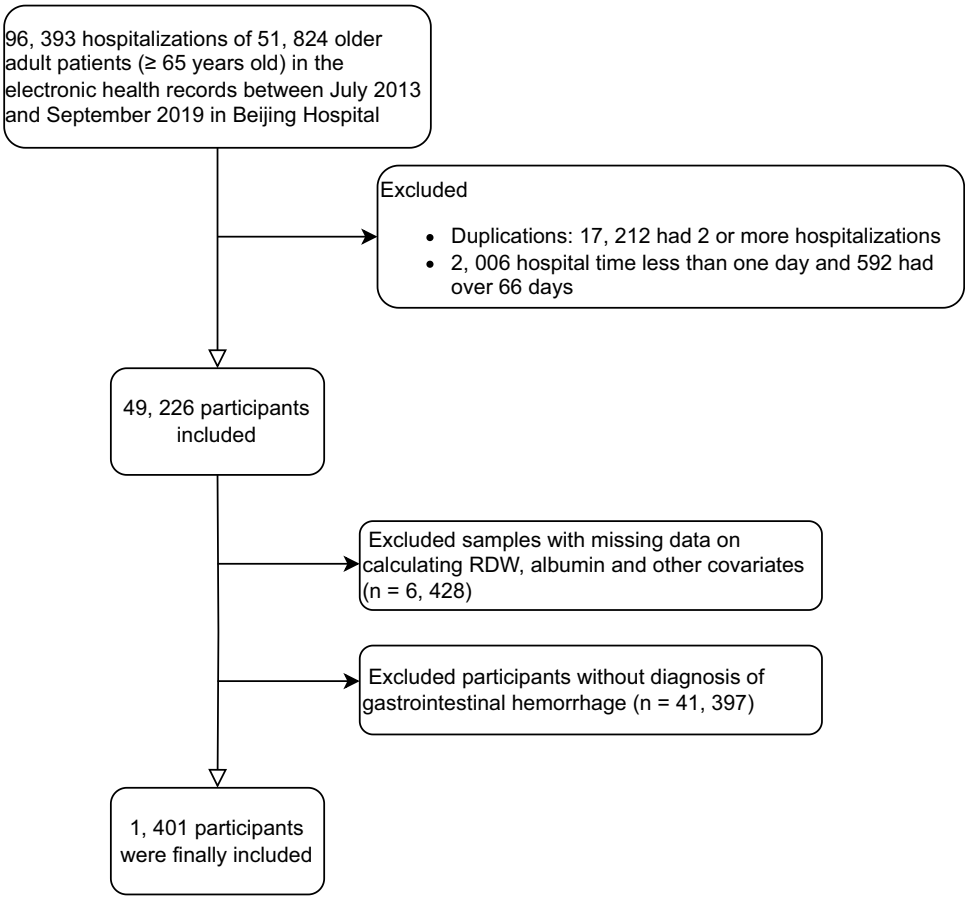

Figure 1 Flow chart for inclusion and exclusion of the study population.

Statistical Analysis

The baseline characteristics of participants were summarized and compared between those who experienced adverse outcomes and those who did not. Continuous variables were expressed as mean (±SD) and compared using either a *t*-test or Wilcoxon rank-sum test, based on the outcome of the Kolmogorov–Smirnov normality test. Categorical variables were presented as frequency (percentage) and compared using the Chi-square test.

The RAR is calculated using the following formula: [RDW (%) / serum albumin (g/dL)]. The potential nonlinear associations between the RAR and adverse outcomes, as well as in hospital mortality, were examined using restricted cubic spline (RCS) curves. These curves were positioned at specific percentiles (10%, 25%, 75%, and 90%) of the RAR distribution. Multivariable-adjusted logistic regression analyses were performed to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between RAR and both adverse outcomes and in hospital mortality. To prevent over-adjustment and maximize the utility of the available data, two models were developed. Model 1 adjusted for age, sex, education, BMI, CKD, COPD and cancer, while Model 2 included total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), WBC, eGFR, hemoglobin, heart failure, BUN and heart rate in addition to the adjustments in Model 1.

A two-sided $P< 0.05$ was considered statistically significant. All analyses were performed using SPSS version 26.0 (IBM Corp, Armonk, NY) and R (version 4.3.2).[19,20]

Results

Study Participants and Baseline Characteristics

In the final cohort, 1401 adults were included, of whom 648 experienced adverse outcomes (Table 1). The mean age of participants was 77.99 ± 7.34 years, with males accounting for 55.7% of the sample. The average RDW, albumin, and

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Table 1 Baseline Characteristics of Participants

	Overall (n=1, 401)	No Adverse Outcome (n=753)	Adverse Outcome (n=648)	P value
Age (years)	77.99 (7.34)	76.36 (7.27)	79.89 (6.96)	<0.001
Sex (Male %)	781 (55.7)	390 (51.8)	391 (60.3)	0.002
BMI (kg/m^2)	22.72 (3.43)	23.36 (3.48)	21.98 (3.23)	<0.001
WBC (10^9/L)	8.81 (10.50)	6.96 (3.17)	10.97 (14.77)	<0.001
Hemoglobin (g/L)	105.08 (26.51)	111.17 (25.00)	98.00 (26.46)	<0.001
Education (%)				0.541
Less Than High School	717 (52.0)	396 (53.2)	321 (50.7)	
College	586 (42.5)	312 (41.9)	274 (43.3)	
High School	75 (5.4)	37 (5.0)	38 (6.0)	
Total Bilirubin (umol/L)	15.00 (29.88)	11.47 (8.62)	19.10 (42.56)	<0.001
Fasting Glucose (mmol/L)	6.99 (3.47)	6.40 (2.51)	7.67 (4.24)	<0.001
TC (mmol/L)	3.70 (1.08)	3.92 (1.00)	3.39 (1.11)	<0.001
TG (mmol/L)	1.32 (1.00)	1.29 (0.74)	1.38 (1.29)	0.138
HDL (mmol/L)	0.96 (0.35)	1.05 (0.32)	0.82 (0.35)	<0.001
LDL (mmol/L)	2.21 (0.87)	2.37 (0.83)	1.99 (0.88)	<0.001
BUN (mmol/L)	9.33 (6.95)	7.54 (4.63)	11.42 (8.46)	<0.001
eGFR (mL/min/1.73m^2)	91.68 (48.24)	95.21 (39.65)	87.57 (56.35)	0.003
RDW	14.71 (2.63)	13.95 (2.13)	15.60 (2.86)	<0.001
Albumin (g/dL)	3.47 (0.54)	3.70 (0.43)	3.21 (0.54)	<0.001
RAR	4.40 (1.36)	3.83 (0.84)	5.07 (1.54)	<0.001
Heart rate (per min)	84.63 (20.04)	79.37 (14.07)	90.75 (23.87)	<0.001
Hypertension (%)	852 (60.8)	470 (62.4)	382 (59.0)	0.204
SBP (mmHg)	134.42 (22.24)	138.02 (19.76)	130.23 (24.16)	<0.001
DBP (mmHg)	72.05 (13.15)	73.81 (12.25)	70.01 (13.86)	<0.001
Heart Failure (%)	478 (34.1)	167 (22.2)	311 (48.0)	<0.001
Stroke (%)	371 (26.5)	198 (26.3)	173 (26.7)	0.913
CKD (%)	287 (20.5)	85 (11.3)	202 (31.2)	<0.001
COPD (%)	99 (7.1)	36 (4.8)	63 (9.7)	<0.001
Diabetes Mellitus (%)	428 (30.5)	220 (29.2)	208 (32.1)	0.267
Cancer (%)	359 (25.6)	112 (14.9)	247 (38.1)	<0.001
Syncope (%)	9 (0.6)	6 (0.8)	3 (0.5)	0.657
Length-of stay (days)	19.82 (14.69)	14.92 (10.61)	25.51 (16.60)	<0.001
Hospitalization Charges (RMB)	62179.90 (66,090.26)	33,375.95 (34,899.87)	95,651.16 (77,124.17)	<0.001

Abbreviations: BMI, Body mass index; WBC, White blood cell; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; RDW, red blood cell distribution width; RAR, red blood cell distribution width to albumin ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease.

RAR were 14.71 ± 2.63, 3.47 ± 0.54, and 4.40 ± 1.36, respectively. In the adverse outcome group, a distinct pattern emerged: this group was characterized by a higher proportion of older individuals and males, lower BMI and hemoglobin, and elevated WBC counts. Additionally, this group exhibited increased levels of bilirubin, blood glucose, and lipids, along with reduced eGFR and higher BUN, RAR and heart rate. The prevalence of chronic conditions, including CKD, COPD, heart failure and cancer, was significantly higher. Furthermore, these individuals had elevated blood pressure, longer hospital stays, and higher rates of hospital discharge.

Associations between RAR, Adverse Outcomes, and in Hospital Mortality

Among the total participants, 648 individuals (46.25%) experienced adverse outcomes, and 427 individuals (30.48%) died. The relationship between the RAR, adverse outcomes, and in hospital mortality was further analyzed using RCS curves, as shown in Figure 2A and B. The RCS analysis revealed that RAR, treated as a continuous variable, was significantly associated with an increased adjusted risk of in hospital mortality (*P overall = 0.0335; P non-linear =*

0.348). Additionally, a significant linear relationship was observed between RAR and adverse outcomes (*P overall* < *0.001; P non-linear* = *0.542*). Notably, a turning point was observed in both Figure 2A and B, where the RAR reached 4.06.

A multivariable logistic regression analysis was conducted to investigate the association between RAR and the risks of adverse outcomes and mortality, as presented in Table 2 and Table 3. When analyzed as a continuous variable, RAR was significantly associated with an increased risk of adverse outcomes and mortality, even after adjusting for multiple covariates. When categorized into quartiles, in the unadjusted model (Model 0), participants in the Q2, Q3, and Q4 groups demonstrated significantly higher risks of mortality and adverse outcomes compared to the Q1 group ($P < 0.001$). This trend persisted in Model 1, which adjusted for age, sex, educational level, and the presence of CKD, COPD, and cancer. In Model 2, which included additional adjustments for total cholesterol, HDL, LDL, WBC, eGFR, hemoglobin, heart failure, BUN and heart rate, the Q4 group continued to exhibit significantly higher risks of mortality compared to the Q1 group ($P < 0.01$). Similarly, both the Q3 and Q4 groups showed significantly higher risks of adverse outcomes compared to the Q1 group ($P < 0.001$). These findings highlight the robust and independent association between RAR and adverse health outcomes, underscoring its predictive value in older adult populations.

Discussion

Our study investigated the association between the RAR and adverse outcomes, including in-hospital mortality, in elderly patients hospitalized with GIB. The findings revealed that patients with higher RAR experienced significantly increased risks of adverse outcomes and mortality compared to those with lower RAR. Notably, these associations persisted even after adjusting for demographic and clinical covariates, underscoring the independent predictive value of the RAR in this vulnerable population.

RDW reflects variations in the size of red blood cells and has been recognized as a novel prognostic marker in various pathophysiological conditions. A previous study suggested that RDW could serve as a reliable and independent indicator of gastrointestinal bleeding following heart surgery.[10] In addition, Hu et al[21] found that elevated RDW at admission may be associated with poor outcomes in both the short- and long-term in both adults and neonates. However, the mechanisms underlying the association between increased RDW and adverse outcomes still remain unclear, and several plausible explanations have been proposed. First, elevated RDW may reflect systemic inflammation, as it is correlated with common inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate.[22] Inflammatory cytokines like TNF-α and IL-6 inhibit erythropoietin production, resulting in the release of immature reticulocytes into peripheral circulation,[23] which leads to RDW increase. Second, oxidative stress is known to disrupt erythropoiesis and reduce the flexibility of erythrocyte membranes, resulting in a shortened lifespan of red blood cells and, as a consequence, an increase in RDW.[24]

Several studies have demonstrated that both higher RDW and lower serum albumin concentrations are associated with an increased risk of chronic diseases and mortality in the general population. Moreover, the RAR has been shown to have predictive value for disease prognosis. Yoo et al[25] conducted a study on adult patients in a medical ICU and found that the RAR was associated with 60-day mortality in patients with acute respiratory distress syndrome. Jeong et al[26] performed a prospective study on critically ill patients with pneumonia requiring invasive mechanical ventilation and found that a high RAR demonstrated comparable predictive accuracy for 28-day mortality to the lactate-to-albumin ratio. Furthermore, the RAR has been identified as a potential prognostic biomarker for predicting mortality in patients with diabetic retinopathy, stroke, and cancer.[16,27,28]

In our study, the RAR was also found to be a reliable prognostic biomarker, consistent with previous findings in diverse patient populations. For instance, Qiu et al[29] demonstrated that RAR was associated with hospital mortality in ICU patients with COPD. This further supports the role of RAR as an effective predictor of disease prognosis, which is similarly validated in our study involving elderly patients with gastrointestinal bleeding.

Although our findings offer meaningful insights, additional research is necessary to confirm the validity of RAR in larger, multicenter cohorts and assess its relevance in various healthcare environments. Furthermore, prospective studies are needed to explore the effects of RAR-based interventions on long-term outcomes in this patient population. Such efforts will be crucial in further defining the role of RAR in improving care for older adults with GIB, ultimately enhancing their prognosis and quality of life.

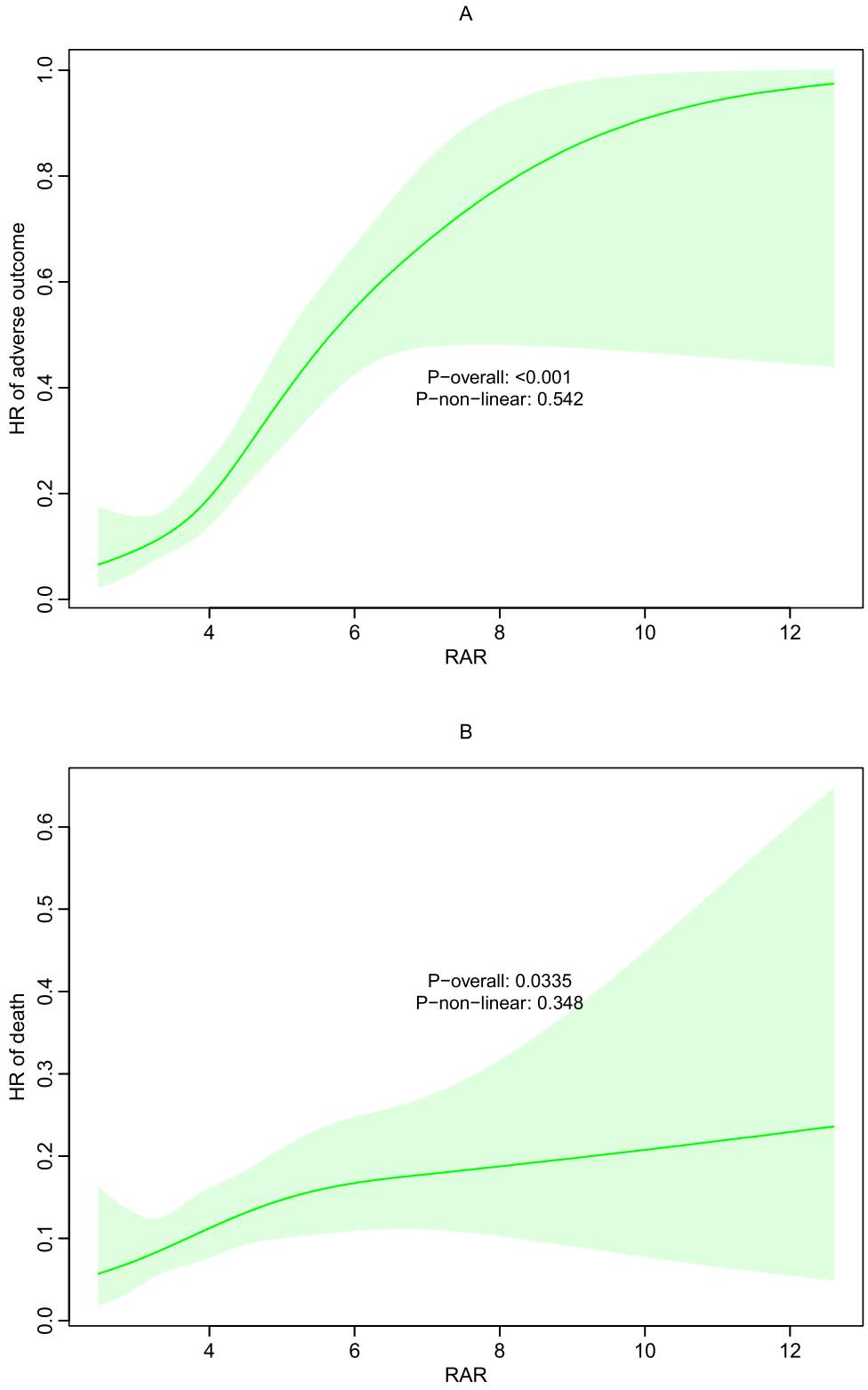

Figure 2 (**A**) Restricted cubic spline (RCS) for the association between RAR and the risks of adverse outcome in patients with gastrointestinal bleeding; (**B**) RCS for the association between RAR and the risks of in hospital death in patients with gastrointestinal bleeding.

Table 2 Adjusted Odds Ratio and 95% CI for the Associations Between RAR and in Hospital Mortality

RAR	Model 0 1.800 (1.629,1.990) ***	Model 1[a] 1.582 (1.423,1.759) ***	Model 2[b] 1.297 (1.080,1.558) **
Q1	Ref	Ref	Ref
Q2	3.001 (1.944, 4.634) ***	2.22 (1.394,3.536) ***	1.581 (0.858,2.915)
Q3	5.423 (3.567, 8.246) ***	3.262 (2.070,5.141) ***	1.511 (0.772,2.961)
Q4	10.627 (7.010,16.110) ***	5.931 (3.783,9.300) ***	2.803 (1.308,6.006) **

Notes: [a]Model 1 adjusted for age, sex, education, BMI, CKD, COPD and cancer. [b]Model 2 adjusted for age, sex, education, BMI, CKD, COPD, cancer, total cholesterol, HDL, LDL, WBC, eGFR, hemoglobin, heart failure, BUN and heart rate. ***P* < *0.01*, ****P* < *0.001*.

Table 3 Adjusted Odds Ratio and 95% CI for the Associations Between RAR and Adverse Outcome

RAR	Model 0 2.822 (2.468,3.226) ***	Model 1[a] 2.393 (2.081,2.751) ***	Model 2[b] 2.604 (2.004,3.384) ***
Q1	Ref	Ref	Ref
Q2	2.562 (1.791, 3.666) ***	1.900 (1.281, 2.816) ***	1.579 (0.907, 2.751)
Q3	6.441 (4.533, 9.154) ***	4.071 (2.759, 6.006) ***	3.099 (1.661, 5.784) ***
Q4	18.442 (12.594,27.005) ***	11.288 (7.468,17.061) ***	12.478 (5.856,26.587) ***

Notes: [a]Model 1 adjusted for age, sex, education, BMI, CKD, COPD and cancer. [b]Model 2 adjusted for age, sex, education, BMI, CKD, COPD, cancer, total cholesterol, HDL, LDL, WBC, eGFR, hemoglobin, heart failure, BUN and heart rate. ****P* < *0.001*.

Limitations

This study has several limitations. First, the data were collected from a single tertiary general hospital, which may limit the generalizability of our findings to other hospitals in China. To enhance external validation, multicenter studies with larger datasets and comprehensive follow-up information are needed. Second, follow-up data after discharge were not available, restricting our ability to evaluate the long-term predictive value of RAR for adverse events among elderly inpatients. Additionally, the absence of a linkage between hospital medical records and national death registries or medical records from other healthcare institutions poses a significant challenge for assessing long-term outcomes. Finally, due to incomplete documentation of certain clinical variables—such as liver disease history—pre-endoscopic risk scores (eg, Glasgow-Blatchford scores) could not be calculated in this study. We will strive to incorporate more comprehensive clinical assessments, including validated risk scores, in future research.

Conclusion

In our study, a high RAR emerged as a novel and significant predictor of death and adverse outcomes in hospitalized elderly patients with gastrointestinal hemorrhage, further emphasizing its potential as a valuable prognostic tool in managing older adult populations. These findings suggest that RAR could serve as a simple, reliable, and cost-effective indicator for identifying individuals at high risk of mortality in clinical settings.

Data Sharing Statement

Data would be available on reasonable request with Email to Fan Zhang (zfdobest@163.com).

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Clinical Research Ethics Committee of the Beijing Hospital, Beijing, China (2018BJYYEC-121-02) and individual consent for this retrospective analysis was waived. We declare that our study complies with ethical guidelines, ensures

patient data confidentiality, and that all data were anonymized or maintained with strict confidentiality. No private information, such as patient names or addresses, will be disclosed.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declared no conflicts of interest.

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