Received: August 5, 2025
Accepted: August 14, 2025

Acad Med J 2025;5(3):32-40
UDC:616.155.19:616.24-005.7-036.8
https://www.doi.org/10.53582/AMJ255332p
Original article

RED BLOOD CELL DISTRIBUTION WIDTH IN THE ASSESSMENT OF EARLY MORTALITY RISK IN PATIENTS WITH ACUTE PULMONARY EMBOLISM

Pocesta Bekim, Poposka Lidija, Vrajnko Elif, Konjanovski Tomislav, Boshevski Marijan, Georgievska-Ismail Ljubica

University Clinic for Cardiology, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia
e-mail: bekimpoc@yahoo.com

Abstract

Introduction: Pulmonary embolism (PE) is a life-threatening condition with variable clinical presentation and prognosis. Early identification of patients at increased risk of mortality remains a challenge, especially in intermediate-risk categories. Red blood cell distribution width (RDW), a routinely measured hematologic parameter, has emerged as a potential prognostic marker in various cardiovascular conditions.

Aim: To evaluate the predictive value of RDW for early (30-day) mortality in patients with acute PE.

Material and methods: This retrospective study included 58 consecutive patients with CTPA-confirmed acute PE treated at a tertiary cardiac center between 2023 and 2024. Patients were stratified into early mortality risk groups according to the 2019 ESC guidelines. RDW and other hematologic and biochemical parameters were recorded on admission. Correlation, logistic regression, and receiver operating characteristic (ROC) analyses were used to assess associations with 30-day mortality.

Results: Seven patients (12.1%) died within 30 days. RDW values were significantly higher among non-survivors with a moderate positive correlation with mortality (r=0.363, p=0,005). ROC analysis revealed an AUC of 0.771 for RDW in predicting early mortality, with an optimal cut-off of ≥14.05% (sensitivity 83.3%, specificity 59.6%). In logistic regression, RDW was an independent predictor of 30-day mortality (OR 1.637, 95% CI: 1.058-2.535; p= 0.027). Traditional clinical scores such as PESI and sPESI were not significantly associated with mortality.

Conclusion: RDW is an independent, easily obtainable predictor of early mortality in acute PE and may enhance risk stratification, particularly in intermediate-risk patients. Its integration into clinical assessment could improve early decision-making and patient management.

Keywords: pulmonary embolism, red blood cell distribution width, early mortality

Introduction

Pulmonary embolism (PE) is a common medical emergency that can significantly compromise patient health. The in-hospital mortality rate is estimated at 14%, while the 3-month mortality rate may reach 20%[1,2]. Timely diagnosis and appropriate therapy have reduced PE-related mortality in recent years[2]. One of the most important factors influencing treatment success is the early prediction of mortality risk upon admission.

The Pulmonary Embolism Severity Index (PESI) and its simplified version (sPESI) are frequently used to assess disease severity. In combination with the presence of hemodynamic

instability, right ventricular (RV) dysfunction, detected by transthoracic echocardiography (TTE) or computed tomography pulmonary angiography (CTPA), and elevated troponin levels, these scores help stratify the 30-day mortality risk into high, intermediate-high, intermediate–low, and low categories[2].

However, a patient's clinical condition may deteriorate rapidly, and initial risk assessments may not remain constant and the hemodynamic status may quickly change within hours. This is especially important in intermediate- and high-risk patients, who represent approximately one-third of all PE cases and in whom risk stratification remains challenging[2]. Thus, there is a need for additional biomarkers that can enhance early risk prediction - ideally those that are readily available and routinely assessed upon admission.

Red blood cell distribution width (RDW) is a standard parameter reported in complete blood counts. It reflects the heterogeneity in red blood cell size and morphology. RDW is inexpensive, rapidly obtainable, and automatically measured. Previous studies have linked elevated RDW with increased mortality in critically ill patients[3,4], including those with acute PE[5-8].

The aim of this study was to investigate the predictive value of RDW in early mortality in patients with acute PE.

Material and methods

Study population

The study retrospectively enrolled 58 consecutive patients who were diagnosed with acute PE during 2023 and 2024 and treated in Intensive care unit at the University Clinic for Cardiology. Adult patients (≥18 years) were eligible if PE was confirmed by CTPA, defined as the direct visualization of a thrombus on at least two projections, either as a filling defect or amputation of a pulmonary arterial branch[2].

Exclusion criteria were: death within 48 hours of admission, prior thrombolytic or anticoagulant therapy before laboratory testing, documented recent infection, blood transfusion or corticosteroid/immunosuppressive use within the preceding two weeks, advanced hepatic or renal disease (including dialysis), known hematologic disorders, and acute or chronic inflammatory diseases.

The study was approved by the Ethics Committee of the Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, N. Macedonia. Due to the retrospective design, informed consent was not obtained, but de-identified data were extracted from the hospital's electronic health records.

Methods

Collected data included demographics, comorbidities and risk factors for PE, vital signs on admission, diagnostic imaging methods (CTPA, TTE and lower extremity Doppler ultrasonography), blood test results (including RDW) at the time of PE diagnosis, PESI and sPESI scores and ESC 2019 risk classification for early mortality[2].

Complete blood counts, including RDW, were obtained on admission and processed in the hospital's central laboratory. The laboratory reference range for RDW was 10.8%–16.0%. Patients were managed according to current ESC guidelines[2], and follow-up was conducted through clinical visits for up to 30 days.

Statistical analysis

Data were presented as means ± standard deviations, medians (min-max) or percentages. Group comparisons for categorical variables were conducted using the Pearson Chi-square test. For continuous variables, either the Student's t-test or Mann-Whitney U test was used as appropriate. ANOVA with Bonferroni post-hoc correction was applied for

comparisons among four mortality risk groups (low, intermediate-low, intermediate-high, high). Correlations were assessed using Pearson and/or Spearman correlation coefficients. To evaluate the predictive value of RDW and other parameters for mortality, stepwise backward logistic regression was performed. Receiver operating characteristic (ROC) analysis was used to determine the discriminatory power of RDW and identify an optimal cut-off value for predicting mortality as well to test for sensitivity and specificity of the predictive model.

All statistical analyses were performed using SPSS software, version 25 (IBM Corp., Armonk, NY, USA). A p-value <0.05 was considered statistically significant.

Results

A total of 58 consecutive patients with confirmed acute pulmonary embolism (PE) by computed tomography pulmonary angiography (CTPA) were included. The mean age was 65.3 ± 12.2 years (range: 37-89), and 28 (48.3%) were female patients.

Baseline characteristics

Identified PE risk factors included: prior PE (8.6%), previous venous thromboembolism (15.5%), active cancer (17.2%), recent immobility (5.2%), surgery (10.3%), and fracture (5.2%). The most common presenting symptoms were dyspnea (58.6%), chest pain (36.8%), fatigue (41.4%), and suffocation sensation (36.2%). Lower-limb pain and edema were each reported in 8.6%. Mean systolic and diastolic blood pressure were 137.5 ± 24.8 mmHg and 86.7 ± 13.1 mmHg, respectively. Median heart rate was 104.9 ± 20.7 bpm, and oxygen saturation was 89.2 ± 8.5% (range: 62-98%).

Atrial fibrillation on ECG findings was detected in 15.5%, while RV dysfunction on echocardiography was present in 43.9% of all patients. Deep vein thrombosis (DVT) was detected in 35.0% of patients examined.

Median PESI and sPESI scores were 2.97 ± 1.2 and 0.8 ± 0.4, respectively. Mean hospital stay was 10.3 ± 4.2 days (range: 3-23 days).

Early mortality risk groups

Patients were classified per ESC 2019 early (in-hospital or 30 day) mortality risk stratification (2): low risk (n=11, 19.0%), intermediate-low (n=23, 39.7%), intermediate-high (n=19, 32.8%), and high risk (n=5, 8.6%).

Table 1. Demographic characteristics and vital signs according to the risk group

Variable	Low n=11	Intermediate-low n=23	Intermediate-high n=19	High n=5	*p*
Age (years)	64.45 11.48	64.39 13.75	67.00 10.31	65.40 15.48	0.912
m/f (n/%)	8/3/(72.7/27.3)	14/9/(60.9/39.1)	6/13/(31.6/68.4)	2/3/(40/60%)	0.108
HTN (n/%)	7/63.6	12/52.2	13/68.4	0	0.048
DM (n/%)	2/18.2	4/17.4	5/26.3	3/40.0	0.682
COPD (n/%)	2/18.2	2/8.7	2/10.5	1/20.0	0.808
HR (bpm)	94.82 20.62	100.83 20.52	112.26 18.76	117.8017.93	0.045
SBP (mmHg)	139.55 17.38	133.52 23.45	142.37 30.84	133.8022.52	0.692
DBP (mmHg)	89.98 7.35	84.13 9.76	90.37 18.40	79.40 8.47	0.233
SpO2 (%)	91.83 5.45	93.20 5.11	88.11 6.30	75.00 15.68	0.0001

high *vs*. low (p=0.004). high vs. intermediated-high (p=0.011). high vs. intermediated-low (p=0.0001). HTN=hypertention. DM=diabetes mellitus. COPD=chronic obstructive pulmonary disease. HR=heart rate. SBP=systolic blood pressure. DBP=diastolic blood pressure. SpO2=oxygen saturation

The main demographic characteristics and vital signs of all study groups (n=58) are shown in Table 1. There were no significant differences in age or sex between groups. Hypertension was more prevalent in the intermediate-high group versus the low-risk group (p =0.048). Heart

rate was significantly higher (p=0.045). and SpO_2 significantly lower (p<0.001) in the high-risk group.

Laboratory parameters across risk groups

As shown in Table 2. no significant differences were observed in red blood cell count. hemoglobin. hematocrit. lymphocytes. platelets or platelet/lymphocyte ratio (PLR). However. white blood cell count. neutrophils. and neutrophil/lymphocyte ratio (NLR) were significantly elevated in higher-risk groups (p=0.011. 0.014. and 0.034. respectively). RDW was highest in the high-risk group but did not reach statistical significance across groups (p=0.168).

Table 2. Hematologic biomarkers according to risk groups

Variable	Low n=11	Intermediate-low n=23	Intermediate-high n=19	High n=5	*p*
RBC (10^{12}/L)	4.50 0.53	4.61 0.61	4.57 0.71	4.43 0.91	0.931
Hb (g/L)	133.18 18.70	135.26 16.72	135.26 18.44	134.6039.17	0.993
Htc (%)	0.44 0.18	0.41 0.04	0.41 0.06	0.400.10	0.793
RDW (n/%)	13.62 1.70	14.73 2.78	14.21 1.21	16.122.43	0.168
WBC (10^3/L)	8.44 2.44	10.80 2.96	12.91 4.46	13.485.91	0.011
low vs. intermediate-high risk (p=0.014)					
NEUT (10^9/L)	9.79 13.90	7.65 2.78	10.80 4.40	10.664.73	0.014
intermediate-low vs. intermediate-high risk (p=0.014)					
LYMPH (10^9/L)	4.45 9.63	2.39 3.28	1.43 0.65	7.8014.11	0.165
NLR	4.26 3.02	5.68 3.95	9.77 7.23	8.547.47	0.034
low vs. intermediate-high risk (p=0.061)					
PLT (10^9/L)	227.00 80.45	228.74 90.93	248.47 156.56	264.6091.98	0.880
PLR	171.52 124.51	164.20 106.99	192.15 101.10	208.49 164.65	0.795
CRP (mg/L)	39.94 44.03	44.14 35.68	41.99 26.37	114.05 117.74	0.018
low vs. high risk (p=0.027). intermediate-low vs. high risk (p=0.022). intermediate-high vs. high risk (p=0.019)					
hsTnI (ng/ml)	27.29 59.92	147.16 210.05	262.12 371.77	348.79 580.00	0.0001
D-dimer (mol/L)	7113.14 9015.28	18464.33 18782.09	11002.42 13423.94	9522.27 15228.89	0.032
BUN (mmol/L)	7.87 4.41	6.66 2.23	10.86 6.52	7.24 4.10	0.035
intermediate-low vs. intermediate-high risk (p=0.028)					
Creatinine (mol/L)	96.71 33.62	94.57 23.85	105.54 31.54	125.31 83.29	0.332
eGFR (ml/min/1.73m^2)	72.64 20.91	72.52 21.13	56.74 20.50	56.20 33.38	0.061
aPTT (sec)	32.15 3.42	54.65 56.94	48.09 28.61	26.83 10.68	0.427
PT (sec)	14.04 8.20	11.97 0.99	13.55 3.74	13.08 4.39	0.631
TT (sec)	21.38 5.91	40.42 44.92	52.10 49.22	29.03 12.28	0.299

RBC=red blood cell count (erythrocyte). Hb=hemoglobin. Htc=hematocrit. RDW=red cell distribution width. WBC=white blood cells (leucocyte). NEUT=neutrophils. LYMPH =lymphocites. NLR=netrophil-lymphocite ratio. PLT=platelet count. PLR=platelet-lymphocite ratio. CRP=C-reactive protein. hsTnI=high sensitive troponin. BUN=blood urea nitrogen. aPTT=activated partial thromboplastin clotting time. PT=prothrombin time. TT=thrombin time

Troponin I. CRP. and D-dimer levels were significantly higher in high-risk groups (p< 0.001. 0.018. and 0.032. respectively). BUN was elevated in the intermediate-high group (p= 0.035). Although creatinine was highest and eGFR was lowest in the high-risk group. differences among risk groups were not statistically significant (p=0.332 and 0.061).

Coagulation markers (aPTT. PT. TT) tended to be shorter in the high-risk group. though not statistically significant (p value 0.427. 0.631. 0.299. respectively).

RDW showed a significant negative correlation with lymphocyte count (r= -0.305. p=0.020) and positive correlation with NLR (r=0.281. p=0.034). while no significant associations were found with other hematologic or inflammatory biomarkers.

30-Day mortality and predictive analysis

Seven patients (12.1%) died within 30 days; four of these deaths (6.9%) occurred during hospitalization.

Correlation analysis revealed that early mortality was significantly associated with: higher RDW (r=0.363. p=0.005) (Figure 1). lower lymphocyte count (r= -0.283. p=0.031). higher NLR (r=0.390. p=0.003) and PLR (r=0.404. p=0.002). higher BUN (r=0.328. p=0.012) and creatinine (r=0.432. p=0.001). and lower eGFR (r= -0.422. p=0.001). prior atrial fibrillation (r=0.324. p=0.013) and in-hospital clinical deterioration (r=0.521. p<0.001). Neither PESI nor sPESI scores were significantly correlated with early mortality.

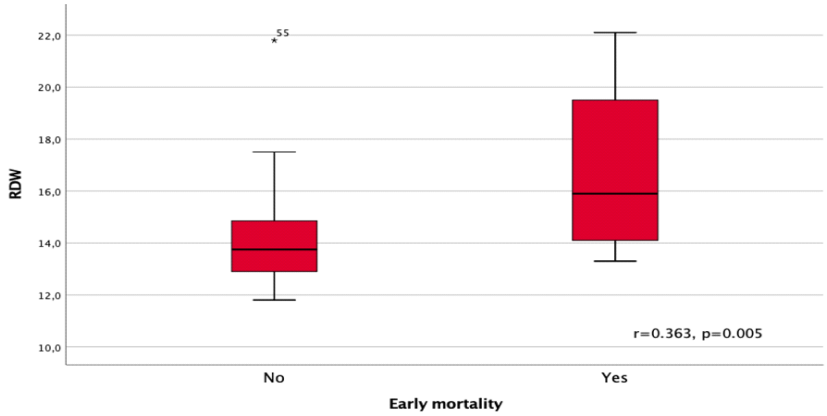


Fig. 1. Association between red cell distribution width (RDW) and early mortality in patients with acute pulmonary embolism.
Box plots show RDW values in patients who survived (no) and those who died (yes) within 30 days. A significantly higher RDW was observed in the mortality group (p=0.005). A moderate positive correlation between RDW and early mortality was found (r=0.363. p=0.005).

RDW as a mortality predictor

Receiver operating characteristic (ROC) analysis demonstrated that RDW had good discriminative power for predicting 30-day mortality. with an AUC of 0.771 (95% CI: 0.587-0.955; p=0.031). The optimal RDW cut-off value was ≥14.05%. yielding a sensitivity of 83.3% and specificity of 59.6% (Figure 2).

Logistic regression analysis (Table 3) of hematological variables significantly related with early mortality showed that higher RDW% (OR 1.637. 95% CI: 1.058–2.535; $p = 0.027$) was a significant independent predictor of early mortality. Higher NLR (OR 1.190. 95% CI: 0.992-1.427; p=0.061) and PLR (OR 1.008. 95% CI: 0.998-1.019; p=0.119) showed a trend toward significance but did not reach statistical thresholds.

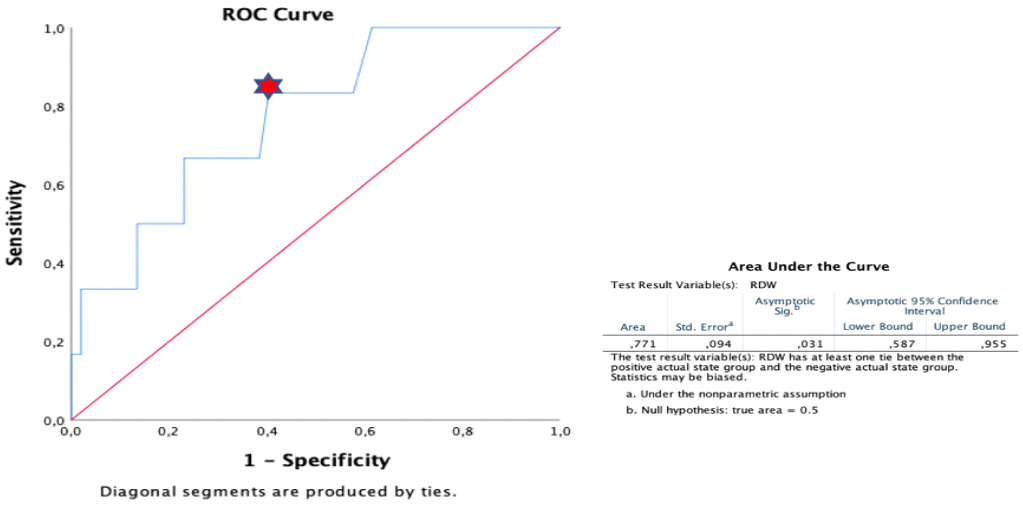


Fig. 2. Receiver Operating Characteristic (ROC) curve for red cell distribution width (RDW) in predicting 30-day mortality in patients with acute pulmonary embolism. The red star marks the optimal cutoff point based on the best trade-off between sensitivity and specificity.

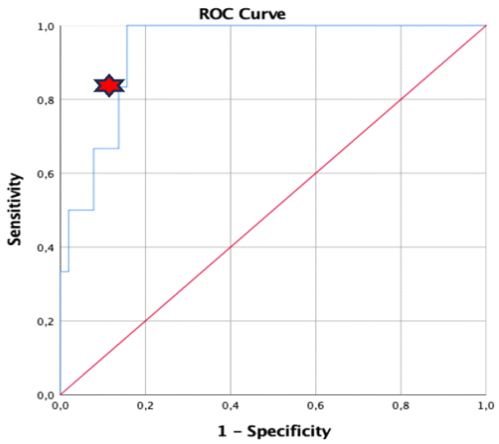
Table 3. Logistic regression analysis in order to identify independent predictors of early mortality

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	PLR	,011	,004	6,866	1	,009	1,011	1,003	1,020
	Constant	-4,760)	1,296	13,501	1	,000	,009		
Step 2[b]	RDW	,353	,180	3,850	1	,050	1,423	1,000	2,023
	PLR	,011	,005	5,116	1	,024	1,011	1,001	1,020
	Constant	-10,074)	3,280	9,432	1	,002	,000		
Step 3[c]	RDW	,493	,223	4,891	1	,027	1,637	1,058	2,535
	NLR	,174	,093	3,518	1	,061	1,190	,992	1,427
	PLR	,008	,005	2,425	1	,119	1,008	,998	1,019
	Constant	-13,713)	4,816	8,109	1	,004	,000		

a. Variable(s) entered on step 1: PLR.
b. Variable(s) entered on step 2: RDW.
c. Variable(s) entered on step 3: NLR.

However. the combined model demonstrated excellent discriminatory performance with an area under the curve (AUC) of 0.902. sensitivity of 85%. and specificity of 90%. indicating strong predictive ability for early mortality (Figure 3).



Area Under the Curve

Test Result Variable(s): Predicted probability

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
,935	,036	,001	,864	1,000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Fig. 3. Receiver Operating Characteristic (ROC) curve for the multivariable model including red cell distribution width (RDW). neutrophil-to-lymphocyte ratio (NLR). and platelet-to-lymphocyte ratio (PLR) in predicting 30-day mortality in patients with acute pulmonary embolism.
The red star marks the optimal cutoff point based on the best trade-off between sensitivity and specificity.

Discussion

In this retrospective study. red blood cell distribution width (RDW). a routine hematological parameter. was significantly associated with early (30-day) mortality in patients with acute pulmonary embolism (PE). RDW values were higher in non-survivors. and the variable remained an independent predictor in multivariable analysis. Receiver operating characteristic (ROC) analysis confirmed the prognostic accuracy of RDW. with an area under the curve (AUC) of 0.771 and an optimal cut-off of ≥14.05%. yielding 83.3% sensitivity and 59.6% specificity.

These findings support previous reports that elevated RDW is a marker of poor prognosis in patients with acute PE. Zorlu *et al.*[4] first demonstrated that admission RDW predicts early mortality in PE. with an AUC of 0.73. closely aligning with our results. Similar conclusions were reached in subsequent studies. including those by Oszu *et al.* [5]. Zhou *et al.*[8]. Kucuk *et al.*[9]. and Jurin *et al.*[10]. who noted that RDW improved the prognostic performance of the PESI score. Collectively. These data reinforce the growing evidence that RDW is a valuable. cost-effective biomarker for early risk stratification in PE.

The pathophysiological link between RDW and adverse outcomes in PE may be multifactorial. Elevated RDW reflects anisocytosis. which may arise from inflammation. oxidative stress. impaired erythropoiesis. and nutritional deficiencies-common features in acutely ill patients[3.6]. Inflammation may suppress erythropoietin production and alter red blood cell membrane deformability. contributing to a broader distribution of erythrocyte size. Our results support this. as RDW showed moderate correlations with established inflammatory markers such as lymphocyte count and neutrophil–lymphocyte ratio (NLR).

Interestingly. while PESI and sPESI scores are widely used to estimate early mortality in PE. they were not significantly associated with death in our cohort. This may be due to the limited sample size or the fact that PESI may underestimate risk in some intermediate-risk patients. particularly those with subclinical hemodynamic compromise. Our results are consistent with Jurin *et al.*[10]. who also found that RDW added incremental value to PESI-based risk stratification. Furthermore. Akgedik *et al.* [7] and Sanri *et al.* [11] noted that RDW correlates with both short-term mortality and PE severity scores.

Besides RDW. other parameters such as NLR. PLR. BUN. and creatinine were associated with early mortality. However. only RDW retained independent significance in multivariable analysis. further underscoring its utility as a robust prognostic biomarker. Notably. our combined model including RDW. NLR. and PLR achieved excellent discriminative capacity.

suggesting that RDW-based composite indices might improve prognostic accuracy beyond single markers.

Despite the promising findings. some limitations must be acknowledged. First. the retrospective. single-center design and relatively small sample size may limit generalizability. Second. although we excluded patients with known inflammatory or hematologic conditions. subclinical confounders affecting RDW could not be completely ruled out. Third. temporal changes in RDW during hospitalization were not assessed; serial measurements may offer additional prognostic insight. as suggested by Elshahaat *et al*.[12]. Finally. while RDW showed predictive power. it should be considered an adjunct. not a replacement. for comprehensive clinical assessment.

Conclusion

RDW is a readily available. inexpensive. and independent predictor of 30-day mortality in patients with acute pulmonary embolism. Its incorporation into initial risk assessment models. particularly for intermediate-risk patients. may improve early identification of individuals at higher risk for adverse outcomes. Future prospective. multicenter studies with larger cohorts are warranted to validate these findings and define the role of RDW in clinical decision-making.

Conflict of interest statement. None declared.

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