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Red blood cell distribution width is an independent predictor of mortality following amputation for diabetic foot

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Red blood cell distribution width (RDW) is a prognostic factor in various disorders. This study aimed to assess the prognostic value of RDW in patients undergoing amputation for diabetic foot. We retrospectively analyzed data on 415 patients who underwent diabetic foot amputation between January 2009 and January 2019. After establishing an optimal cutoff value of preoperative RDW for all-cause mortality, univariable and multivariable analyses with Cox proportional hazard model for survivorship and logistic regression analysis for prolonged hospital length of stay (> 30 days) were performed to identify significant prognostic factors. A preoperative RDW of 14.5% was the optimal cutoff value for predicting all-cause mortality. RDW ≥ 14.5% was significantly associated with increased all-cause mortality (hazard ratio, 2.55; 95% confidence interval [CI], 1.55–4.19; *P* < 0.001) on multivariable Cox proportional model analysis. Preoperative RDW ≥ 14.5% was also associated with a prolonged hospital length of stay after surgery (odds ratio, 2.17; 95% CI, 1.29–3.66; *P* = 0.004). Higher preoperative RDW was an independent predictive factor for increased all-cause mortality and prolonged hospital length of stay after diabetic foot amputation. These results suggest that RDW may be a useful laboratory parameter for risk stratification in patients undergoing amputation for diabetic foot.

Keywords Diabetic foot, Amputation, Red blood cell distribution width, Mortality, Hospital length of stay

The impact of the global burden of diabetes mellitus continues to increase at an alarming rate. The number of patients with diabetes worldwide is expected to increase by 51% from 463 million in 2019 to approximately 700 million by 2045[1]. The longer the duration of diabetes, the higher the risk of developing diabetic foot complications, including ulcers and gangrene[2]. Therefore, the explosive increase in diabetes will lead to a corresponding rise in the prevalence of diabetic foot. Diabetic foot ulcers failing to respond to conservative management eventually require amputation, an operation performed approximately every 30 s worldwide[3]. The 5-year survival rate of patients with diabetic foot is comparable to that of individuals with malignant tumors, highlighting the substantial medical and social burden of this condition[4].

As most patients with diabetes have multiple comorbidities or complications, their clinical assessment is difficult. Diabetic foot is the result of complex interactions between neuropathy, vasculopathy, and other underlying conditions. Thus, a multidisciplinary team approach is necessary for optimal patient management. It is also important to identify factors predictive of the prognosis of diabetic foot disease. These factors should not only easily and accurately detect risk, but they should also not be an economic burden to the patient.

Red blood cell distribution width (RDW), which represents the heterogeneity of erythrocyte volume, has been traditionally used in determining the cause of anemia[5]. Recently, RDW has emerged as a useful prognostic factor

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in various human disorders[5]. The clinical usefulness of RDW as a prognostic marker has been demonstrated in cardiovascular disease[6], cancer[7,8], kidney disease[9,10], and diabetes[11,12]. Several recent studies evaluated the predictive value of RDW as a prognostic factor in patients with diabetic foot ulcers[13,14]. However, the findings of these studies varied, and the clinical usefulness of RDW for predicting mortality and hospital length of stay (LOS) after diabetic foot amputation has not been established. The objective of this study was to investigate the prognostic value of preoperative RDW in patients undergoing amputation for diabetic foot. We hypothesized that RDW would be an independent predictor of all-cause mortality and prolonged hospital length of LOS after diabetic foot amputation.

Material and methods

Patients and study design

This study was performed according to the Declaration of Helsinki and was approved by institutional review board of Severance Hospital, which waived the requirement for informed consent because of its retrospective nature (approval number 4-2024-0629). Between January 2009 and January 2019, 444 consecutive patients with diabetes mellitus underwent lower extremity amputation (LEA) at our institution. LEA was indicated for persistent wet gangrene despite aggressive conservative treatment, painful dry gangrene combined with peripheral artery disease, osteomyelitis, and failed reconstruction of Charcot neuroarthropathy. We excluded 29 patients with traumatic LEA, soft tissue malignant tumors, or LEA in the previous 12 months (to reduce carryover effects). Consequently, 415 patients were included in this study. Figure 1 is a flowchart depicting patient participation.

Preoperative evaluation

Electronic medical records and databases at our institution were retrospectively reviewed for all eligible patients. We collected demographic data, including age, sex, and body mass index (BMI), at the time of LEA. BMI was classified as normal or obese based on a cutoff value of 25 kg/m^2. Before surgery, all patients underwent comprehensive evaluation to confirm the indication for surgery and the appropriateness of surgery based on their comorbidities. Preoperative assessment including laboratory tests, chest radiography, electrocardiography, and further evaluation at the discretion of the clinicians. The following preoperative laboratory data were collected: hemoglobin (g/dL), RDW (%), white blood cell ($\times 10^3/\mu L$) count, lymphocyte count ($\times 10^3/\mu L$), erythrocyte sedimentation rate (mm/h), c-reactive protein (mg/L), glycated hemoglobin (HbA1c; %), serum albumin (g/dL), and estimated glomerular filtration rate (eGFR; mL/min/1.73 m^2). eGFR was determined using the modification of diet in renal disease equation. If more than one result was available within 60 days preoperatively, the result closest to the date of surgery was used. Renal function was classified according to the eGFR and need for dialysis: normal, eGFR > 60 mL/min/1.73 m^2; chronic kidney disease, eGFR > 15 and < 60 mL/min/1.73 m^2; and end-stage renal disease (ESRD), eGFR < 15 mL/min/1.73 m^2 and requiring dialysis.

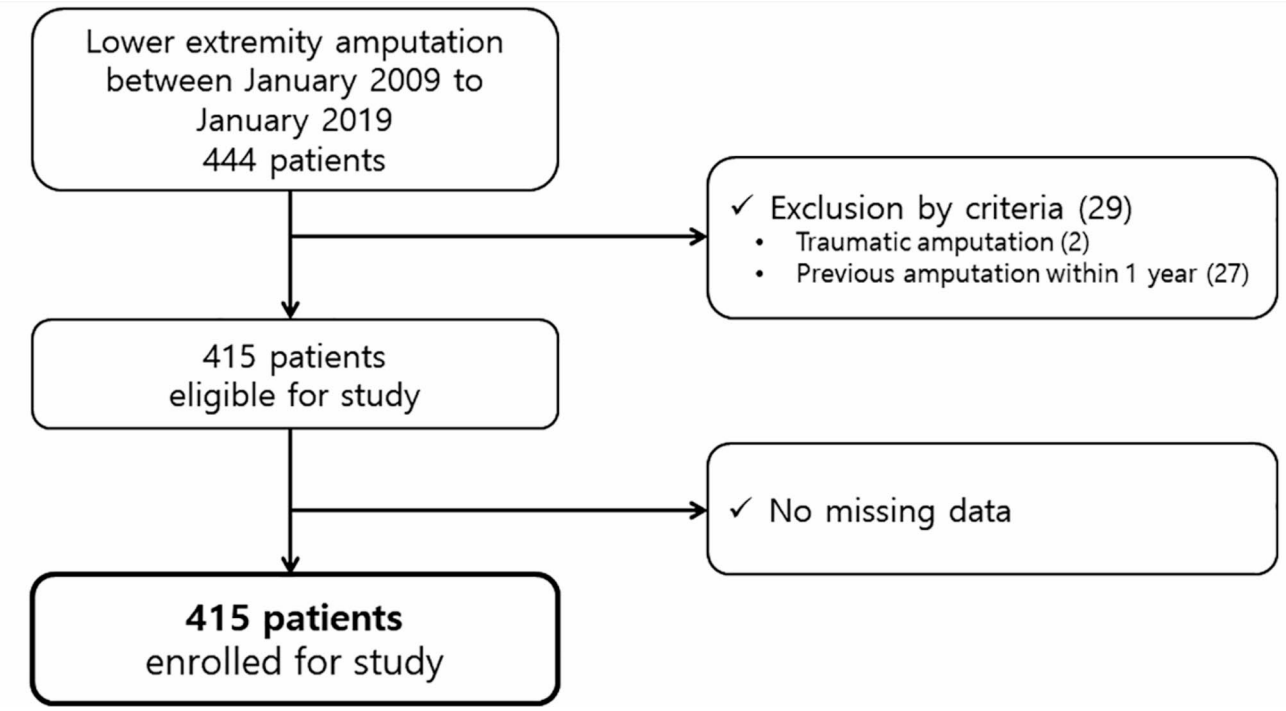

Fig. 1. Flowchart of patient participation in the study.

Amputation procedure, postoperative management, and discharge

All LEAs were performed under general, spinal, or regional anesthesia. The final amputation level was a balance between maintaining the greatest residual limb length and removing all nonviable or infected tissue and securing sufficient soft tissue coverage. Amputations above the level of the ankle joint were considered major amputations, while those below the ankle joint were considered minor amputations. After the amputation, the stump wound was managed with daily sterile compression dressing changes. Discharge planning began when wound healing was stable and there was no evidence of stump infection. The timing of hospital discharge was ultimately determined using a multidisciplinary team approach, including consultation with each clinician on the team.

Primary and secondary endpoints

The primary study endpoint was mortality. Duration of survival was based on the date of last visit to our institution, and death was confirmed by review of electronic medical records. The secondary endpoint was prolonged LOS, defined as > 30 days after amputation. LOS was calculated from the day of amputation to the day of hospital discharge. If death occurred during the hospital stay after amputation within 30 days, they were excluded from the LOS analysis.

Statistical analysis

Patient characteristics and clinical data are presented as mean ± standard deviation or count (percentage). To obtain the optimal cutoff value of RDW, we used the maximally selected rank statistics method for all-cause mortality and receiver operating characteristics (ROC) curve analysis for hospital LOS. The Kolmogorov–Smirnov test was used to verify the normality of distribution for all variables. For subgroup comparisons, the Student t test or Mann–Whitney test was performed for continuous variables, and the Pearson chi-square test was used for categorical variables. Cox proportional hazard and logistic regression models were used to identify variables associated with mortality and LOS, respectively. Factors significant ($P < 0.05$) in univariable analysis were entered into the multivariable Cox regression model. The probability of all-cause mortality was estimated using Kaplan–Meier analysis with log-rank tests. P values < 0.05 were considered statistically significant. All statistical analyses were performed using R (version 4.0.0, R Foundation for Statistical Computing).

Results

Patient demographics and baseline characteristics

Patient characteristics based on clinical information and preoperative laboratory results are presented in Table 1. Mean patient age at the time of LEA was 64.1 ± 11.9 years, and 75.7% of patients were male. Hypertension was the most frequent comorbidity, followed by coronary artery disease and kidney disease. Mean preoperative RDW was 14.3 ± 1.8%, and mean HbA1c was 8.0 ± 1.9%. Minor amputations accounted for 88.9% of all LEAs, and the remaining 11.1% were major amputations. Mean duration of follow-up after LEA was 3.1 ± 2.9 years. High RDW group (n = 145) was associated with lower BMI, higher prevalence of hypertension, coronary artery disease, cerebrovascular accident and ESRD.

Primary and secondary endpoints

Total 92 mortality event occurred (Table 2). The most common cause for mortality was septic shock (23 patients [25.0%]), followed by pneumonia (16 patients [17.4%]), multi-organ failure (6 patients [6.5%]), heart failure (6 patients [6.5%]) and coronary artery disease (6 patients [6.5%]). Estimated overall survival rates for the entire cohort were as follows: 1-year, 89.4%; 3-year, 82.8%; 5-year, 75.7%; and 7-year, 68.7%. Based on maximally selected rank statistics analysis, the optimal cutoff value of preoperative RDW as a predictor of mortality was 14.5% (Fig. 2). On ROC analysis, RDW ≥ 14.5% was also a significant predictor of prolonged hospital LOS after LEA, with an area under the curve (AUC) of 0.619 (95% confidence interval [CI], 0.554–0.683; $P < 0.001$), a sensitivity of 53.1%, and a specificity of 67.1% (Fig. 3).

The results of univariable and multivariable Cox proportional hazard regression analyses for predictors of all-cause mortality are shown in Table 3. After adjusting for variables significant on univariable analysis, RDW ≥ 14.5% remained significantly associated with all-cause mortality after diabetic foot amputation on multivariable analysis (adjusted hazard ratio [aHR], 2.24; 95% CI, 1.43–3.51; $P < 0.001$). Other variables positively associated with mortality were increased age (aHR, 1.06; 95% CI, 1.04–1.09; $P < 0.001$), presence of ESRD (aHR, 2.21; 95% CI, 1.39–3.517; $P = 0.001$) and low lymphocyte level (aHR 0.65; 95% CI, 0.43–0.99; $P = 0.044$). Cumulative survival curves showed significantly inferior survivorship after LEA in the higher preoperative RDW group (RDW ≥ 14.5%), compared with the lower preoperative RDW group (RDW < 14.5%; $P < 0.001$) (Fig. 4). Confined to minor amputation, increased age, presence of ESRD and RDW ≥ 14.5% were significant predictor of all-cause mortality (Table 4).

Mean hospital LOS after LEA was 24.6 ± 24.7 days. 4 patients were excluded from the LOS analysis because they died during the hospital stay within 30 days. The results of univariable and multivariable logistic regression analyses for predictors of prolonged LOS (> 30 days) are shown in Table 5. Preoperative RDW ≥ 14.5% was the only variable associated with prolonged LOS on multivariable analysis (adjusted odds ratio [aOR], 1.96; 95% CI, 1.17–3.28; $P = 0.011$). Confined to minor amputation, RDW ≥ 14.5%, low lymphocyte level and high erythrocyte sedimentation rate level were significant predictor of prolonged LOS (Table 6).

Discussion

Our results showed that high preoperative RDW values were significantly associated with increases in both mortality and length of hospitalization after LEA in patients with diabetic foot, even after adjusting for

Variable	Subgroup	RDW < 14.5 (n = 268)	RDW ≥ 14.5 (n = 147)	P value
Age, year		63.3 ± 12.3	65.7 ± 11.0	0.08[a]
Duration of diabetes, year		17.5 ± 10.5	19.2 ± 9.9	0.128[a]
Sex	Female	62 (23.1)	39 (26.5)	0.474[b]
	Male	206 (76.9)	108 (73.5)	
BMI, kg/m^2		23.4 ± 3.4	22.7 ± 3.3	**0.037[c]**
	< 25	188 (70.1)	118 (80.3)	**0.027[b]**
	≥ 25	80 (29.9)	29 (19.7)	
Comorbidities	Hypertension	195 (72.8)	125 (85.0)	**0.005[b]**
	CAD	57 (21.3)	61 (41.5)	**< 0.001[b]**
	PAD	160 (59.7)	101 (68.7)	0.072[b]
	Previous CVA	34 (12.7)	30 (20.4)	**0.046[b]**
	COPD	24 (9.0)	13 (8.8)	1.000[b]
	Solid organ transplantation	25 (9.3)	14 (9.5)	1.000[b]
	CKD	79 (29.5)	36 (24.5)	0.303[b]
	ESRD	37 (13.8)	60 (40.8)	**< 0.001[b]**
Level of amputation	Minor	244 (91.0)	125 (85.0)	0.072[b]
	Major	24 (9.0)	22 (15.0)	
Preoperative laboratory results	Hb, g/dL	10.8 ± 1.9	10.0 ± 1.4	**< 0.001[a]**
	RDW, %	13.3 ± 0.8	16.2 ± 1.6	**< 0.001[a]**
	WBC count, × 10^3/μL	11.9 ± 6.0	10.4 ± 5.2	**0.002[a]**
	Lymphocyte count, × 10^3/μL	1.43 ± 0.5	1.41 ± 0.7	0.186[a]
	ESR, mm/h	86.3 ± 29.6	83.7 ± 33.2	0.677[a]
	CRP, mg/L	85.7 ± 89.2	63.7 ± 68.1	0.074[a]
	HbA1c, %	8.1 ± 1.9	7.6 ± 1.8	**0.008[a]**
	Albumin, g/dL	3.1 ± 0.7	3.0 ± 0.6	0.671[a]
Follow-up duration, years		3.8 ± 3.1	2.5 ± 2.7	**< 0.001[a]**
Mortality		39 (14.6)	53 (36.1)	**< 0.001[b]**
Prolonged LOS		50 (18.7)	52 (35.4)	**< 0.001[b]**

Table 1. Patient demographic and preoperative laboratory results. "Significant values are in [bold]" [a]Mann-Whitney U test. [b]Chi-square test. [c]Student *t* test. BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, c-reactive protein; CVA, cerebrovascular accident; ESR, erythrocyte sedimentation rate; ESRD, end-stage renal disease; Hb, hemoglobin; HbA1c, glycated hemoglobin; LOS, length of stay; PAD, peripheral artery disease; RDW, red blood cell distribution width; SD, standard deviation; WBC, white blood cell.

Cause	N (%)
Septic shock	23 (25.0)
Unknown (Death on arrival or death on other hospital by unknown cause)	19 (20.7)
Pneumonia	16 (17.4)
Multi-organ failure	6 (6.5)
Heart failure	6 (6.5)
Coronary artery disease	6 (6.5)
Malignancy	4 (4.3)
Gastrointestinal bleeding	4 (4.3)
Renal failure	3 (3.3)
Arrythmia	3 (3.3)
Panperitonitis	1 (1.1)
Suicide	1 (1.1)

Table 2. Causes of death.

confounding variables. The practicality of RDW values was confirmed by identifying an optimal cutoff RDW value. Specifically, a preoperative RDW ≥ 14.5% was associated with not only higher mortality but also prolonged hospitalization, and preoperative RDW was an independent predictor of both outcomes in patients undergoing diabetic foot amputation.

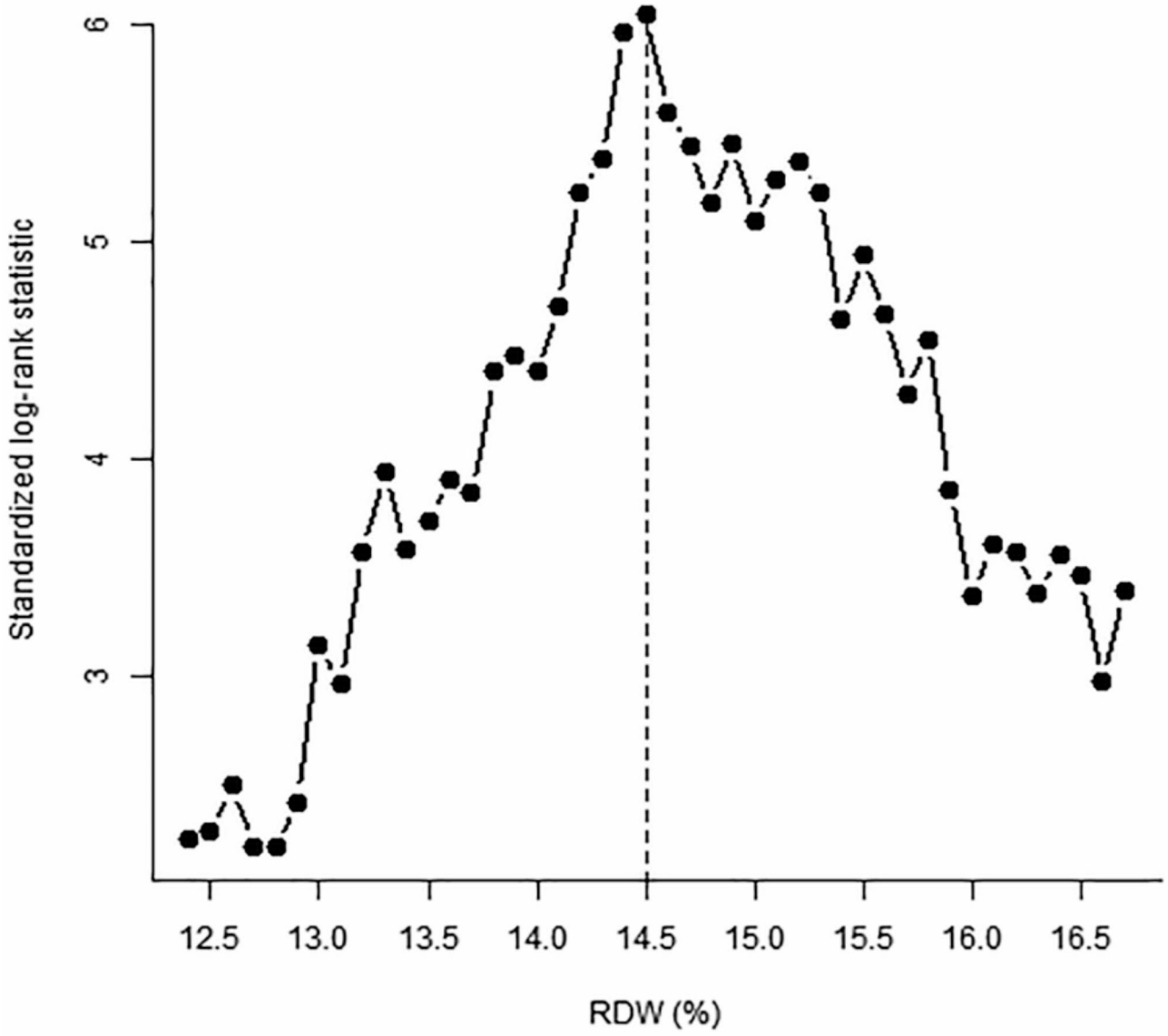

Fig. 2. Maximally selected rank statistics analysis for determining the optimal cutoff value of red blood cell distribution width (RDW) for predicting all-cause mortality after diabetic foot amputation.

Several previous studies examined the relationship between diabetes mellitus and RDW. The chronic inflammatory process associated with diabetes can affect red blood cell (RBC) production and increase RDW by reducing RBC half-life and deformability[11]. Elevated RDW values have also been associated with diabetes-associated complications. Atalay et al.[15] reported that low RDW values were strongly associated with diabetic ketoacidosis (DKA), and that the RDW/mean corpuscular volume (MCV) ratio was a stronger predictor of DKA risk than RDW or MCV alone. Additionally, Al-Kindi et al.[16] found that RDW was highly associated with cardiovascular mortality in patients with diabetes, and Zhang et al.[17] reported that RDW was associated with microalbuminuria, which is an early indicator of diabetic nephropathy, in patients with type 2 diabetes. More recently, Ma et al.[18] reported significantly increased RDW in patients with diabetic retinopathy and confirmed that increased RDW was an independent risk factor for diabetic retinopathy. The authors concluded that RDW is a simple, inexpensive, and reliable parameter that could be a useful biomarker for diabetic retinopathy[18].

Several recent studies have examined the relationship between RDW and diabetic foot ulcers, a potentially fatal complication of diabetes. Arıcan et al.[13] reported that in patients with diabetic foot ulcers, RDW > 13.4% was significantly associated with the need for major amputation. Hong et al.[14] reported that two factors, RDW and RDW/albumin ratio, were independent predictors of mortality in patients with diabetic foot ulcers. Furthermore, the RDW/albumin ratio was superior to RDW for predicting mortality in younger and less severely ill patients[14]. In contrast, Yammine et al.[19] analyzed the prognostic value of various laboratory markers for predicting the severity of diabetic foot infection and reported that RDW was not associated with infection severity. In the present study, we found that RDW was an independent risk factor for both all-cause mortality and prolonged hospital LOS after diabetic foot amputation. These findings support the results of previous studies revealing an

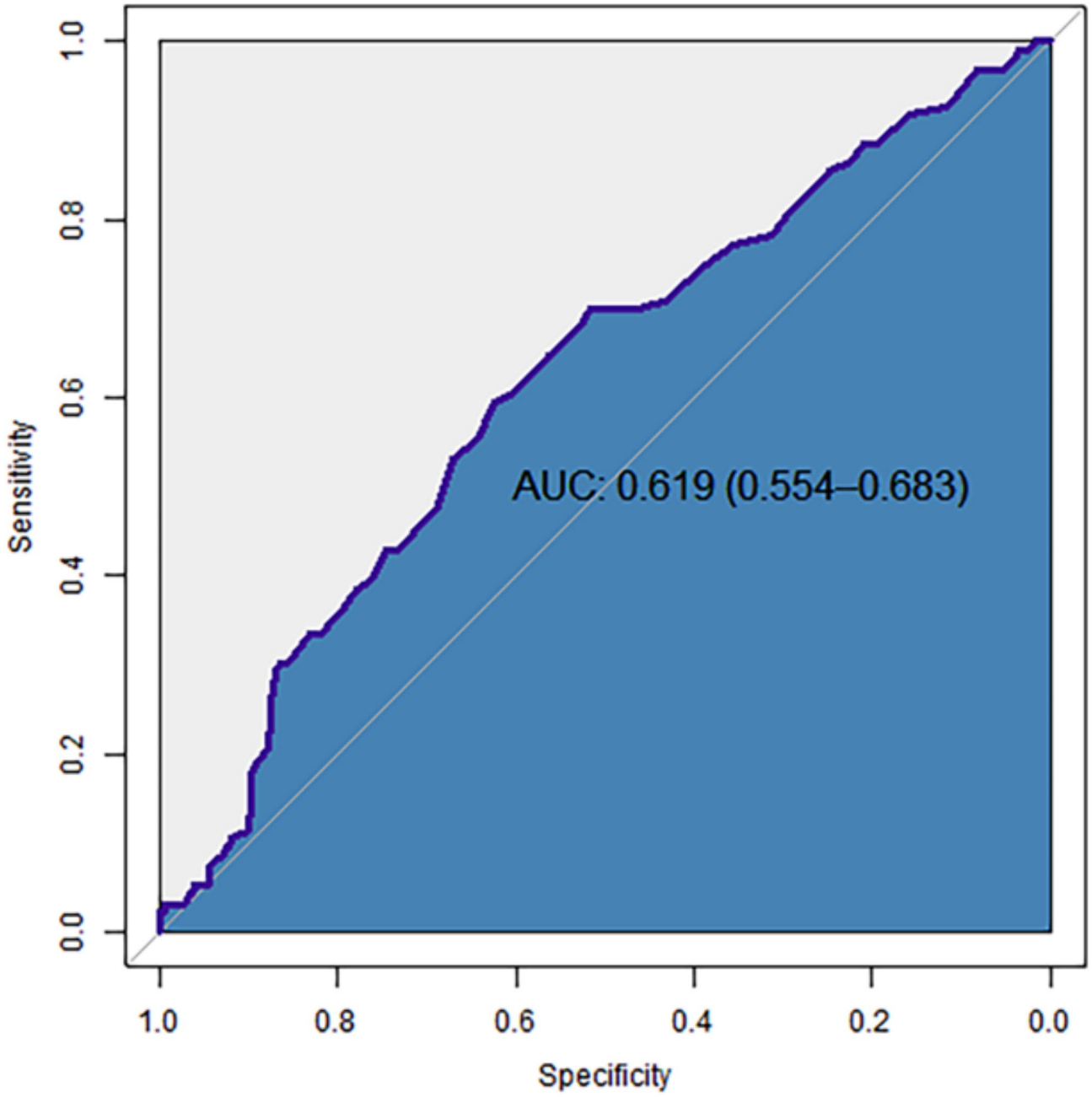

Fig. 3. Receiver operating characteristics curve for predicting prolonged hospital length of stay after diabetic foot amputation. Shown are the results for a red blood cell distribution width (RDW) cutoff value of 14.5%. The AUC of RDW was 0.619, 95% CI: 0.554–0.683. AUC, area under the curve. CI: confidence interval.

association between elevated RDW levels and poorer prognosis in patients with diabetic foot ulcers[13,14]. We also identified two other independent risk factors for all-cause mortality after diabetic foot LEA: age and ESRD. These are known prognostic factors after diabetic foot LEA[20–25].

Another interesting finding of our study is that high RDW was significantly associated with a prolonged hospital LOS. In addition to medical necessity, LOS is determined by various other factors, including patient socioeconomic status and type of health care insurance, and prolonged LOS can lead to substantial financial and social burdens[26–28]. However, our study was conducted in Korea, where > 95% of the population is enrolled in the National Health Insurance program and has easy access to medical care. Thus, the impact of socioeconomic status and insurance type on LOS was likely minimized. In previous studies, erythrocyte sedimentation rate, HbA1c, white blood cell count, c-reactive protein, serum albumin, wound severity, BMI, and history of cerebrovascular accident or coronary artery disease were evaluated as factors potentially associated with the duration of hospitalization in patients with diabetic foot ulcers[29,30]. This is the first study to examine the role

Variable		Univariable		Multivariable	
		HR (95% CI)	*P* value	HR (95% CI)	*P* value
Sex	Female	Reference			
	Male	0.88 (0.56–1.38)	0.567		
Age		**1.06 (1.03–1.08)**	**< 0.001**	**1.06 (1.04–1.09)**	**< 0.001**
BMI, kg/m^2		0.95 (0.89–1.01)	0.087		
Level of amputation	Minor	Reference			
	Major	1.62 (0.88–2.98)	0.120		
Hypertension		**2.70 (1.36–5.37)**	**0.005**	1.47 (0.71–3.04)	0.294
CAD		**1.97 (1.30–2.99)**	**0.001**	1.25 (0.80–1.96)	0.336
Previous CVA		**2.33 (1.45–3.76)**	**0.001**	1.54 (0.93–2.56)	0.097
COPD		1.09 (0.61–1.96)	0.777		
Solid organ transplantation		0.91 (0.47–1.75)	0.774		
CKD		1.12 (0.72–1.72)	0.621		
ESRD		**2.76 (1.81–4.20)**	**< 0.001**	**2.21 (1.39–3.51)**	**0.001**
Hb		**0.81 (0.72–0.92)**	**0.001**	0.91 (0.80–1.04)	0.158
RDW, %	< 14.5	Reference			
	≥ 14.5	**3.48 (2.29–5.27)**	**< 0.001**	**2.24 (1.43–3.51)**	**< 0.001**
WBC count		0.96 (0.92–1.00)	0.079		
Lymphocyte count		**0.65 (0.44–0.96)**	**0.032**	**0.65 (0.43–0.99)**	**0.044**
ESR		1.00 (0.99–1.01)	0.785		
CRP		1.00 (1.00–1.00)	0.517		
HbA1c		0.94 (0.83–1.06)	0.315		
Albumin		0.77 (0.56–1.05)	0.097		

Table 3. Univariable and multivariable Cox regression analysis of potential predictors of all-cause mortality after diabetic foot amputation. "Significant values are in [bold]" BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, c-reactive protein; CVA, cerebrovascular accident; ESR, erythrocyte sedimentation rate; ESRD, end-stage renal disease; Hb, hemoglobin; HbA1c, glycated hemoglobin; HR, hazard ratio; RDW, red blood cell distribution width; WBC, white blood cell.

of RDW in predicting hospital LOS after diabetic foot amputation. We confirmed a statistically significant relationship between RDW ≥ 14.5% and prolonged hospital LOS (> 30 days).

Although exact mechanisms of the relationship between high RDW and prognosis after diabetic foot amputation have not been established, several theories have been proposed. For example, short telomere length can lead to an increased RDW and also adversely affect mortality and long-term hospitalization[31]. It has been reported that shorter telomere length is associated with a lower RBC count and hemoglobin and an elevated MCV and RDW. Shorter telomere length is also known to be associated with aging in general[32,33], as well as various diseases. It is also associated with the development of DM foot ulcers and risk of lower extremity amputation in patients with type 1 diabetes[34,35]. Another theory focuses on the association between increased RDW and oxidative stress. Increased oxidative stress leads to the production of free radicals that damage RBCs, changing their morphology. Changes in erythrocyte morphology can negatively affect blood flow and gas exchange in small blood vessels[36]. Furthermore, peroxidase protects RBCs from oxidative damage, and selenium supplementation in humans increases glutathione peroxidase activity in erythrocytes. Serum selenium can inhibit the increase in RDW by protecting erythrocytes from oxidative damage[37]. These observations suggest that oxidative stress may be a biological mechanism leading to increased RDW[38]. A third theory involves the role of inflammation as a potential trigger of increased RDW. Inflammation can impair erythrocyte maturation and allow immature erythrocytes to enter the bloodstream, which can be achieved by promoting anisocytosis through impaired iron metabolism and interruption of the erythropoietin response[39]. Inflammation can also induce a condition in which immature and mature erythrocytes are mixed together, and the overall survival rate of erythrocytes is reduced[40]. It is thought that this will eventually lead to an increased RDW. Core aspects of these theories regarding the causes of high RDW are similar to those related to the pathophysiology of diabetic foot ulcers and other diabetes complications. In this regard, high RDW may be a marker of poor general health and healing abilities of patients with diabetic foot ulcers.

This study has a couple of major strengths. One strength was the identification of a prognostic factor that is easily evaluated using inexpensive, routine laboratory tests. Financial concerns are a major problem for many patients with diabetes, and RDW is a test that satisfies both economic feasibility and accessibility. Another strength is that the study considered not only all-cause mortality but also hospital LOS after diabetic foot amputation at a tertiary medical institution. Hospital LOS can be a significant socioeconomic burden, especially when hospitalization is prolonged.

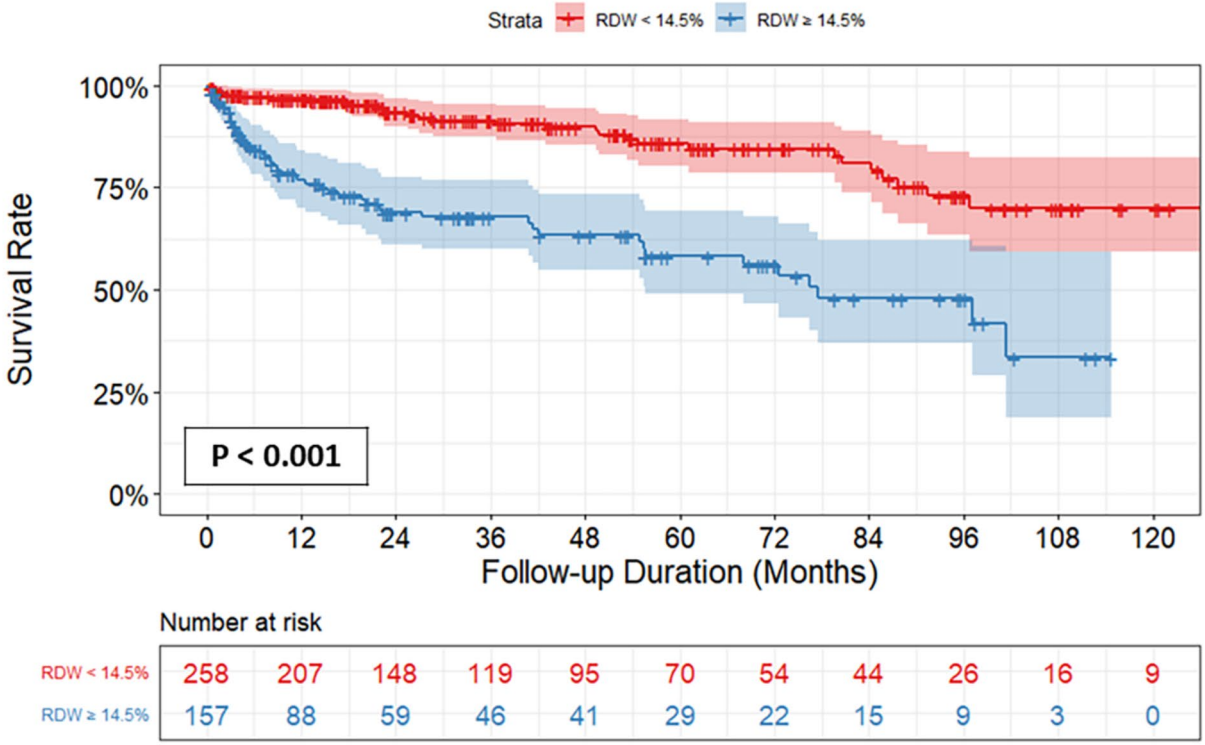

Fig. 4. Kaplan–Meier curves of all-cause mortality according to red blood cell distribution width (RDW) value. Shaded areas indicate the 95% confidence intervals.

The study also has some limitations. For example, there is a risk of assessment bias based on the retrospective design of this study. To reduce this risk, the senior author was blinded to the data collection and analysis process. Another limitation was that the mean follow-up period was relatively short for evaluating exact mortality rates. In addition, this study was conducted in a single tertiary medical center. Patients cared for at a tertiary center often have a worse general medical condition and more comorbidities than patients treated elsewhere, so our study cohort may differ from the general population of patients with diabetic foot. This difference may have affected the results of our predictive factor analysis.

In conclusion, preoperative RDW ≥ 14.5% was an independent predictive factor for increased all-cause mortality and prolonged LOS after diabetic foot amputation. RDW is an inexpensive, easily accessible value that may be a useful parameter for risk stratification of patients undergoing LEA for diabetic foot. Our results suggest that patients with a high preoperative RDW should undergo more intensive, multidisciplinary management and careful monitoring to improve outcomes after diabetic foot amputation.

Variable		Univariable		Multivariable	
		HR (95% CI)	*P* value	HR (95% CI)	*P* value
Sex	Female	Reference			
	Male	0.98 (0.60–1.61)	0.942		
Age		**1.06 (1.04–1.08)**	**< 0.001**	**1.07 (1.05–1.10)**	**< 0.001**
BMI, kg/m^2		0.94 (0.88–1.01)	0.081		
Hypertension		**2.56 (1.23–5.32)**	**0.012**	1.39 (0.64–3.01)	0.405
CAD		**2.08 (1.33–3.26)**	**0.001**	1.38 (0.85–2.24)	0.196
Previous CVA		**2.31 (1.38–3.86)**	**0.001**	1.52 (0.88–2.63)	0.132
COPD		1.39 (0.77–2.52)	0.277		
Solid organ transplantation		0.68 (0.31–1.47)	0.322		
CKD		1.11 (0.69–1.78)	0.662		
ESRD		**2.71 (1.72–4.25)**	**< 0.001**	**2.29 (1.37–3.80)**	**0.001**
Hb		**0.83 (0.73–0.94)**	**0.005**	0.94 (0.82–1.09)	0.402
RDW, %	< 14.5	Reference			
	≥ 14.5	**2.97 (1.91–4.61)**	**< 0.001**	**1.90 (1.18–3.06)**	**0.009**
WBC count		0.98 (0.93–1.02)	0.278		
Lymphocyte count		**0.64 (0.42–0.98)**	**0.041**	0.63 (0.39–1.01)	0.053
ESR		1.00 (0.99–1.01)	0.691		
CRP		1.00 (1.00–1.00)	0.666		
HbA1c		0.99 (0.87–1.12)	0.817		
Albumin		**0.70 (0.50–0.99)**	**0.044**	0.73 (0.50–1.07)	0.102

Table 4. Univariable and multivariable Cox regression analysis of potential predictors of all-cause mortality after diabetic foot minor amputation. "Significant values are in [bold]" BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, c-reactive protein; CVA, cerebrovascular accident; ESR, erythrocyte sedimentation rate; ESRD, end-stage renal disease; Hb, hemoglobin; HbA1c, glycated hemoglobin; HR, hazard ratio; RDW, red blood cell distribution width; WBC, white blood cell.

Variable		Univariable		Multivariable	
		HR (95% CI)	*P* value	HR (95% CI)	*P* value
Sex	Female	Reference			
	Male	0.80 (0.48–1.34)	0.399		
Age		0.99 (0.98–1.01)	0.540		
BMI, kg/m^2		0.98 (0.92–1.05)	0.625		
Level of amputation	Minor	Reference			
	Major	**1.96 (1.03–3.74)**	**0.041**	1.395 (0.70–2.80)	0.349
Hypertension		1.03 (0.60–1.75)	0.924		
CAD		**1.73 (1.08–2.78)**	**0.024**	1.48 (0.88–2.48)	0.141
Previous CVA		0.93 (0.50–1.74)	0.818		
COPD		1.40 (0.87–2.25)	0.168		
Solid organ transplantation		1.23 (0.59–2.57)	0.581		
CKD		0.98 (0.60–1.62)	0.946		
ESRD		**2.12 (1.29–3.47)**	**0.003**	1.36 (0.78–2.36)	0.274
Hb		**0.77 (0.67–0.89)**	**< 0.001**	0.86 (0.74–1.01)	0.059
RDW, %	< 14.5	Reference			
	≥ 14.5	**2.39 (1.51–3.77)**	**< 0.001**	**1.96 (1.17–3.28)**	**0.011**
WBC count		1.02 (0.98–1.06)	0.318		
Lymphocyte count		**0.51 (0.32–0.79)**	**0.003**	0.66 (0.41–1.07)	0.089
ESR		**1.01 (1.00–1.02)**	**0.035**	1.00 (1.00–1.01)	0.32
CRP		**1.00 (1.00–1.01)**	**0.027**	1.00 (1.00–1.01)	0.119
HbA1c		1.02 (0.91–1.15)	0.747		
Albumin		0.76 (0.54–1.08)	0.130		

Table 5. Univariable and multivariable logistic regression analysis of potential predictors of prolonged hospital length of stay (> 30 days) after diabetic foot amputation. "Significant values are in [bold]" BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, c-reactive protein; CVA, cerebrovascular accident; ESR, erythrocyte sedimentation rate; ESRD, end-stage renal disease; Hb, hemoglobin; HbA1c, glycated hemoglobin; OR, odds ratio; RDW, red blood cell distribution width; WBC, white blood cell.

Variable		Univariable		Multivariable	
		HR (95% CI)	*P* value	HR (95% CI)	*P* value
Sex	Female	Reference			
	Male	0.92 (0.53–1.60)	0.766		
Age		1.00 (0.98–1.02)	0.961		
BMI, kg/m^2		0.97 (0.90–1.05)	0.451		
Hypertension		1.03 (0.58–1.84)	0.918		
CAD		**1.90 (1.14–3.18)**	**0.014**	1.75 (1.00–3.07)	0.051
Previous CVA		1.24 (0.65–2.36)	0.523		
COPD		1.34 (0.66–2.74)	0.421		
Solid organ transplantation		1.03 (0.45–2.37)	0.943		
CKD		0.83 (0.47–1.46)	0.511		
ESRD		**2.39 (1.41–4.06)**	**0.001**	1.42 (0.78–2.58)	0.247
Hb		**0.79 (0.68–0.92)**	**0.003**	0.89 (0.76–1.06)	0.894
RDW, %	< 14.5	Reference			
	≥ 14.5	**2.22 (1.35–3.64)**	**0.002**	**1.84 (1.04–3.25)**	**0.036**
WBC count		1.02 (0.98–1.06)	0.395		
Lymphocyte count		**0.43 (0.25–0.71)**	**0.001**	**0.56 (0.33–0.96)**	**0.036**
ESR		**1.01 (1.00–1.02)**	**0.003**	**1.01 (1.00–1.02)**	**0.045**
CRP		**1.00 (1.00–1.01)**	**0.019**	1.00 (1.00–1.01)	0.153
HbA1c		1.07 (0.94–1.21)	0.326		
Albumin		0.80 (0.54–1.18)	0.259		

Table 6. Univariable and multivariable logistic regression analysis of potential predictors of prolonged hospital length of stay (> 30 days) after diabetic foot minor amputation. "Significant values are in [bold]" BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, c-reactive protein; CVA, cerebrovascular accident; ESR, erythrocyte sedimentation rate; ESRD, end-stage renal disease; Hb, hemoglobin; HbA1c, glycated hemoglobin; OR, odds ratio; RDW, red blood cell distribution width; WBC, white blood cell.

Data availability

The data sets used and analyzed during the current study are available from the corresponding author at a reasonable request.

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Author contributions

All authors drafted the manuscript. KH Park and JW Lee coordinated the project. JW Lee, KH Park, JH Park and SH Han generated the concept of the study. The acquisition of data and analysis was done by YK Yoon, DW Shim, W Lee, HH Cho and JH Park. The interpretation of data was done by YK Yoon, DW Shim, HH Cho, W Lee JH Park and JW Lee. YK Yoon, SH Han, JW Lee and KH Park revised the final draft critically for important intellectual content and approved the version to be submitted. JW Lee, SH Han and KH Park made final approval of the version to be published.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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