Journal of Surgery
Zhang Y-Q, et al. J Surg 9: 11172
www.doi.org/10.29011/2575-9760.11172
www.gavinpublishers.com
Research Article

Study on the Relationship Between Red Cell Distribution Width and Prognosis in Newly Initiated Hemodialysis Patients

Yun-Qiang Zhang, Sheng-Rong Li, Jian-Hong Zhang, Min-Jia Li*

Blood Purification Center, The Third Affiliated Hospital, Sun Yat-Sen University, Yuedong Hospital, Meizhou city, Guangdong province 514700, China

***Corresponding author:** Min-Jia Li, Blood purification center, The Third Affiliated Hospital, Sun Yat-Sen University, Yuedong Hospital, Meizhou city, Guangdong province 514700, China

Citation: Zhang Y-Q, Li S-R, Zhang J-H, Li M-J (2024) Study on the Relationship Between Red Cell Distribution Width and Prognosis in Newly Initiated Hemodialysis Patients. J Surg 9: 11172 DOI: 10.29011/2575-9760.11172

Received Date: 25 October 2024; Accepted Date: 02 November 2024; Published Date: 05 November 2024

Abstract

Background: This study aims to assess the impact of varying levels of Red Cell Distribution Width (RDW) on all-cause mortality among hemodialysis patients.

Methods: This retrospective cohort study comprised 377 patients who began hemodialysis at our center from September 1, 2015, to December 31, 2022. We stratified patients into quartiles based on RDW values and employed Cox regression to evaluate the correlation between RDW levels and mortality rates, while adjusting for confounders like age, albumin, and ferritin levels.

Results: Significantly, elevated RDW levels correlated with increased all-cause mortality among hemodialysis patients. Those in the Highest RDW Quartile (Q4) faced a mortality risk (HR = 1.378, 95% CI: 1.144–1.659, p = 0.001) substantially greater than those in the Lowest Quartile (Q1). RDW persisted as an independent mortality predictor (HR = 1.237, 95% CI: 1.015–1.508, p = 0.035) after adjusting for age, albumin, and ferritin, which themselves were significant predictors.

Conclusion: RDW, a commonly measured hematological marker, demonstrates considerable potential for evaluating mortality risk in hemodialysis patients. Future research should delve into the causal dynamics between RDW levels and mortality to identify intervention strategies that could enhance survival outcomes for these individuals.

Keywords: All-Cause Mortality; Newly Initiated Hemodialysis; Prognosis; Red Cell Distribution Width (RDW); Retrospective Cohort Study

Introduction

Chronic Kidney Disease (CKD) represents a significant global public health issue. As the disease progresses, some patients will develop End-Stage Renal Disease (ESRD), necessitating renal replacement therapy. Hemodialysis (HD) is one of the most common forms of renal replacement therapy, effectively removing metabolic waste and excess fluid from the body. However, despite dialysis treatment, the mortality rate remains significantly high, with cardiovascular diseases and infections continuing to be the leading causes of death [1]. Recent studies indicate that the mortality rate among dialysis patients may be up to 6 to 8 times higher than in the general population, highlighting the severe impact of this condition [1]. Red Cell Distribution Width (RDW) is a routine hematological parameter reflecting variability in red blood cell size. Recently, RDW has been associated not only with anemia diagnosis but also with the prognosis of various chronic diseases. Studies have shown that elevated RDW is linked to higher mortality and hospitalization rates in cardiovascular disease patients [2]. In patients with Chronic Kidney Disease (CKD), elevated RDW has been associated with cardiovascular events and all-cause mortality, potentially reflecting inflammation, oxidative stress, and erythropoiesis disorders [3]. Although these findings underscore RDW's potential prognostic value, its specific role in the outcomes of hemodialysis patients, especially during the initial

stages of treatment, requires further investigation.

Although the prognostic role of Red Cell Distribution Width (RDW) has been validated in Chronic Kidney Disease (CKD) and cardiovascular diseases, yet its role in patients at the onset of hemodialysis treatment remains insufficiently explored. Given the physiological changes experienced by patients during the early stages of HD, RDW may serve as a crucial predictor of mortality. This study posits that higher RDW levels correlate significantly with increased mortality rates among patients newly initiated on hemodialysis and asserts that RDW may serve as an independent prognostic marker for assessing mortality risk in these patients. This study aims to evaluate the ability of red cell distribution width (RDW) as an independent predictor of mortality in patients newly initiated on hemodialysis. By employing Cox regression analysis, it will rigorously assess the relationship between RDW levels and mortality risk, thereby exploring RDW's potential clinical applications in prognostic assessments. The findings could provide vital clinical insights to enhance risk evaluation and individualized management for hemodialysis patients.

Methodology

Study Design and Population

This study utilized a retrospective cohort design, executed at the Blood Purification Center of The Third Affiliated Hospital of Sun Yat-sen University, Yuedong Hospital. It included 377 patients who began hemodialysis from September 1, 2015, to December 31, 2022. The patients were categorized into four groups based on the quartiles of their red cell distribution width (RDW) values for detailed analysis.

Inclusion and Exclusion Criteria

Inclusion Criteria

1.Patients aged 18 years or older.

2. Patients who commenced hemodialysis treatment between September 1, 2015, and December 31, 2022.

3. Patients who had been undergoing hemodialysis for a minimum of three months.

4. Patients with comprehensive baseline data and consistent follow-up records.

Exclusion Criteria

1. Individuals receiving temporary dialysis treatment due to acute kidney injury.

2. Patients who underwent kidney transplantation either before or during the study period.

3. Patients lacking complete baseline data or follow-up information.

Data Collection

Baseline data were collected, including age, gender, hemoglobin, albumin, serum iron, ferritin, total iron-binding capacity, transferrin saturation, parathyroid hormone, carbon dioxide combining power, C-reactive protein, and red cell distribution width (RDW). Laboratory data were collected 3 to 6 months following the initiation of hemodialysis. RDW values were then utilized for quartile grouping for analytical purposes, and survival data were continuously collected until December 31, 2022.

Statistical Analysis

Baseline Data Analysis: The baseline characteristics of the participants were summarized and analyzed by dividing the patients into quartiles based on their RDW levels. Continuous variables were presented as means ± standard deviation (SD) and analyzed using the independent samples t-test. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test.

Univariate Cox Regression Analysis: Each baseline variable was evaluated through univariate Cox regression analysis to determine its association with all-cause mortality. Variables that showed a P-value of less than 0.1 were selected for inclusion in the subsequent multivariate analysis.

Multivariate Cox Regression Analysis: Variables that were significant in the univariate analysis were further analyzed using multivariate Cox regression to identify independent predictors of all-cause mortality. The results were presented as Hazard Ratios (HR) with 95% Confidence Intervals (CI). A P-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in compliance with the Declaration of Helsinki and was approved by the Ethics Committee of The Third Affiliated Hospital of Sun Yat-sen University, Yuedong Hospital. Informed consent was obtained from all participants or their legal guardians prior to the collection of data.

Results

Baseline Characteristics

The study included a total of 377 patients who were divided into Quartiles (Q1-Q4) based on their red cell distribution width (RDW). Significant differences were observed among the quartiles in terms of age, gender, hemoglobin, albumin, and serum iron. Specifically, there was a notable age difference among the groups ($p = 0.003$), with older patients predominantly in the Highest RDW Quartile (Q4). In terms of gender distribution, significant variations were observed ($p = 0.033$), with a higher proportion of males in the Lowest RDW Quartile (Q1). Furthermore, significant differences were noted in hemoglobin levels ($p < 0.001$), total iron-binding

capacity (p = 0.007), and transferrin saturation (p = 0.038) across the groups. Detailed baseline characteristics are presented in Table 1.

Variable	Overall (n=377)	Q1 (n=92)	Q2 (n=91)	Q3 (n=100)	Q4 (n=94)	p-value
Age (years)	63.50 (54.00, 71.00)	61.50 (52, 69)	61.00 (50, 71)	67.00 (59, 75)	64.00 (53, 72)	0.003
Male (%)	242 (64.19%)	67 (72.83%)	64 (70.33%)	56 (56.00%)	55 (58.51%)	0.033
Red cell distribution width (RDW, %)	14.80 (13.30, 16.00)	13.5 (12.9, 13.5)	14.3 (14.1, 14.5)	15.3 (15.0, 15.5)	17.5 (16.2, 18.8)	<0.001
Albumin (g/L)	36.65 (34.80, 39.00)	37.15 (34, 39)	36.70 (34, 39)	36.85 (34, 39)	36.20 (33, 38)	0.151
Hemoglobin (g/L)	93.48 ± 21.57	98.98 ± 23.44	94.48 ± 19.76	95.02 ± 18.02	85.48 ± 22.84	<0.001
Serum iron (μmol/L)	9.00 (7.00, 12.00)	9.65 (7, 14)	8.70 (6, 12)	9.20 (7, 11)	8.10 (6, 10)	0.181
Ferritin (ng/mL)	116.85 (60.00, 258.00)	143.00 (92, 280)	126.90 (84, 282)	112.70 (59, 241)	75.50 (34, 210)	0.118
Total iron-binding capacity (μmol/L)	43.50 (36.00, 50.00)	41.30 (37, 48)	43.95 (39, 49)	43.95 (39, 49)	47.00 (40, 54)	0.007
Transferrin saturation (%)	21.45 (17.00, 31.00)	23.22 (17, 31)	22.06 (16, 32)	22.74 (15, 31)	16.59 (12, 28)	0.038
Parathyroid hormone (pg/mL)	310.40 (160.00, 485.00)	330.65 (157, 510)	332.10 (191, 507)	301.45 (181, 547)	278.30 (122, 432)	0.202
CO2CP (mmol/L)	21.34 ± 60.15	30.87 ± 121.59	17.70 ± 3.55	18.39 ± 3.74	18.70 ± 3.67	0.383
C-reactive protein (mg/L)	4.80 (2.00, 10.00)	5.10 (2, 10)	4.00 (1, 10)	4.80 (2, 9)	4.00 (2, 10)	0.223
Survival Time (Months)	35.00 (18.00, 58.00)	36.50 (15, 63)	47.00 (23, 67)	35.00 (18, 57)	23.00 (11, 39)	<0.001
Number of Deaths□%□	104(27.586%)	20(17.70%)	24(17.78%)	30(23.26%)	30(23.26%)	0.421

Table 1: Baseline Data Comparison.

Univariate Cox Regression Analysis

The univariate Cox regression analysis revealed that several baseline variables were significantly associated with all-cause mortality. Specifically, age (HR = 1.061, 95% CI: 1.042–1.081, p < 0.001), albumin (HR = 0.899, 95% CI: 0.856–0.944, p < 0.001), serum iron (HR = 0.963, 95% CI: 0.824–1.003, p = 0.071), and red cell distribution width (RDW) (HR = 1.378, 95% CI: 1.144–1.659, p = 0.001) all showed significant associations with mortality. The findings indicate that higher age and RDW are linked to an increased risk of mortality, whereas higher albumin levels are associated with a reduced risk of mortality. Other variables like ferritin, parathyroid hormone, and transferrin saturation did not demonstrate significant associations. Detailed results are presented in Table 2.

Variable	B	SE	Wald	df	p-value	Exp(B) (HR)	95% Confidence Interval for Exp(B)
Age (years)	0.06	0.01	38.997	1	<0.001	1.061	1.042-1.081
Male (%)	0.105	0.209	0.253	1	0.615	1.111	0.738-1.671
Red cell distribution width (RDW, %)	0.32	0.095	11.435	1	0.001	1.378	1.144-1.659
Albumin (g/L)	-0.107	0.025	18.209	1	<0.001	0.899	0.856-0.944
Serum iron (μmol/L)	-0.038	0.021	3.25	1	0.071	0.963	0.824-1.003
Ferritin (ng/mL)	-0.001	0	7.039	1	0.008	0.999	0.998-1.000
Total iron-binding capacity (μmol/L)	-0.003	0.01	0.068	1	0.795	0.997	0.978-1.017
Transferrin saturation (%)	-0.011	0.007	2.514	1	0.113	0.989	0.975-1.003
Parathyroid hormone (pg/mL)	-0.001	0	8.93	1	0.003	0.999	0.999-1.000
CO2CP (mmol/L)	0	0.007	0.002	1	0.961	1	0.985-1.014
C-reactive protein (mg/L)	0.006	0.007	0.674	1	0.412	1.006	0.993-1.020

Table 2: Univariate Cox Regression Analysis Results.

Multivariate Cox Regression Analysis

In the multivariate Cox regression analysis, after adjusting for confounding factors such as age and albumin, the quartiles of Red Cell Distribution Width (RDW) remained significantly associated with all-cause mortality (HR = 1.237, 95% CI: 1.015–1.508, p = 0.035). Age (HR = 1.055, 95% CI: 1.035–1.075, p < 0.001) and albumin (HR = 0.915, 95% CI: 0.867–0.964, p = 0.001) also continued to show significant associations with mortality risk. Ferritin, though less impactful (HR = 0.999, 95% CI: 0.998–1.000, p = 0.048), remained significant after adjustment. However, parathyroid hormone did not reach statistical significance (p = 0.065). Detailed results are presented in Table 3.

Variable	B	SE	Wald	df	p-value	Exp(B) (HR)	95% Confidence Interval for Exp(B)
Age (years)	0.053	0.01	30.058	1	<0.001	1.055	1.035-1.075
Red cell distribution width (RDW, %)	0.213	0.101	4.423	1	0.035	1.237	1.015-1.508
Albumin (g/L)	-0.089	0.027	10.878	1	0.001	0.915	0.867-0.964
Serum iron (μmol/L)	0.013	0.027	0.221	1	0.638	1.013	0.961-1.067
Ferritin (ng/mL)	-0.001	0.001	3.925	1	0.048	0.999	0.998-1.000
Parathyroid hormone (pg/mL)	-0.001	0	3.4	1	0.065	0.999	0.999-1.000

Table 3: Multivariate Cox Regression Analysis Results.

In this study, we identified key predictors of all-cause mortality among hemodialysis patients. Age, albumin, ferritin, and red cell distribution width (RDW) were found to be significant independent predictors in the multivariate analysis. RDW was particularly noteworthy as a robust independent predictor, linked to higher mortality rates even after accounting for age and albumin. It was observed that patients in the highest RDW quartile had a median survival time of only 23 months compared to 47 months in the lowest quartile, emphasizing RDW's potential for clinical use in risk stratification and management. On the other hand, while parathyroid hormone initially showed some potential links to mortality in the univariate analysis, it did not reach statistical significance in the multivariate analysis, suggesting its influence might be less critical than other factors. These insights are crucial for improving the prognosis and individualized treatment planning for patients undergoing hemodialysis, underscoring the importance of including RDW in routine assessments.

Discussion

This study found that elevated Red Cell Distribution Width (RDW) is significantly associated with all-cause mortality in hemodialysis patients. After adjusting for confounding factors such as age and albumin, RDW remained an independent predictor of mortality. Patients with higher RDW levels had significantly lower median survival times compared to those with lower RDW levels. Additionally, age and albumin were also significantly associated with mortality, underscoring their importance in evaluating patient outcomes. Ferritin also showed significance in the multivariate analysis, suggesting its potential relevance in the context of mortality among these patients. Although parathyroid hormone appeared to be a potential risk factor in the univariate analysis, it did not reach statistical significance in the multivariate model, indicating that its impact might be less substantial than that of other variables. The findings of this study align with the existing literature. Previous research has demonstrated that RDW serves as a prognostic marker in patients with cardiovascular disease and chronic kidney disease. Zhang et al. demonstrated that elevated RDW significantly correlates with increased mortality and cardiovascular events in patients with chronic kidney disease [4]. Similarly, Similarly, Sangoi et al. identified RDW as a crucial predictor of mortality in patients with coronary artery disease [5]. Further studies confirm RDW's association with increased mortality among hemodialysis patients [6-8]. Our study reinforces the prognostic value of RDW in hemodialysis patients and supports its application in a broader spectrum of diseases. The association between RDW and mortality may involve several mechanisms. Research indicates that elevated RDW is closely linked to chronic inflammation [9], oxidative stress [10], impaired erythropoiesis [11], and endothelial dysfunction [12]. In patients with chronic kidney disease, prevalent chronic inflammation may alter erythropoiesis, subsequently elevating RDW. Oxidative stress directly impacts erythropoiesis and enhances mortality risk by accelerating atherosclerosis and cardiovascular disease development. Malnutrition and anemia, prevalent among dialysis patients, are potential contributors to elevated RDW. Lower albumin levels, indicative of malnutrition, along with elevated RDW, correlate with poor prognosis, as confirmed by multiple studies [13]. Consequently, RDW may encapsulate various physiological dysfunctions and serve as a comprehensive marker of mortality risk.

The findings of this study underscore the significant clinical utility of Red Cell Distribution Width (RDW) as a prognostic tool in hemodialysis patients. RDW, being a routine, easily accessible, and cost-effective hematological marker, offers clinicians a valuable method for early identification of high-risk patients. This early detection enables the implementation of more targeted and aggressive interventions, potentially improving patient outcomes. Furthermore, RDW's association with multiple physiological abnormalities, such as malnutrition and chronic inflammation, suggests its broader relevance in patient management. By integrating RDW with other nutritional and inflammatory markers, clinicians can enhance their assessment capabilities, leading to more accurate predictions of mortality risk. This comprehensive approach could facilitate a more personalized and effective treatment strategy for hemodialysis patients, ultimately contributing to better clinical management and patient care. Future studies should aim to validate the predictive value of RDW in larger, multicenter cohorts to confirm its effectiveness across diverse populations. Additionally, given the potential links between RDW and nutritional and inflammatory statuses, it is crucial to explore targeted interventions that could mitigate these risk factors, potentially reducing mortality in hemodialysis patients.

Conclusion

This study demonstrates a significant association between Red Cell Distribution Width (RDW) and all-cause mortality in hemodialysis patients, persisting even after adjusting for confounders like age and albumin. As a routinely measured hematological marker, RDW presents valuable clinical potential for identifying patients at high risk. Future research should further delineate the causal mechanisms linking RDW to mortality and evaluate intervention strategies to enhance survival outcomes in this vulnerable population.

Limitations of the Study

This study's findings, while highlighting a significant link between Red Cell Distribution Width (RDW) and mortality in hemodialysis patients, are limited by its retrospective cohort design, which could include unmeasured confounding factors such as lifestyle or medication usage. Additionally, the data from a single medical center and a small sample size may not be generalizable. The study also did not assess how RDW changes over time affect patient outcomes, which could be crucial for understanding its prognostic value. Future research should explore these dynamics through longitudinal studies and larger, more diverse populations to enhance the findings' applicability.

References

1. Chirakarnjanakorn S, Navaneethan SD, Francis GS (2017) Cardiovascular impact in patients undergoing maintenance hemodialysis: Clinical management considerations. Int J Cardiol 232: 12-23.
2. Felker GM, Allen LA, Pocock SJ (2007) Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. Journal of the American College of Cardiology 50: 40-47.
3. Roumeliotis S, Stamou A, Roumeliotis A (2020) Red blood cell distribution width is associated with deterioration of renal function and cardiovascular morbidity and mortality in patients with diabetic kidney disease 10: 301.
4. Zhang T, Li J, Lin Y (2017) Association between red blood cell distribution width and all-cause mortality in chronic kidney disease patients: a systematic review and meta-analysis[J]. Archives of medical research 48: 378-385.
5. Sangoi MB, Rödel AP, Zorzo P (2014) Prognostic value of red blood cell distribution width in prediction of in-hospital mortality in patients with acute myocardial infarction. Clinical laboratory 60: 1351-1356.
6. Vashistha T, Streja E, Molnar MZ (2016) Red cell distribution width and mortality in hemodialysis patients. American journal of kidney diseases 68: 110-121.
7. Yoon HE, Kim SJ, Hwang HS (2015) Progressive rise in red blood cell distribution width predicts mortality and cardiovascular events in end-stage renal disease patients. PLoS One 10: e0126272.
8. Chen X, Shen B, Zou J (2016) The prognostic value of red blood cell distribution width in patients on maintenance hemodialysis. Blood purification 42: 314-321.
9. Lippi G, Targher G, Montagnana M (2009) Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Archives of pathology & laboratory medicine 133: 628-632.
10. Hunziker S, Celi L A, Lee J (2012) Red cell distribution width improves the simplified acute physiology score for risk prediction in unselected critically ill patients. Critical care 16: 1-8.
11. Förhécz Z, Gombos T, Borgulya G (2009) Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. American heart journal 158: 659-666.
12. Solak Y, Gaipov A, Turk S (2014) Red cell distribution width is independently related to endothelial dysfunction in patients with chronic kidney disease. The American journal of the medical sciences 347: 118-124.
13. Tekce H, Kin Tekce B, Aktas G (2014) The evaluation of red cell distribution width in chronic hemodialysis patients. International journal of nephrology 2014: 754370.