Prognostic Value of Red Blood Cell Distribution Width and D-Dimer in Diffuse Large B-cell Lymphoma: Systematic Review and Meta-analysis.

Maryam Rahchamani [1], Mohammad Sedghi [2], Ali Hakimi [3], Mahdi Nejatianfar [4], Tohid Javaheri [5], Reza Tavakoli [6], Ramtin Ahmadi [5], Nazanin Azmi-Naei [7], Neda Kamandi [3], AmirMohammad Soleimanian[3], Mansoureh Makarem [8], Saeid Zahmatkesh Sangani [8], Rasoul Shavaleh [9], Kazem Rahmani[9], and Moloud Foogerdi[10]

[1]Tehran University of Medical Sciences
[2]Islamic Azad University
[3]Mashhad University of Medical Sciences
[4]Ferdowsi University of Mashhad
[5]Islamic Azad University Mashhad Branch
[6]Arak University of Medical Sciences
[7]Shahrood University of Medical Sciences
[8]Torbat-e Jam Faculty of Medical Sciences and Health
[9]Iran University of Medical Sciences
[10]Birjand University of Medical Sciences

July 20, 2023

Abstract

Background: The significant role of red blood cell distribution width (RDW) and D-Dimer as prognostic factors in patients with some blood malignancies has been reported recently. Aim: We designed and performed a meta-analysis to investigate the prognostic roles of RDW and D-Dimer in subjects with diffuse large B-cell lymphoma (DLBCL). Materials and Methods: We systematically reviewed PubMed-Medline, SCOPUS, EMBASE, Web of Science Core Collection, and Google Scholar up to 30 April 2023 to look for publications on prognostic effects of RDW and D-Dimer in DLBCL patients. For investigation of the associations between RDW and D-Dimer with the overall survival (OS) and progression-free survival (PFS) of the DLBCL cases, hazard ratio (HR) with 95% confidence intervals (CIs) was used. Results: We included 13 eligible studies in the present meta-analysis. The results of pooled analysis showed that increased levels of RDW was related to poor OS (HR=2.01, 95% CI: 1.62-2.48, P value<0.01) and poor PFS (HR=1.52, 95% CI: 1.24-1.85, P value<0.01) among the DLBCL patients. On the other hand, a significant relationship was found between increased D-Dimer and poor OS (HR=2.30, 95% CI: 1.03-5.14, P value<0.05) of the DLBCL patients as well. Conclusion: Our finding clearly confirmed that elevated RDW levels and D-Dimer were associated with adverse OS and PFS in DLBCL.

Introduction

Among common types of non-Hodgkin's lymphoma, diffuse large B-cell lymphoma (DLBCL) accounts for approximately 35% of lymphoma cases in western countries (1-3). Most often, chemoimmunotherapy with standard regimens such as R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine prednisone) is the treatment for DLBCL patients. However, prognosis of these patients is highly heterogeneous and it is

very difficult to predict the final outcome of the disease in the patients. In addition, about 40% of DLBCL patients experience relapse or are resistant to treatment (4, 5).

In the recent years, several prognostic factors such as Hemoglobin, Lymphocyte/Monocyte Ratio, Beta-2 microglobulin, and Neutrophil/Lymphocyte Ratio have been proposed to project the survival rate of DLBCL patients (6-9). Nevertheless, easier and more available factors with high sensitivity are required for prediction of prognosis of DLBCL patients. Red blood cell distribution width (RDW) is considered a systemic inflammatory response marker that can be easily evaluated through the Complete Blood Count (CBC) test and has acceptable sensitivity in many diseases such as cardiovascular and autoimmune diseases and sepsis (10-13). D-Dimer as a sensitive index of the process of fibrin formation and destruction is widely used in the deep venous thrombosis detection, intravascular coagulation, sickle cell anemia, and myocardial infarction (14-18). Recent studies introduced that tumor-related degradation products for the coagulation and fibrinolytic system, such as D-Dimer, can be used as outcomes prediction for tumor (19). Furthermore, scientific evidence recently revealed the association of RDW and D-Dimer with many cancers such as breast cancer (20-22), lung cancer (23, 24), blood cancers (25-27), prostate cancer (28), and other malignancies (29-32). However, the prognostic roles of RDW and D-Dimer in cancer and its possible mechanism in tumor progression are being discussed. Besides, several studies indicated that D-Dimer had a possible role in proliferation of cancer cells, adhesion, and angiogenesis, which may bring about malignant tumors growth. Cancer patients usually face hypercoagulable states that increase the risk of embolism. Hence, D-Dimer levels have prognostic role and are associated with survival of patients with cancer. Considering the differences between the results of the studies regarding sample sizes, study designs, and the controversy among the results, we deemed it necessary to conduct a meta-analysis regarding comprehensively investigating the RDW and D-Dimer prognostic roles among patients with DLBCL.

Materials and Methods

We utilized the Checklist of Meta-analysis of Observational Studies (33) and preferred reporting items for systematic reviews and meta-analyses (PRISMA) standard (34) to perform this study. The protocol was registered with the number of CRD42023417907 at the international prospective register of systematic reviews database (PROSPERO).

Search Strategy

A systematic search in PubMed, Medline, SCOPUS, Web of Science Core Collection, EMBASE, and Google Scholar databases was carried out to find the records from inception to 30 April 2023. Using the keywords including RDW, red blood cell distribution width, DLBCL, diffuse large B-cell lymphoma, lymphoma diffuse, large B-cell, fibrin fragment D, D-dimer, D-dimer fibrin, and D-dimer fragments, two researchers (KR and RS) searched in the mentioned databases separately and blindly. Inconsistencies in some articles were also solved by other researchers (NAN, MR, MF and NK). Finally, duplicates were identified by title of the papers, authors' names, and journals' names.

Eligibility Criteria

We included all the observational studies which examined the role of RDW and D-dimer as prognostic factors in DLBCL cases and also published in English without time and place restriction. On the other hand, studies such as case reports, case series, letters, and correspondence studies were among our exclusion criteria (Flowchart 1). The articles conducted regarding autoimmune diseases, Immunosuppression, patients with mental disorders, and those undergoing dialysis were excluded as well. In addition, the studies with lack of sufficient information on overall survival (OS) as well as progression-free-survival (PFS) of DLBCL subjects were excluded from the review process.

Data Extraction and Quality Assessment

Articles were screened independently by two researchers (RT and RM) (according to Flowchart 1) and disagreements resolved through discussions with other researchers. The extracted information included author's first name, study location, study type, type of marker investigated, year of publication, type of

survival analysis performed, mean follow-up period, sample size, and a summary of the cut-off points for the markers investigated. OS is usually the time length from the beginning of medical treatment until outcome occurrence (death whether or end of the follow-up period of the patient). PFS is the duration when the treatment is started until tumor progresses or death happens for any reason. In order to evaluate quality of the articles, two researchers (MR and AH) independently used the checklist of Newcastle Ottawa Scale (NOS) (35). The articles with a total score of [?]7 were considered as high-quality.

Statistical Analysis

We used R version 4.3.0 for performing the statistical analysis. I^2 and χ^2 statistics were applied for assessing the heterogeneity of the studies and the significance level for heterogeneity between the studies was considered $I^2 > 50\%$ and P value <0.1. We used a random effect model so as to compute Pooled Hazard Ratio with 95% confidence interval and the Inverse Variance method was applied to weight the studies. The researchers also used funnel plot and Eggers' test to check the publication bias in the studies and the asymmetric funnel plot was considered as a possible publication bias. Sensitivity analysis was utilized to examine the heterogeneity source between the records. The significance level in this study was considered < 0.05.

Figure 1. PRISMA flow diagram illustrating the process of selection studies in the meta-analysis

Results

A total of 13 studies (1, 6, 7, 16, 19, 36-43) were included in our study (PRISMA flow diagram) based on the searched databases. Overall, eight studies (1, 6, 7, 37, 39-41, 43) focused on the role of RDW and the remaining five studies (16, 19, 36, 38, 42) focused on D-Dimer levels in DLBCL patients. The included studies were published from 2015 to 2022. All included articles were retrospective cohorts. Eight studies were conducted in China (7, 16, 19, 36, 38-40, 43) and others were conducted in Croatia (41), Iraq (37), Japan (42), Peru (1), and Spain (6). The total sample size of the meta-analysis was 3972 people (1252 and 2720 patients in the studies were related to prognostic roles of D-Dimer and RDW in DLBCL patients, respectively) varying from 81 to 992 people in the included studies. Other details of the included studies are shown briefly in Table 1.

Overall Survival in RDW and D-Dimer

To examine the relationship between the RDW in DLBCL patients and OS, seven studies (1, 7, 37, 39-41, 43) with 1728 patients were included. Our findings showed that RDW levels had relationship with OS. The pooled analysis presented a significant association between increased RDW and adverse OS of the patients (HR_{Pooled}= 2.01, 95% CI: 1.62-2.48, P value<0.01) (Table 1) (Plot 2). Examining the correlation between the D-Dimer and OS among the patients with DLBCL was performed by four studies (16, 19, 38, 42) with 1066 patients and D-Dimer levels correlated with poorer OS. The combined results also demonstrated that increased D-Dimer was associated with worse OS of the patients (HR_{Pooled}= 2.30, 95% CI: 1.03-5.14, P value<0.05) (Plot 3).

Progression-Free-Survival and RDW

Five studies (6, 7, 37, 39, 43) with 2169 patients reported the relationship between the RDW levels and PFS. In this study, the pooled HRs showed that increased RDW correlated with worse PFS in the DLBCL patients (HR_{Pooled}=1.52, 95% CI: 1.24-1.85, P value<0.01) (Plot 4).

Sensitivity Analysis

With respect to the sensitivity analysis, the results did not show significant difference between the included articles regarding the relationship between RDW and D-Dimer and OS, and the relationship between RDW and PFS among the DLBCL patients (supplementary file Figs 1, 2 and 3).

Publication Bias

The Funnel Plot and Eggers' test were used so as to evaluate publication bias of the studies. We found no significant bias in the articles included in this study (Eggers' test P value > 0.05). (Figs 5, 6 and 7).

Table1- Summary of studies on the prognostic factors such as RDW and D-Dimer among patients with DLBCL

First Author	Type of Study	Country	Year	Type of Marker	Description
Atsushi Tanaka (42)	Retrospective	Japan	2018	D-Dimer	Cut-off value of D-dimer <
Yu-di GENG (19)	Retrospective	China	2019	D-Dimer	Cut-off value of D-dimer 0.9
Shaobo Duan (36)	Retrospective	China	2022	D-Dimer	-
Bin Liu (16)	Retrospective	China	2018	D-Dimer	Cut-off value of D-dimer [?]
Haobo Huang (38)	Retrospective	China	2021	D-Dimer	Cut-off value of D-dimer [?]
Brady E. Beltran (1)	Retrospective	Peru	2019	RDW	High RDW (> 14.6%) and
Leyre Bento (6)	Retrospective	Spain	2019	RDW	RDW ratio>0.96 according
Kawa Muhamedamin Hasan (37)	Retrospective	Iraq	2021	RDW	High RDW ([?] 14.85%) an
Vlatka Periša (41)	Retrospective	Croatia	2015	RDW	Elevated RDW >15%, Norı
Danhui Li (39)	Retrospective	China	2022	RDW	High RDW ([?] 13.40%), Lo
Shujuan Zhou (43)	Retrospective	China	2017	RDW	High RDW ([?] 14.1%) and
Manman Li (40)	Retrospective	China	2019	RDW	High RDW (> 14.35%) and
Haizhu Chen (7)	Retrospective	China	2022	RDW	High RDW ([?] 14.50%) an

LD ; Low D-Dimer, **HD** ; High D-Dimer, **OS** ; Overall Survival, **PFS** ; Progression Free Survival, **EFS** ; Event Free Survival, **NOS** ; Newcastle–Ottawa Quality Assessment Scale.

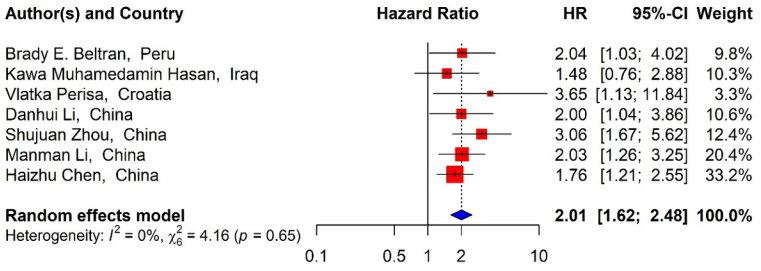

Fig 2- Forest plots of studies evaluating the relationship between RDW and OS

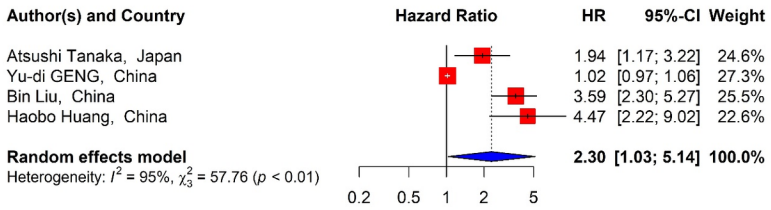

Fig 3- Forest plots of studies evaluating the relationship between D-Dimer and OS

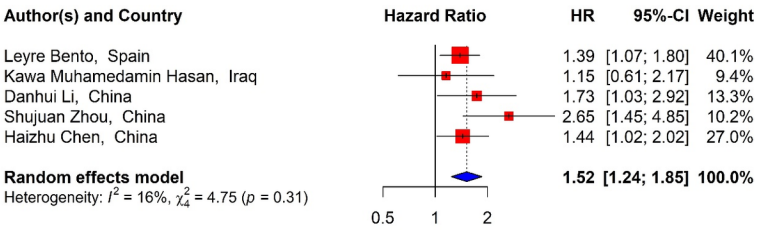

Fig 4- Forest plots of studies evaluating the relationship between RDW and PFS

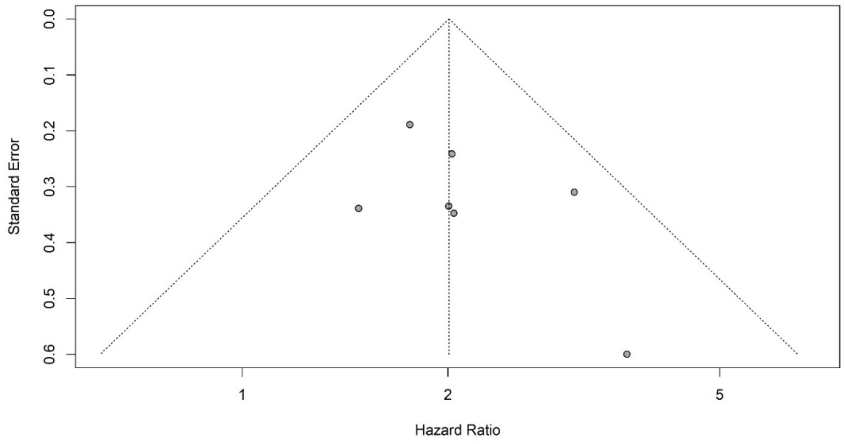

Fig 5 - Funnel Plot with pseudo 95% Confidence Limits for RDW and OS

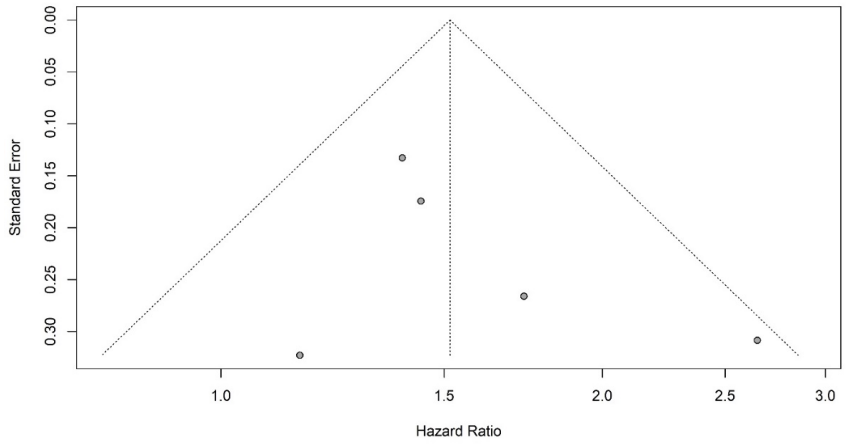

Fig 6 - Funnel Plot with pseudo 95% Confidence Limits for RDW and PFS

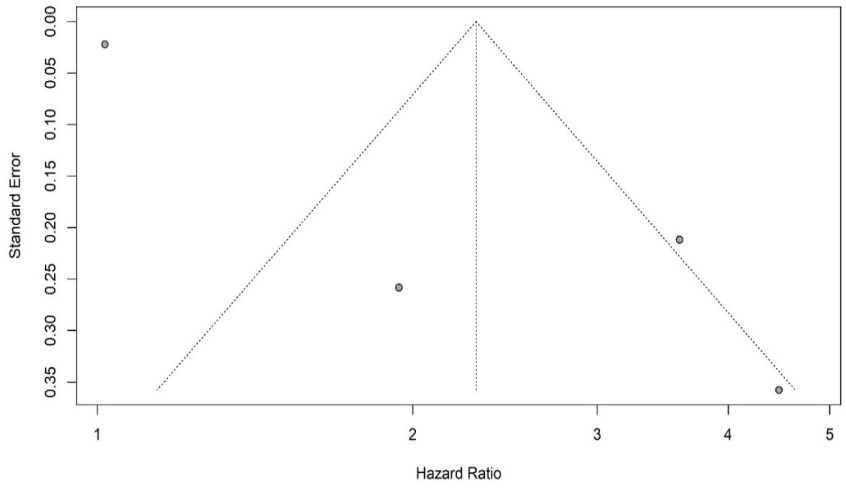

Fig 7 - Funnel Plot with pseudo 95% Confidence Limits for D-Dimer and OS

Discussion

The prognostic roles of RDW and D-Dimer were explored in subjects with DLBCL. We observed that high RDW and D-Dimer were two prognostic factors related to OS and PFS among DLBCL cases. Recently, evidence has been confirmed the relationship between RDW and poor prognosis in various cancers (44, 45). Furthermore, increased RDW was associated with worse prognosis in blood malignancies such as chronic myeloid leukemia (46), chronic lymphocytic leukemia (47), NK/T lymphoma (48), multiple myeloma (49), and DLBCL (40).

Inflammation is a pivotal factor which plays a role in progression of tumor and is known as one of its prominent features (25, 50). In this study, the pooled analysis results revealed that high values of RDW

were associated with poor PFS and OS. Although the main mechanism of the relationship between RDW and the prognosis of DLBCL patients has not been clearly and fully investigated, high RDW can be attributed to the disturbance in erythropoiesis and the changes in red blood cell maturation (51).

Some findings have provided evidence that there is an association between RDW and some markers such as IL-6, CRP (C - reactive protein), TNF-I and II (Tumor Necrosis Factor), TK (Thymidine Kinase), ESR (Erythrocyte Sedimentation Rate), and Ferritin which the accuracy and sensitivity in DLBCL patients are in a state of ambiguity (13). The relationship between RDW and malnutrition conditions might be explained by treatment with poor response and poor prognosis of patients who suffer from cancer (41). In addition, the disruption in iron absorption and metabolism mechanism observed in most cancers also contributes to increase the level of RDW (52), and increased RDW is considered as a turning point in the relationship between inflammation and worse prognosis of subjects who suffer from DLBCL. On the other hand, poor coagulation conditions are associated with poor prognosis and the outcomes such as VTE (venous thrombosis embolism) and DIC (disseminated intravascular coagulation).

Treatment of various cancers is associated with hypercoagulable states and according to the evidence, the changes in coagulation and fibrinolysis pathways have a great impact on cancer prognosis (19).Moreover, tumor-related degradation products such as D-Dimer as a prognostic factor of the final outcome should be used in all types of cancer (20, 26, 29). Some studies have indicated that elevated D-Dimer values as a suitable factor in solid tumor patients is associated with poor prognosis (53) and D-Dimer decreases significantly after the first chemotherapy (19). Also, it has been proved that there is an association between values of D-Dimer and tumor progression, distant metastasis, and tumor volume (54, 55). However, our pooled analysis results showed that by increasing in the D-Dimer values as a prognostic factor, we witnessed worsening OS in the DLBCL patients.

In this study, our findings determined the prognostic role of RDW and D-Dimer in DLBCL patients. Since the values of RDW and D-Dimer can be easily accessible in the patient tests at low cost, considering to these prognostic indicators would be helpful in the prognosis of DLBCL patients. However, the present study had some limitations. As a result of small number of publications on the role of D-Dimer in DLBCL patients, it was not possible to provide PFS in this study. On the other hand, the basic values for grouping the individuals based on RDW were different in the studies. Therefore, we could not be able to conduct subgroup analysis.

Conclusion

This meta-analysis indicated that high values of RDW and D-Dimer were significantly associated with low prognosis and poor OS and PFS in DLBCL patients. Due to availability in routine laboratory tests and affordability, they could be helpful in disease progression and prognosis of DLBCL patients and also in clinical decisions. Nevertheless, doing further studies in this field seems necessary.

Author contribution:

KR, RSH, MN and MF designed and implemented the study, performed analysis, interpreted the data, and contributed to drafting the manuscript. MR and AH assessed quality of studies. KR, NK, AMS and MS interpreted the data, drafted and revised the manuscript. RT and RM extracted the data and contributed to the data management. All authors read and approved the submitted manuscript.

Acknowledgment:

Not applicable.

Funding:

Not applicable.

Conflict of interest statement:

Not applicable.

Data availability:

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethnical approval statement:

Not applicable.

Patient consent statement:

Not applicable.

References:

1. Beltran BE, Paredes S, Castro D, Cotrina E, Sotomayor EM, Castillo JJ. High red cell distribution width is an adverse predictive and prognostic factor in patients with diffuse large B-Cell lymphoma treated with chemoimmunotherapy. Clinical Lymphoma Myeloma and Leukemia. 2019;19(9):e551-e7.

2. Coiffier B, Lepage E, Brière J, Herbrecht R, Tilly H, Bouabdallah R, et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. New England Journal of Medicine. 2002;346(4):235-42.

3. Martelli M, Ferreri AJ, Agostinelli C, Di Rocco A, Pfreundschuh M, Pileri SA. Diffuse large B-cell lymphoma. Critical reviews in oncology/hematology. 2013;87(2):146-71.

4. Friedberg JW. New Strategies in Diffuse Large B-cell Lymphoma: Translating Findings from Gene Expression Analyses into Clinical PracticeDLBCL Gene Expression Profiling. Clinical Cancer Research. 2011;17(19):6112-7.

5. Vaidya R, Witzig T. Prognostic factors for diffuse large B-cell lymphoma in the R (X) CHOP era. Annals of oncology. 2014;25(11):2124-33.

6. Bento L, Díaz-Lopez A, Barranco G, Martin-Moreno AM, Baile M, Martin A, et al. New prognosis score including absolute lymphocyte/monocyte ratio, red blood cell distribution width and beta-2 microglobulin in patients with diffuse large B-cell lymphoma treated with R-CHOP: Spanish Lymphoma Group Experience (GELTAMO). British journal of haematology. 2020;188(6):888-97.

7. Chen H, Zhong Q, Zhou Y, Qin Y, Yang J, Liu P, et al. Enhancement of the International prognostic index with β2-microglobulin, platelet count and red blood cell distribution width: a new prognostic model for diffuse large B-cell lymphoma in the rituximab era. BMC cancer. 2022;22(1):583.

8. Li Z-M, Huang J-J, Xia Y, Sun J, Huang Y, Wang Y, et al. Blood lymphocyte-to-monocyte ratio identifies high-risk patients in diffuse large B-cell lymphoma treated with R-CHOP. PloS one. 2012;7(7):e41658.

9. Wang J, Zhou X, Liu Y, Li Z, Li X. Prognostic significance of neutrophil-to-lymphocyte ratio in diffuse large B-cell lymphoma: A meta-analysis. PLoS One. 2017;12(4):e0176008.

10. Förhécz Z, Gombos T, Borgulya G, Pozsonyi Z, Prohászka Z, Jánoskuti L. 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. 2009;158(4):659-66.

11. Jo YH, Kim K, Lee JH, Kang C, Kim T, Park H-M, et al. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. The American journal of emergency medicine. 2013;31(3):545-8.

12. Lee WS, Kim T-Y. Relation between red blood cell distribution width and inflammatory biomarkers in rheumatoid arthritis. Archives of pathology & laboratory medicine. 2010;134(4):505-6.

13. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Archives of pathology & laboratory medicine. 2009;133(4):628-32.

14. Bick RL, Baker WF. Diagnostic efficacy of the D-dimer assay in disseminated intravascular coagulation (DIC). Thrombosis research. 1992;65(6):785-90.

15. Fronas S, Wik HS, Dahm AEA, Jørgensen CT, Gleditsch J, Raouf N, et al. Safety of D-dimer testing as a stand-alone test for the exclusion of deep vein thrombosis as compared with other strategies. Journal of Thrombosis and Haemostasis. 2018;16(12):2471-81.

16. Liu B, Li B, Zhou P, Yue W, Wang T, Wang J, et al. Prognostic value of pretreatment plasma D-dimer levels in patients with diffuse large B cell lymphoma (DLBCL). Clinica Chimica Acta. 2018;482:191-8.

17. Puurunen MK, Enserro D, Xanthakis V, Larson MG, Benjamin EJ, Tofler GH, et al. Biomarkers for the prediction of venous thromboembolism in the community. Thrombosis Research. 2016;145:34-9.

18. Rowbotham B, Whitaker A, Masci P. Plasma cross-linked fibrin degradation product (XLFbDP) assays in an in vivo model of fibrinolysis. Blood coagulation & fibrinolysis: an international journal in haemostasis and thrombosis. 1990;1(6):653-61.

19. Geng Y-d, Chen Y-r, Jin J, Wang X-d, Zhang S, Li D-j. Prognostic value of D-dimer in patients with diffuse large B-cell lymphoma: a retrospective study. Current Medical Science. 2019;39:222-7.

20. Desch A, Gebhardt C, Utikal J, Schneider SW. D-dimers in malignant melanoma: Association with prognosis and dynamic variation in disease progress. International Journal of Cancer. 2017;140(4):914-21.

21. Takeuchi H, Abe M, Takumi Y, Hashimoto T, Miyawaki M, Okamoto T, et al. Elevated red cell distribution width to platelet count ratio predicts poor prognosis in patients with breast cancer. Scientific reports. 2019;9(1):1-7.

22. Yao D, Wang Z, Cai H, Li Y, Li B. Relationship between red cell distribution width and prognosis in patients with breast cancer after operation: a retrospective cohort study. Bioscience Reports. 2019;39(7).

23. Koma Y, Onishi A, Matsuoka H, Oda N, Yokota N, Matsumoto Y, et al. Increased red blood cell distribution width associates with cancer stage and prognosis in patients with lung cancer. PloS one. 2013;8(11):e80240.

24. Wang Y, Zhou Y, Zhou K, Li J, Che G. Prognostic value of pre-treatment red blood cell distribution width in lung cancer: a meta-analysis. Biomarkers. 2020;25(3):241-7.

25. Ai L, Mu S, Hu Y. Prognostic role of RDW in hematological malignancies: a systematic review and meta-analysis. Cancer cell international. 2018;18:1-8.

26. Geng Y, Jian C, Yang S, Wu S, Zhou J, Li D. The prognostic value of d-dimer in de novo acute myeloid leukemia. The American Journal of the Medical Sciences. 2016;352(2):129-33.

27. Herraez I, Bento L, Del Campo R, Sas A, Ramos R, Ibarra J, et al. Prognostic role of the red blood cell distribution width (RDW) in Hodgkin lymphoma. Cancers. 2020;12(11):3262.

28. Albayrak S, Zengin K, Tanik S, Bakirtas H, Imamoglu A, Gurdal M. Red cell distribution width as a predictor of prostate cancer progression. Asian Pacific Journal of Cancer Prevention. 2014;15(18):7781-4.

29. Feng J-F, Yang X, Chen S, Zhao Q, Chen Q-X. Prognostic value of plasma D-dimer in patients with resectable esophageal squamous cell carcinoma in China. Journal of Cancer. 2016;7(12):1663.

30. Han F, Liu Y, Cheng S, Sun Z, Sheng C, Sun X, et al. Diagnosis and survival values of neutrophil-lymphocyte ratio (NLR) and red blood cell distribution width (RDW) in esophageal cancer. Clinica Chimica Acta. 2019;488:150-8.

31. Wang P-F, Song S-Y, Guo H, Wang T-J, Liu N, Yan C-X. Prognostic role of pretreatment red blood cell distribution width in patients with cancer: A meta-analysis of 49 studies. Journal of Cancer. 2019;10(18):4305.

32. Yuksel C, Ersen O, Cuclu S, Bakırarar B, Ünal A, Demirci S. Prognostic role of red distribution width (RDW) value in gastric cancer. Journal of the College of Physicians and Surgeons Pakistan. 2021;31(1).

33. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Jama. 2000;283(15):2008-12.

34. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology. 2009;62(10):e1-e34.

35. Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa: Ottawa Hospital Research Institute. 2011;2(1):1-12.

36. Duan S, Zhang Y, Xu S, Jiang P, Qi Q. Contrast-Enhanced Ultrasound Parameters and D-Dimer: New Prognostic Parameters for Diffuse Large B-Cell Lymphoma. Cancer Management and Research. 2022:2535-44.

37. Hasan KM, Elmeshhedany AY. Prognostic value of absolute lymphocyte/monocyte ratio, red cell distribution width and neutrophil/lymphocyte ratio in diffuse large B-cell lymphoma patients. Cellular and Molecular Biology. 2021;67(3):61-8.

38. Huang H, Fan L, Fu D, Lin Q, Shen J. High pretreatment plasma D-dimer levels predict poor survival in patients with diffuse large B-cell lymphoma in the real world. Translational Cancer Research. 2021;10(4):1723.

39. Li D, Li S, Xia Z, Cao J, Zhang J, Chen B, et al. Prognostic significance of pretreatment red blood cell distribution width in primary diffuse large B-cell lymphoma of the central nervous system for 3P medical approaches in multiple cohorts. EPMA Journal. 2022;13(3):499-517.

40. Li M, Xia H, Zheng H, Li Y, Liu J, Hu L, et al. Red blood cell distribution width and platelet counts are independent prognostic factors and improve the predictive ability of IPI score in diffuse large B-cell lymphoma patients. BMC cancer. 2019;19:1-11.

41. Periša V, Zibar L, Sinčić-Petričević J, Knezović A, Periša I, Barbić J. Red blood cell distribution width as a simple negative prognostic factor in patients with diffuse large B-cell lymphoma: a retrospective study. Croatian medical journal. 2015;56(4):334-43.

42. Tanaka A, Shimomura Y, Yabushita T, Ishikawa T. High Pretreatment Plasma D-Dimer Levels Are Associated with Poor Prognosis in Patients with Newly Diagnosed Diffuse Large B-Cell Lymphomas Treated with Immunochemotherapy. Blood. 2018;132:4219.

43. Zhou S, Fang F, Chen H, Zhang W, Chen Y, Shi Y, et al. Prognostic significance of the red blood cell distribution width in diffuse large B-cell lymphoma patients. Oncotarget. 2017;8(25):40724.

44. Riedl J, Posch F, Königsbrügge O, Lötsch F, Reitter E-M, Eigenbauer E, et al. Red cell distribution width and other red blood cell parameters in patients with cancer: association with risk of venous thromboembolism and mortality. PloS one. 2014;9(10):e111440.

45. Yilmaz A, Malya F, Ozturk G, Çitgez B, Ozdenkaya Y, Ersavas C, et al. Effect of pre-operative red blood cell distribution on cancer stage and morbidity rate in patients with pancreatic cancer. International journal of clinical and experimental medicine. 2014;7(9):3072.

46. Iriyama N, Hatta Y, Kobayashi S, Uchino Y, Miura K, Kurita D, et al. Higher red blood cell distribution width is an adverse prognostic factor in chronic-phase chronic myeloid leukemia patients treated with tyrosine kinase inhibitors. Anticancer Research. 2015;35(10):5473-8.

47. Podhorecka M, Halicka D, Szymczyk A, Macheta A, Chocholska S, Hus M, et al. Assessment of red blood cell distribution width as a prognostic marker in chronic lymphocytic leukemia. Oncotarget. 2016;7(22):32846.

48. Luo H, Quan X, Song X-Y, Zhang L, Yin Y, He Q, et al. Red blood cell distribution width as a predictor of survival in nasal-type, extranodal natural killer/T-cell lymphoma. Oncotarget. 2017;8(54):92522.

49. Wang J, Xie X, Cheng F, Zhou X, Xia J, Qian X, et al. Evaluation of pretreatment red cell distribution width in patients with multiple myeloma. Cancer Biomarkers. 2017;20(3):267-72.

50. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. nature. 2008;454(7203):436-44.

51. Demirkol S, Balta S, Cakar M, Unlu M, Arslan Z, Kucuk U. Red cell distribution width: A novel infl ammatory marker in clinical practice. Cardiology Journal. 2013;20(2):209-.

52. Macciò A, Madeddu C, Gramignano G, Mulas C, Tanca L, Cherchi MC, et al. The role of inflammation, iron, and nutritional status in cancer-related anemia: results of a large, prospective, observational study. haematologica. 2015;100(1):124.

53. Ay C, Dunkler D, Pirker R, Thaler J, Quehenberger P, Wagner O, et al. High D-dimer levels are associated with poor prognosis in cancer patients. haematologica. 2012;97(8):1158-64.

54. Dirix LY, Salgado R, Weytjens R, Colpaert C, Benoy I, Huget P, et al. Plasma fibrin D-dimer levels correlate with tumour volume, progression rate and survival in patients with metastatic breast cancer. British journal of cancer. 2002;86(3):389-95.

55. Oya M, Akiyama Y, Okuyama T, Ishikawa H. High preoperative plasma D-dimer level is associated with advanced tumor stage and short survival after curative resection in patients with colorectal cancer. Japanese journal of clinical oncology. 2001;31(8):388-94.