Bull. Pharm. Sci., Assiut University, Vol. 46, Issue 1, 2023, pp. 291-304.

Bulletin of Pharmaceutical Sciences
Assiut University
Website: http://bpsa.journals.ekb.eg/
e-mail: bullpharm@aun.edu.eg

CLINICOPATHOLOGICAL AND PROGNOSTIC SIGNIFICANCE OF PLATELET TO LYMPHOCYTE RATIO IN DIFFUSE LARGE B-CELL LYMPHOMA: A META-ANALYSIS

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Background: *Nowadays, there is a significant but variable correlation between the diffuse large B-cell lymphoma (DLBL) and the platelet-lymphocyte ratio (PLR). This meta-analysis will assess this association.* ***Methods****: A thorough search was done up until June 2022, and 11 research revealed 2284 patients with DLBL. They discovered a connection between DLBL and the PLR. A fixed or random-effect model was used to construct odds ratios (ORs) with 95% confidence intervals (CIs) and examine the prognostic significance of the PLR on overall survival, progression-free survival, and a variety of clinicopathological characteristics.* ***Results:*** *Poor 5-years overall survival (OR, 0.59; 95% CI, 0.36-0.98, p<0.001), poor 2-years progression-free survival subjects (OR, 0.42; 95% CI, 0.27-0.67, p<0.001), and poor 5-years progression-free survival (OR, 0.50; 95% CI, 0.34-0.72, p<0.001) were all significantly correlated with high the PLR. In a similar manner, a high the PLR was strongly correlated with the presence of B-symptoms (OR, 2.22; 95% CI, 1.69-2.93, p<0.001), a high lactate dehydrogenase level (OR, 2.98; 95% CI, 2.19-4.06, p<0.001), a higher tumour stage (OR, 1.84; 95% CI, 1.08-3.13, p=0.03). Nevertheless, there was no significant correlation between a high the PLR and a high Eastern Cooperative Oncology Group performance status ≥2 (OR, 1.44; 95% CI, 0.69-3.02, p=0.33), a high bone marrow infiltration (OR, 1.02; 95% CI, 0.60-1.74, p=0.94), a person's gender (OR, 1.20; 95% CI, 0.93-1.55, p=0.17); age (OR, 0.89; 95% CI, 0.69-1.15, p=0.37); and cell of origin (OR, 1.00; 95% CI, 0.71-1.39, p=0.98).* ***Conclusions:*** *The impact of the PLR on DLBL may be substantial as a technique to enhance prognosis. Patients with DLBL who have a high the PLR may be at an independent risk for having a poor prognosis. To prevent potential problems, we advise keeping track of patients with a high platelet-to-lymphocyte ratio.*

Keywords: *platelet to lymphocyte ratio; Diffuse large B-cell lymphoma; overall survival; progression-free survival; B symptoms; elevated lactate dehydrogenase; higher tumor stage; Eastern Cooperative Oncology Group performance status; international prognostic index; Infiltration of bone marrow*

INTRODUCTION

A typical non-Hodgkin lymphoma subtype that makes up 30–40% of lymphomas worldwide is diffuse large B-cell lymphoma (DLBL)[1&2]. In terms of clinical and biological characteristics, DLBL is a cancer that is aggressive and diverse[3]. More than 60% of DLBLs are cured with the conventional treatment Rituximab (R)-cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), but 30% are recurrent[4]. Prognostic biomarkers have a crucial role in determining treatment options and predicting survival. The International Prognostic Index (IPI), albeit frequently employed in the prediction of DLBL, needs to have better predictive power[5]. Therefore, it is critical to find affordable and accessible prognostic biomarkers. Inflammatory reactions take place during different stages of cancer progression. Indicators derived from haematological factors

Received in 15/11/2022 & Accepted in 8/1/2023

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have recently been researched for cancer prediction[6]. The ratio of platelet counts to lymphocyte counts is known as the platelet-lymphocyte ratio (PLR). The PLR is a prognostic indicator for a number of cancers, including ovarian cancer[7], esophageal cancer[8], DLBL[9], and head and neck squamous cell carcinoma[10]. Despite the fact that a number of recent retrospective studies found a predictive role for the PLR in DLBL, their results were erratic and conflicting[11-21].

In people with DLBL, the PLR was examined to determine whether it was associated with survival. The meta-analysis performed here was to evaluate whether different levels of the PLR are related to higher odds of DLBL prognosis. The study aimed to recognize the relationship between PLR and DLBL subjects' survival.

METHODS

The study performed here followed the meta-analysis of studies in the epidemiology statement,[22] which was conducted following an established protocol.

Study selection

The included studies met the statistical criteria for the relationship between the PLR and DLBL (odds ratio [OR] with 95% confidence intervals [CIs]).

Only human studies in any language were considered. Inclusion was not limited by study size or publication type. Publications excluded were review articles and commentary and studies that did not deliver a measure of association. Figure 1 shows the whole study process.

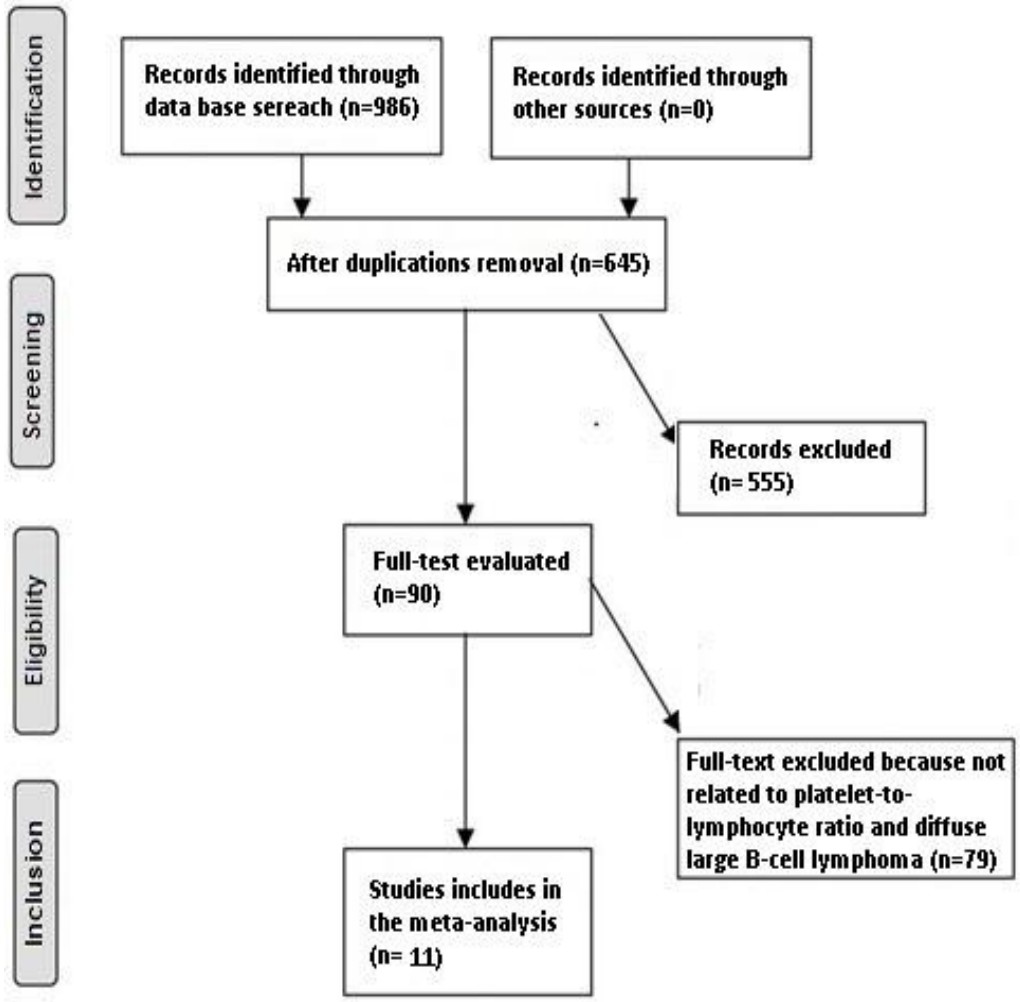

Fig. 1: Flowchart of the study process.

Identification

Based on the PICOS concept[23], we created a search strategy protocol, which we designated as P (population): people with DLBL. "I" (intervention/exposure): different PLR, "C" (comparison): comparisons between persons with DLBL who had differing PLR as a reference (high and low) “O” Poor survival was the outcome of the study and "S" (study design) had no restrictions[24]. Using a combination of keywords and related terms, we first conducted a thorough search of the China Knowledge Resource Integrated Database (CNKI), Embase, PubMed, Cochrane Library, OVID, and Google Scholar up until June 2022. Based on the inclusion and exclusion criteria, all discovered publications were compiled in an EndNote file. Duplicate papers were removed, and the titles and abstracts were updated to omit studies that did not demonstrate a connection between PLR and DLBL. We searched the remaining studies for relevant information.

Screening

Based on study- and topic-related criteria, data were condensed into a specified form. The surname of the first author, the length of the trial, the location of the practise, the research design, the type of study, the sample size, the patient demographics, the method of treatment, the number of participants who had DLBL, the management characteristics, the PLR, the time period for evaluating the PLR with regard to DLBL, the method of evaluation, the information source, and the outcome examination[25]. When there were different data from one study, we extracted them independently. The risk of bias in these studies; individual studies were evaluated using the quality in prognosis studies tool, which evaluates validity and bias in studies of prognostic factors across 6 domains: participation, attrition, prognostic factor measurement, confounding measurement, and account, outcome measurement, and analysis and reporting[26]. Any inconsistencies were addressed by a reevaluation of the original article.

Eligibility

The main discovery focused on the PLR and how it relates to DLBL. Patients with DLBL had their PLR gathered.

Inclusion

Sensitivity studies were limited to articles that discussed the relationship between patients with DLBL and PLR. With different PLR as benchmarks for subcategories and sensitivity analyses, we assessed DLBL participants (high and low).

If the following inclusion criteria were satisfied, the publications were included in the meta-analysis:

1. A retrospective or randomized controlled study design was used for the investigation.
2. The intended subjects consist of those who have DLBL.
3. Patients with DLBL had their PLR assessed as part of the treatment plan.
4. The study used a reference group of patients with DLBL who had different PLR (high and low).

Statistical analysis

The dichotomous method was used to determine the OR on a random or fixed effect model with a 95% confidence interval. The range of the (I2) index was 0 to 100%. The I2 index scale's heterogeneity is classified as zero, low, moderate, and high, or 0%, 25%, 50%, and 75%, respectively[14]. This is thought to be a Random-effect if I2 > 50% and a Fixed-effect if I2 < 50%. By stratifying the results of the initial evaluation into several outcome categories, a subgroup analysis was carried out at the beginning of the evaluation. If the p-value is less than 0.05, the outcome is regarded as statistically significant. The Egger regression test measured publication bias and evaluated it subjectively (if $p \geq 0.05$). The odds ratios' logarithmic funnel plot is therefore contrasted with its standard errors[16]. Utilizing Reviewer Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark), statistics and graphs were produced.

RESULTS AND DISCUSSION

Results

Of the 986 studies found, 11 were included because they satisfied the study's inclusion requirements (between January 2015 and December 2019)[11-21]. In the 11 articles, there were 2284 cases of DLBL. In every study, a PLR was connected to DLBL.

Participants in the trial who had DLBL ranged in number from 59 to 515 at the outset. However, as shown in Table 1, we exclude the Melchardt et al. 2015 study since its cut-off value for the platelet-lymphocyte ratio was higher than three times that of the other ten studies (453 vs. 150, respectively)[14]. Due to their usage of a high cut-off value, we believed that its outcomes might have an impact on the results of the meta-analysis. With regard to overall survival (OS), 10 studies published data stratified patients by the PLR, and ten studies with regard to progression-free survival (PFS). Additionally, the correlation of the platelet to lymphocyte and clinicopathological characteristics were included; seven studies for B-symptoms, six for lactate dehydrogenase level, seven for tumour stage, seven for the international prognostic index (IPI), six for gender, six for age, four for Eastern Cooperative Oncology Group (ECOG) performance status (PS), three for infiltration of bone marrow, and three studies for the tumour microenvironment.

High PLR was significantly related to poor 5-years overall survival (OR, 0.59; 95% CI, 0.36-0.98, $p<0.001$) with high heterogeneity ($I^2 = 81\%$), poor 2-years overall survival (OR, 0.37; 95% CI, 0.24-0.56, $p=0.005$) with moderate heterogeneity ($I^2 = 63\%$), poor 5-years PFS (OR, 0.50; 95% CI, 0.34-0.72, $p<0.001$) with moderate heterogeneity ($I^2 = 63\%$), and poor 2-years PFS subjects (OR, 0.42; 95% CI, 0.27-0.67, $p<0.001$) with moderate heterogeneity ($I^2 = 73\%$) as shown in Figure 2.

Table 1: Characteristics of the selected studies for the meta-analysis.

Study	PLR Cut-off	Duration	Country	Ethnicity	Sample size	Sex (Males /Females)	Age (year)	Stage	Treatment
Melchardt, 2015 [14]	435	2004-2014	Austria	Caucasian	515	270/245	65 (20-92)	I-IV	R-CHOP
Ni, 2016 [15]	270.27	2009-2015	China	Asian	59	36/23	54 (14-75)	I-IV	R-CHOP /CHOP
Periša, 2016 [16]	162.3	2006-2015	Croatia	Caucasian	103	37/66	63 (22-87)	I-IV	R-CHOP
Park, 2016 [13]	150	2004-2012	Korea	Asian	99	53/46	60 (32-81)	I-IV	R-CHOP
Hao, 2017 [17]	150	2003-2014	China	Asian	252	165/87	49 (16-82)	I-IV	R-CHOP /CHOP
Zhao, 2017 [21]	170	2009-213	China	Asian	173	111/62	51 (12-90)	I-IV	R-CHOP
Periša, 2017 [12]	158.65	2006-2013	Croatia	Caucasian	81	29/52	64 (22-85)	I-IV	R-CHOP
Han, 2018 [18]	300	2006-2012	China	Asian	361	203/158	55 (12-91)	III-IV	R-CHOP
Wang, 2018 [20]	150	2005-2016	China	Asian	182	96/86	59 (18-80)	I-IV	R-CHOP
Zhao, 2018 [19]	170	2009-2015	China	Asian	309	186/123	58 (16-90)	I-IV	R-CHOP
Lin, 2019 [11]	143	2013-2017	China	Asian	150	96/54	56 (15-94)	I-IV	R-CHOP /CHOP

R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; PLR: platelet-to-lymphocyte ratio.

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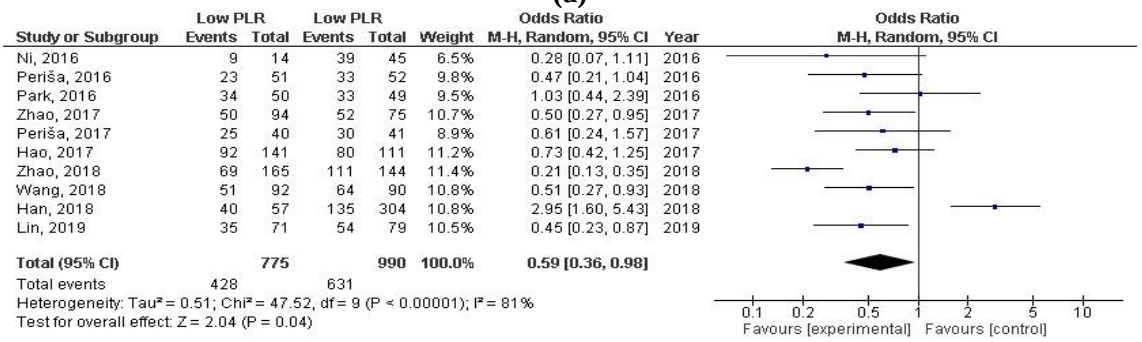

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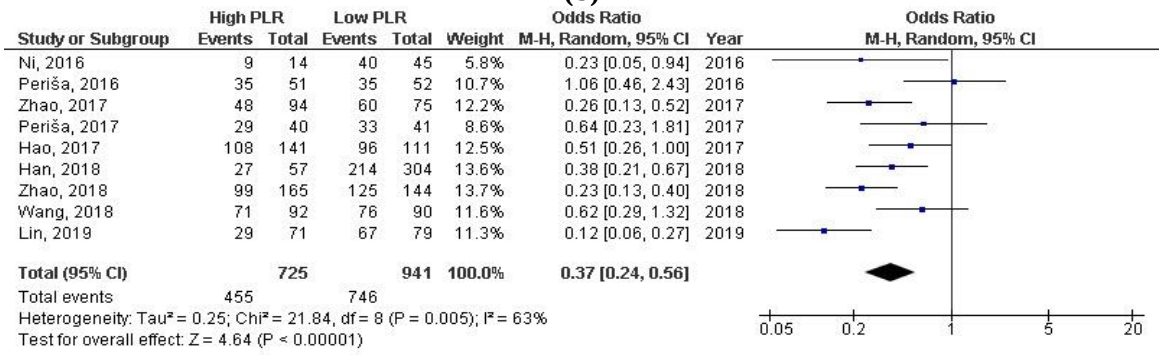

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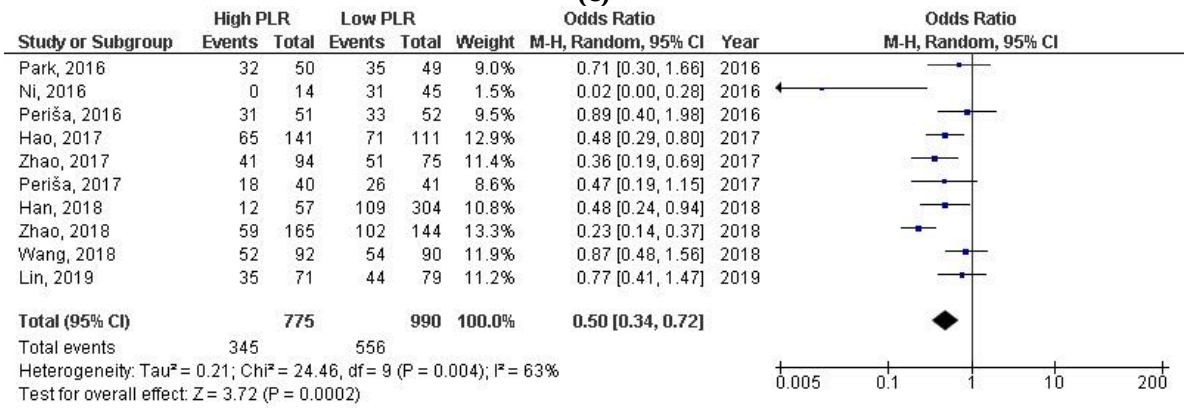

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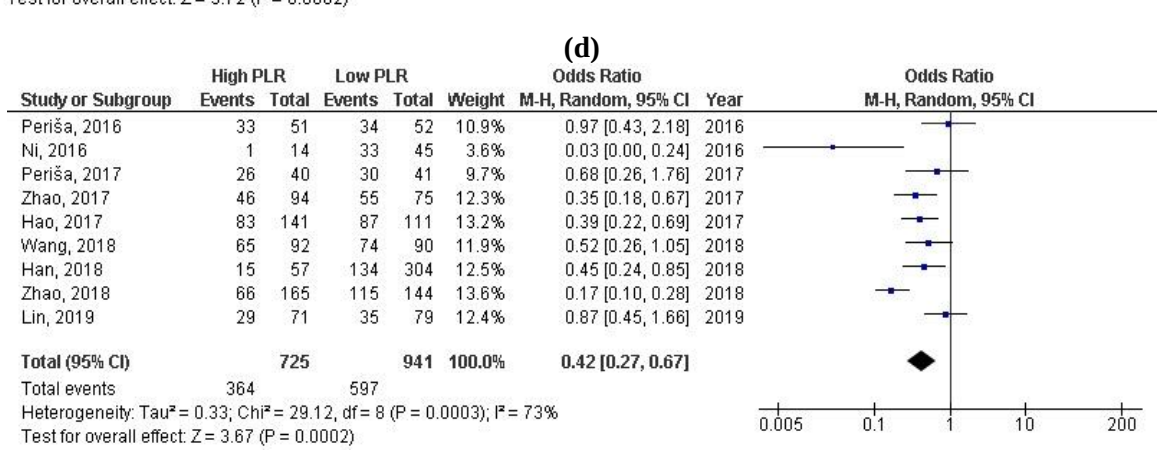

Fig. 2: A forest plot of the PLR in relation to DLBL in a) 5-years overall survival, b) 2-years of overall survival, c) 5-years of PFS, and d) 2-years without progression.

Elevated PLR was significantly related to the presence of B-symptoms (OR, 2.22; 95% CI, 1.69-2.93, p< 0.001) with low heterogeneity (I^2 = 41%); high lactate dehydrogenase (OR, 2.98; 95% CI, 2.19-4.06, p<0.001) with low heterogeneity (I^2 = 26%); higher tumor stage (OR, 1.84; 95% CI, 1.08-3.13, p=0.03) with moderate heterogeneity (I^2 = 72%); and high international prognostic index (OR, 2.41; 95% CI, 1.49-3.91, p<0.001) with moderate heterogeneity (I^2 = 64%) as shown in Figure 3. However, high PLR was not significantly correlated with high ECOG performance status (PS) (OR, 1.44; 95% CI, 0.69-3.02, p=0.33) with moderate heterogeneity (I^2 = 56%); high infiltration of bone marrow (OR, 1.02; 95% CI, 0.60-1.74, p=0.94) with no heterogeneity (I^2 = 0%); gender (OR, 1.20; 95% CI, 0.93-1.55, p=0.17) with no heterogeneity (I^2 = 17%); age (OR, 0.89; 95% CI, 0.69-1.15, p=0.37) with no heterogeneity (I^2 = 0%); or cell of origin (OR, 1.00; 95% CI, 0.71-1.39, p=0.98) with no heterogeneity (I^2 = 0%) as shown in Figure 4.

Stratified analysis of studies that did and did not adjust for different time of PLR detection was not performed because no studies reported or adjusted for this factor or whether higher PLR is related to all cancers or with exact type of cancer.

According to the visual funnel plot analysis and the quantitative Egger regression test evaluation, publication bias was not found (p = 0.88).

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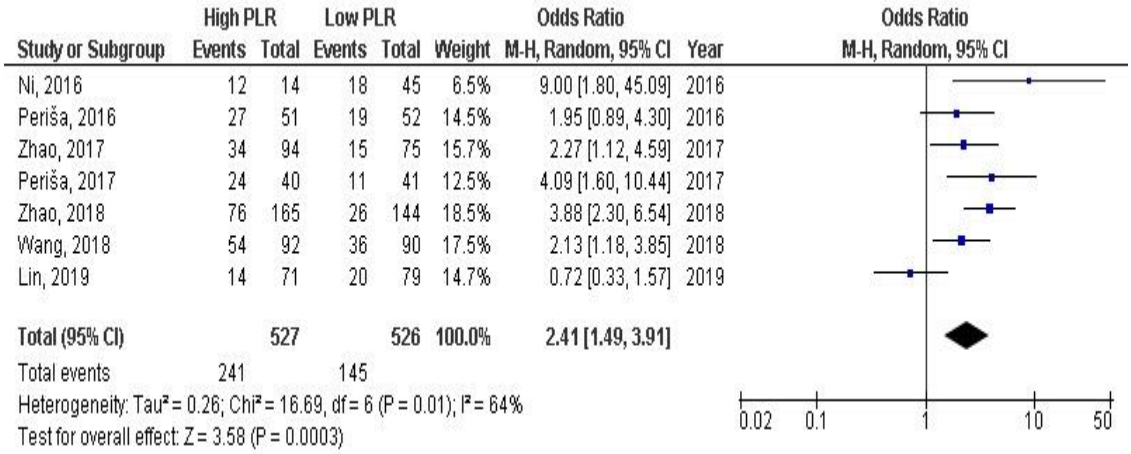

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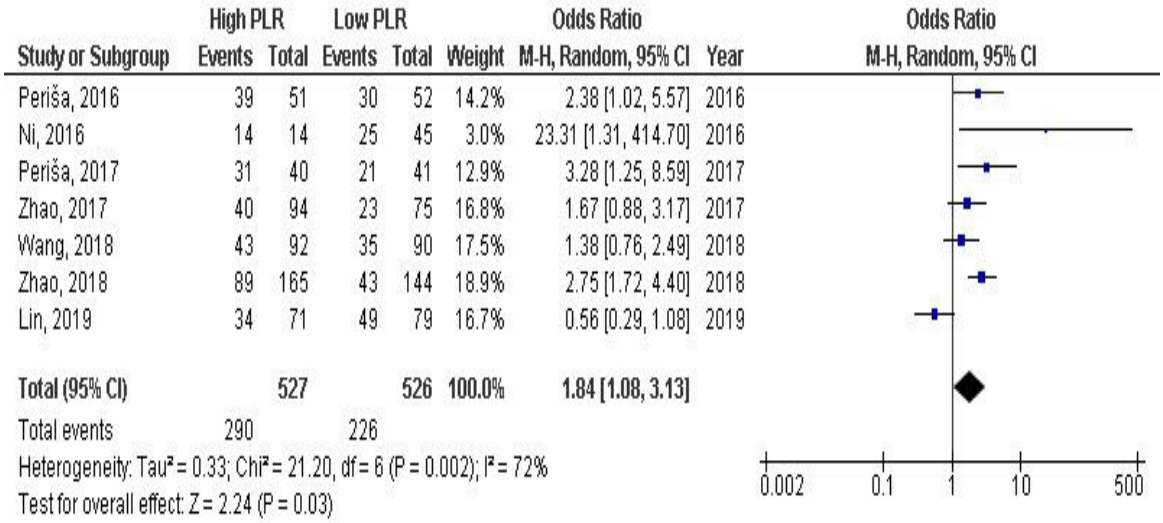

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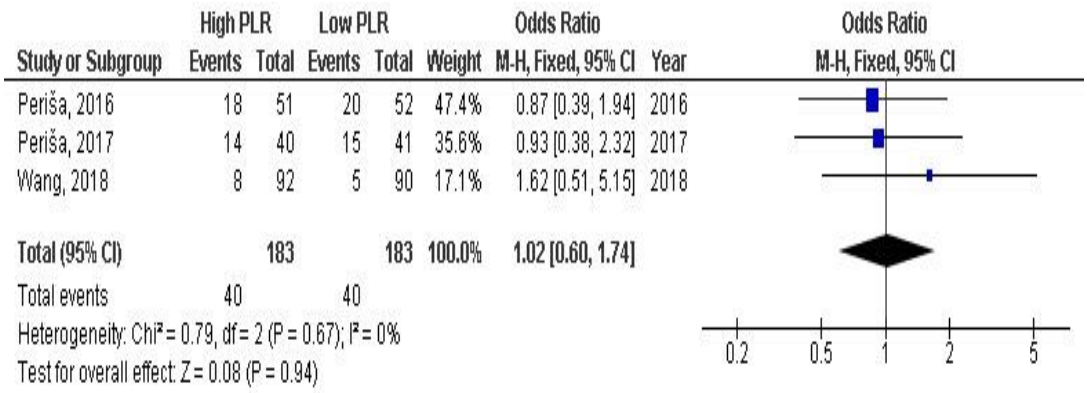

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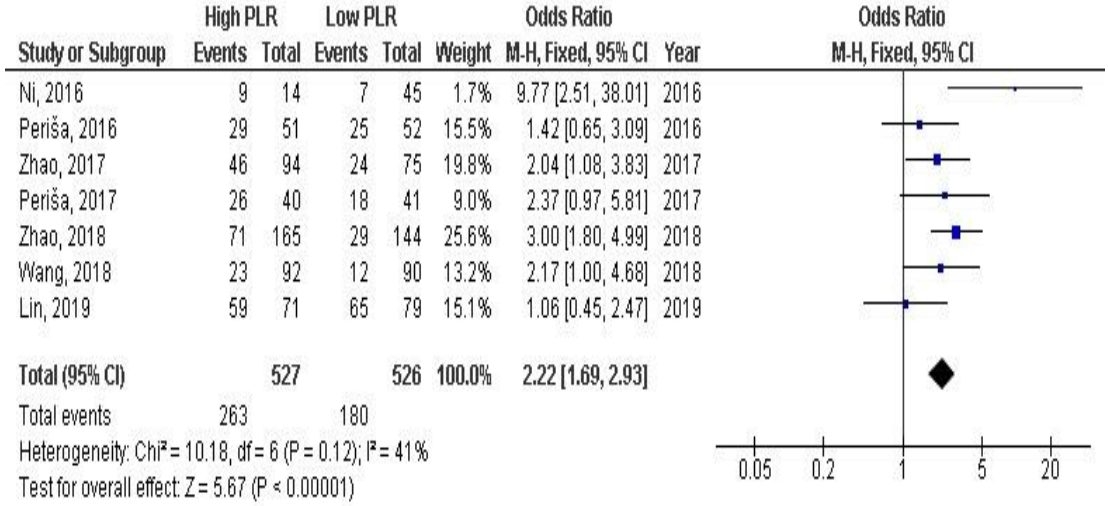

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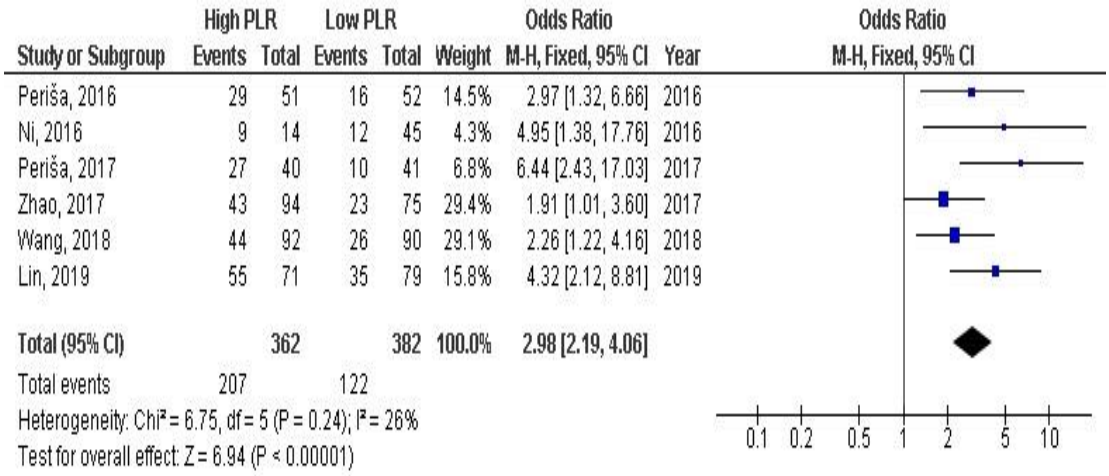
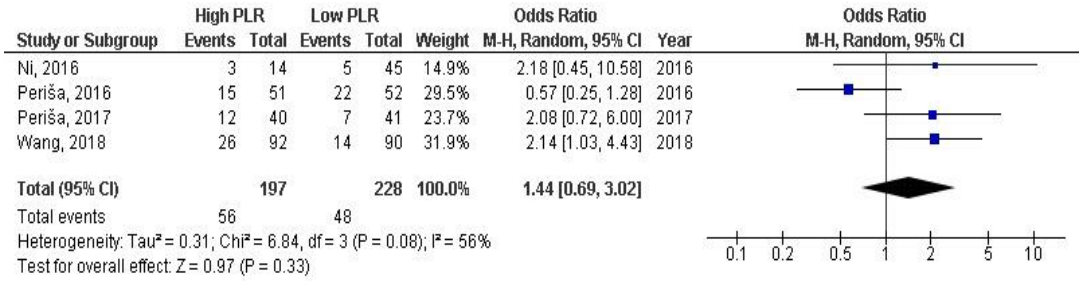


Fig. 3: A forest plot of the PLR in relation to DLBL of the following factors: a) DLBL international prognostic index (IPI) >2; b) DLBL tumour stage (> II); c) DLBL infiltration of bone marrow; d) DLBL B-symptoms; and e) lactate dehydrogenase.

(a)



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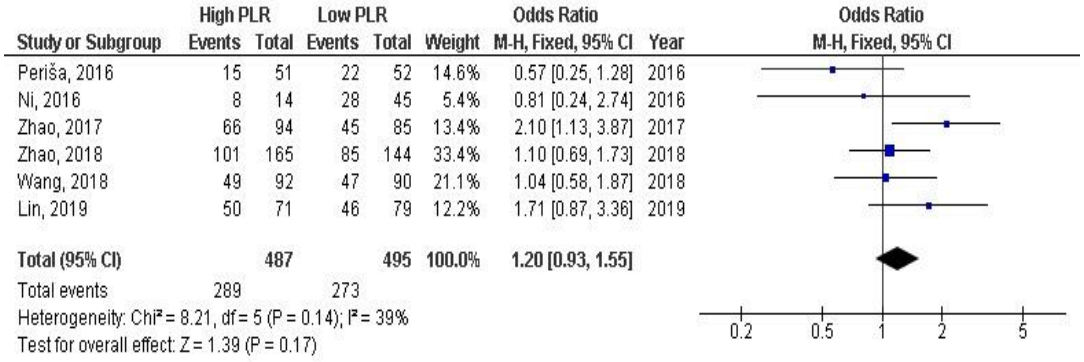

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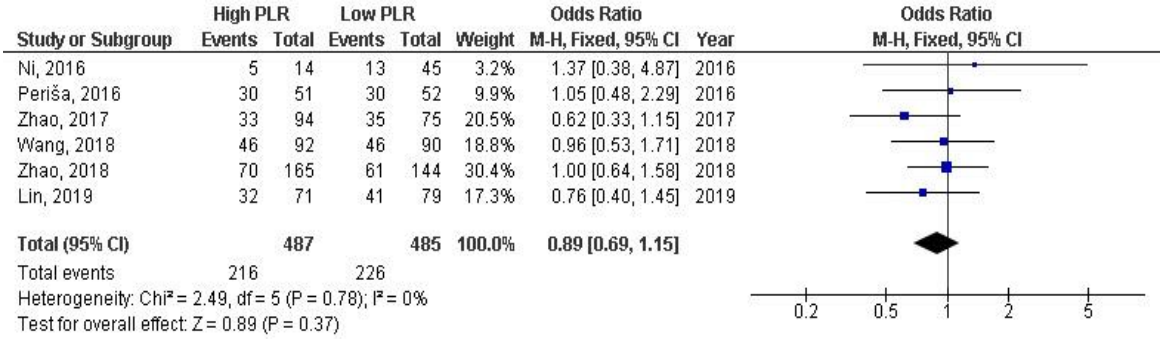

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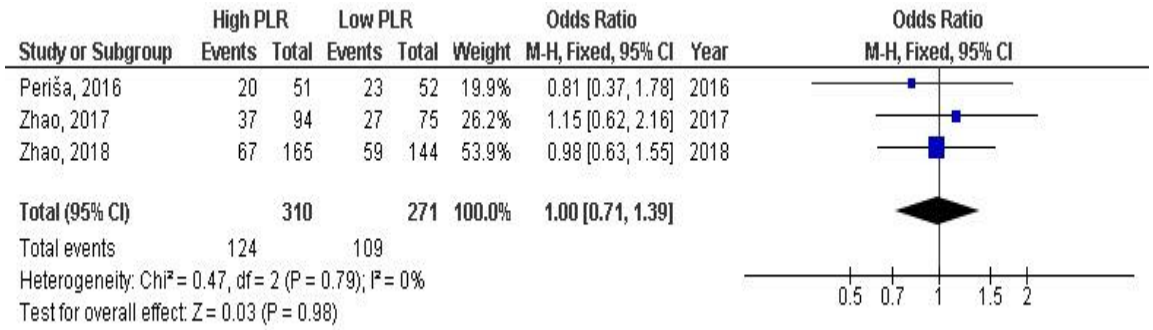

Fig. 4: A forest plot of the PLR in relation to DLBL of the following data: a) an Eastern Cooperative Oncology Group (ECOG) performance status (PS) >2; b) male gender; c) age > 60 years; and; d) cell of origin [germinal center B cell (GCB)].

Discussion

Inflammation has a crucial role in the growth of tumours [27]. Variable results were found when the PLR was examined for the prognosis of patients with DLBL. In patients with DLBL, the PLR has been shown to be predictive, though the results have been mixed [11-21].

We found a higher risk of inadequate overall survival and PFS associated with a high PLR based on 11 studies involving 2284 patients with DLBL [11-21]. According to the statistics, DLBL patients with a high PLR often had poor overall and PFS [28-30].

The only previous meta-analysis on this topic that we could locate stated that DLBL patients with a high PLR have poor overall survival but not PFS [31]. The high the PLR cut-off value from Melchardt et al 2015's study was included in their meta-analysis. This value (453 compared to 150, respectively) was more than thrice that of their other seven studies' lowest the PLR cut-off value [14]. The results of their meta-analysis might have been impacted by the results of this study due to the high the PLR cut-off value [14].

The results also showed a relationship between clinicopathological traits indicative of substantial cancer aggression and the PLR. In this study's DLBL patients, the PLR was a highly significant predictor factor for inadequate overall survival and invasiveness.

A high PLR did not, however, correlate with a high Eastern Cooperative Oncology Group performance. This may be because there were so few studies that met the inclusion criteria for our investigation on the relationship between PLR and Eastern Cooperative Oncology Group performance. The results might be different if other studies with a similar association were found because there was a strong correlation between a high international prognostic score and an elevated PLR. It is suspected that the inflammatory response affects the angiogenesis, growth, and metastasis of cancer[32]. However, the exact mechanism underlying the link between a high PLR and a poor prognosis in patients with DLBL is yet unknown. High platelet counts and low lymphocyte counts can lead to a high PLR. Both the early and late stages of cancer angiogenesis have been linked to platelets [33]. That was obvious in our results where the a high the PLR was strongly correlated with the presence of B-symptoms, a high lactate dehydrogenase level, a higher tumour stage. In the cancer microenvironment, platelets can release a variety of biological chemicals that promote angiogenesis[34]. In addition, platelets start converting growth factor-1 to work with cancer cells to improve pathways connected to the epithelial-mesenchymal transition and promote further metastasis[35]. Immune responses against cancer are negatively impacted by lymphocytes. Cancer cell growth and metastasis can be slowed by lymphocyte-invading tumours, such as CD3+ T cells, CD8+ T cells, and Th1 CD4+ T cells[36]. Therefore, it makes sense to use the PLR as a limit to forecast survival rates in cancer cases.

Changes in PLR measurements may therefore be more useful in predicting DLBL's future stages. People having a higher PLR than those with a lower ratio experienced DLBL with greater power. The need to improve the use of such a crucial haematological marker in predicting DLBL is thus critically raised. Data on the PLR are becoming more readily available and could be utilised as a tool for prognosis and early screening. As a tool for improving early prognosis and therapeutic recommendations in DLBL and identifying those at risk of aggressive DLBL, the PLR is anticipated to have a substantial influence. Changes in PLR measurements may therefore be more useful in predicting the progression of patients with DLBL in the future.

There is a lack of evidence linking an elevated PLR to all cancers or even just some of them.

However, given the results of this study, we advise extending the use of the PLR for DLBL screening and prognosis because it is a simple method for identifying the likelihood of developing DLBL and preventing any unfavourable consequences.

Limitations

The individuals in the 11 studies that were chosen for inclusion were all of the same ethnicity, and all of the investigations were retrospective in nature. We were unable to examine the effects of additional PLR measurements on the stages of DLBL. Furthermore, we were unable to ascertain whether a higher PLR is related to a particular

type of malignancy or all malignancies. The distribution of low and high PLR groups may have been influenced by the fact that different studies used different PLR cut-off values. We were unable to find a significant correlation between a high PLR and Eastern Cooperative Oncology Group performance status due to the dearth of papers exhibiting such a link.

Conclusions

There is a link between a high PLR and a higher likelihood of poor overall survival and PFS. The PLR could be used as a stratification variable in interventional research. Data on the PLR is readily available. Increasing the use of PLR for DLBL screening and prognosis allow early detection of the possibility of risk of DLBL and opposing any possible negative outcome. The PLR was also related to the presence of B-symptoms, high lactate dehydrogenase, higher tumor stage, and high international prognostic index. Large prospective studies with a uniform cut-off value of PLR are needed to validate these findings

List of abbreviations

- CI: confidence interval.
- HR: hazard ratio.
- R-CHOP: rituximab, cyclophosphamide, doxorubicin. vincristine, and prednisone.
- ECOG PS: Eastern Cooperative Oncology Group performance status.
- DLBL: diffuse large B-cell lymphoma.
- PLR: platelet-lymphocyte ratio .
- PFS: progression-free survival.
- IPI: international prognostic index.

REFERENCES

1. K. Gatter and F.Pezzella, "Diffuse large B-cell lymphoma", ***Diagn Histopathol***, 16(2), 69-81 (2010).
2. S. Li, K.H.Young, and L.J.Medeiros, "Diffuse large B-cell lymphoma", ***Pathology,*** 50(1), 74-87 (2018).
3. M. Al-Hamadani, T.M. Habermann, J.R.Cerhan, W.R.Macon, M.J.Maurer, and R.S.Go, "Non-H odgkin lymphoma subtype distribution, geodemographic patterns, and survival in the US: A longitudinal analysis of the N ational C ancer D ata B ase from 1998 to 2011", ***Am J Hematol,*** 90(9), 790-795 (2015).
4. S. Li, Z.Wang, L.Lin, Z.Wu, Q.Yu, F.Gao, J.Zhang, and Y.Xu, "BCL6 rearrangement indicates poor prognosis in diffuse large B-cell lymphoma patients: a meta-analysis of cohort studies", ***J Cancer,*** 10(2), 530-538 (2019).
5. K. Miyazaki, "Treatment of diffuse large B-cell lymphoma", ***J Clin Exp Hematop***, 56(2), 79-88 (2016).
6. A. Meiliana, N.M.Dewi, and A.Wijaya, "The immunobiology of cancer: an update review", ***Indones Biomed J,*** 9(2), 53-72 (2017).
7. Z. Zhao, X.Zhao, J.Lu, J.Xue, P.Liu, and H.Mao, "Prognostic roles of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in ovarian cancer: a meta-analysis of retrospective studies", ***Arch Gynecol Obstet,*** 297(4), 849-857 (2018).
8. J. Deng, P.Zhang, Y.Sun, P.Peng, and Y.Huang, "Prognostic and clinicopathological significance of platelet to lymphocyte ratio in esophageal cancer: a meta-analysis", ***J Thorac Dis,*** 10(3), 1522-1531 (2018).
9. M. Zhang, X.-z.Huang, Y.-x.Song, P.Gao, J.-x.Sun, and Z.-n.Wang, "High platelet-to-lymphocyte ratio predicts poor prognosis and clinicopathological characteristics in patients with breast cancer: a meta-analysis", ***Biomed Res Int,*** 2017, 9503025(2017).
10. Y. Takenaka, R.Oya, Kitamiura, N.Ashida, K. Shimizu, K. Takemura, Y.Yamamoto, and A. Uno, "Platelet count and platelet-lymphocyte ratio as prognostic markers for head and neck squamous cell carcinoma: Meta-analysis", ***Head Neck,*** 40(12), 2714-2723 (2018).
11. H. Lin, Y.Xu, and F.Chen, "Relationship between RDW, PLR and clinical features in patients with DLBCL and its impact on survival prognosis", ***J Clin Hematol (China),*** 32(3), 205-9 (2019).
12. V. Periša, Prognostička vrijednost upalnih bodovnih sustava I širine distribucije eritrocita U bolesnika S B-velikostaničnim limfomom. 2017, Josip Juraj Strossmayer University of Osijek. Faculty of Medicine.

13. L.C. Park, H.S. Lee, E.M. Lee, S.H. Shin , and Y.S. Kim, "prognostic significance of neutrophil lymphocyte ratio and platelet lymphocyte ratio in diffuse large B-cell lymphoma patients treated with R-CHOP", ***Kosin Med J,*** 31(2), 122-133 (2016).
14. T. Melchardt, K.Troppan, L.Weiss, C.Hufnagl, D.Neureiter, W.Tränkenschuh, K.Schlick, F.Huemer, A.Deutsch, and P.Neumeister, "Independent prognostic value of serum markers in diffuse large B-cell lymphoma in the era of the NCCN-IPI", ***J Natl Compr Canc Netw***, 13(12), 1501-1508 (2015).
15. J. Ni, Y.Wang, Y. Zhang, W.Wu, Q. Zeng, M.Yang, and R.Xia, "Value of neutrophil/lymphocyte ratio and platelet/lymphocyte ratio for prognostic evaluation of diffuse large B-cell lymphoma", ***Zhongguo Shi Yan Xue Ye Xue Za Zhi,*** 24(2), 427-432 (2016).
16. V. Periša, A. Knezović, L. Zibar, J. Sinčić-Petričević, D. Mjeda, I. Periša, and I. Aurer, "Comparison of the prognostic impact of neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and glasgow prognostic score in diffuse large B-cell lymphoma", ***Shiraz E-Med,*** 17(7-8), e38209(2016).
17. X. Hao, Y. Wei, X. Wei, L. Zhou, Q.Wei, Y. Zhang, W. Huang, and R. Feng, "Glasgow prognostic score is superior to other inflammation-based scores in predicting survival of diffuse large B-cell lymphoma", ***Oncotarget,*** 8(44), 76740 (2017).
18. Y. Han, Y.Qin, X. He, J. Yang, P. Liu, C. Zhang, L. Zhou, S. Zhou, L. Gui, and Y. Sun, "Prognostic significance of inflammatory indicators for advanced-stage diffuse large B-cell lymphoma", ***Zhonghua Yi Xue Za Zhi,*** 98(16), 1250-1255 (2018).
19. P. Zhao, L. Zang, X. Zhang, Y. Chen, Z. Yue, H. Yang, H. Zhao, Y.Yu, Y.Wang, and Z.Zhao, "Novel prognostic scoring system for diffuse large B-cell lymphoma", ***Oncol Lett,*** 15(4), 5325-5332 (2018).
20. S. Wang, Y.Ma, L.Sun, Y.Shi, S.Jiang, K.Yu, and S.Zhou, "Prognostic significance of pretreatment neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in patients with diffuse large B-cell lymphoma", ***Biomed Res Int,*** 2018(2018).
21. P. Zhao, L.Zang, X.Zhang, Y.Chen, H.Yang, H. Zhao, Y.Yu, Y.Wang, Y. Zhang, and X.Wang, "The Lymphocyte–Monocyte Ratio and the Platelet–Lymphocyte Ratio at Diagnosis as Independent Prognostic Factors in Primary Gastrointestinal Diffuse Large B Cell Lymphoma", ***Indian J Hematol Blood Transfus,*** 33(3), 333-341 (2017).
22. D.F. Stroup, J.A.Berlin, S.C.Morton, I.Olkin, G.D.Williamson, D.Rennie, D.Moher, B.J.Becker, T.A.Sipe, and S.B.Thacker, "Meta-analysis of observational studies in epidemiology: a proposal for reporting", ***Jama***, 283(15), 2008-2012 (2000).
23. A. Gupta, A.Das, K.Majumder, N.Arora, H.G.Mayo, P.P.Singh, M.S.Beg, and S.Singh, "Obesity is Independently Associated With Increased Risk of Hepatocellular Cancer–related Mortality", ***Am J Clin Oncol,*** 41(9), 874-881 (2018).
24. J.A. Hayden, D.A.van der Windt, J.L.Cartwright, P.Côté, and C.Bombardier, "Assessing bias in studies of prognostic factors", ***Ann Intern Med,*** 158(4), 280-286 (2013).
25. J.P. Higgins, S.G.Thompson, J.J.Deeks, and D.G.Altman, "Measuring inconsistency in meta-analyses", ***Bmj,*** 327(7414), 557-560 (2003).
26. M.G. Netea, F.Balkwill, M.Chonchol, F.Cominelli, M.Y.Donath, E.J.Giamarellos-Bourboulis, D.Golenbock, M.S.Gresnigt, M.T.Heneka, and H.M. Hoffman, "A guiding map for inflammation", ***Nat Immunol***, 18(8), 826-831(2017).
27. A.M.A. Ali and M.E.A.Abdelrahim, "Modeling and optimization of terbutaline emitted from a dry powder inhaler and influence on systemic bioavailability using data mining technology", ***J Pharm Innov***, 9(1), 38-47 (2014).
28. M.E. Abdelrahim, K.H.Assi, and H.Chrystyn, "Relative bioavailability of terbutaline to the lung following inhalation, using urinary excretion", ***Br J Clin Pharmacol***, 71(4), 608-610 (2011).

29. M. Abdelrahim, K.H.Assi, and H.Chrystyn, "Dose emission and aerodynamic characterization of the terbutaline sulphate dose emitted from a Turbuhaler at low inhalation flow", ***Pharm Dev Technol,*** 18(4), 944-949 (2013).
30. Y. Chen, Z.Zhang, Q.Fang, and H. Jian, "Prognostic impact of platelet-to-lymphocyte ratio on diffuse large B-cell lymphoma: a meta-analysis", ***Cancer Cell Int***, 19(1), 245 (2019).
31. D. Hanahan and R.A.Weinberg, "The hallmarks of cancer", ***Oxford Textbook of Oncology***, (2016).
32. M.Z. Wojtukiewicz, E.Sierko, D.Hempel, S.C.Tucker, and K.V.Honn, "Platelets and cancer angiogenesis nexus", ***Cancer Metastasis Rev,*** 36(2), 249-262 (2017).
33. C.K. Meikle, C.A.Kelly, P.Garg, L.M.Wuescher, R.A.Ali, and R.G.Worth, "Cancer and thrombosis: the platelet perspective", ***Front Cell Dev Biol,*** 4,147 (2017).
34. P.A. Murphy, V.L.Butty, P.L.Boutz, S. Begum, A. L.Kimble, P.A.Sharp, C.B.Burge, and R.O.Hynes, "Alternative RNA splicing in the endothelium mediated in part by Rbfox2 regulates the arterial response to low flow", ***Elife,*** 7, e29494 (2018).
35. T. Tokito, K.Azuma, A.Kawahara, H.Ishii, K.Yamada, N.Matsuo, T.Kinoshita, N.Mizukami, H.Ono, and M.Kage, "Predictive relevance of PD-L1 expression combined with CD8+ TIL density in stage III non-small cell lung cancer patients receiving concurrent chemoradiotherapy", ***Eur J Cancer,*** 55,7-14 (2016).

Bull. Pharm. Sci., Assiut University, Vol. 46, Issue 1, 2023, pp. 291-304.

نشرة العلوم الصيدلية
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BULL. PHARM. SCI. Assiut Univ.

نوان الأهمية الإكلينيكية والتشخيصية لنسبة الصفائح الدموية إلى الخلايا الليمفاوية في سرطان الغدد الليمفاوية B- الخلية الكبيرة المنتشرة: التحليل التلوي

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في الوقت الحاضر ، هناك ارتباط كبير ولكن متغير بين سرطان الغدد الليمفاوية B-cell الكبيرة المنتشر ونسبة الصفائح الدموية إلى الخلايا الليمفاوية. سيقيم هذا التحليل التلوي هذا الارتباط.

تم إجراء بحث شامل حتى يونيو ٢٠٢٢ ، وكشف ١١ بحثًا عن ٢٢٨٤ مريضًا مصابًا بـ سرطان الغدد الليمفاوية B-CELL الكبيرة المنتشر . اكتشفوا وجود صلة بين سرطان الغدد الليمفاوية B-CELL الكبيرة المنتشر و نسبة الصفائح الدموية إلى الخلايا الليمفاوية. تم استخدام نموذج الأثر الثابت أو العشوائي لإنشاء نسب الأرجحية (ORs) بفواصل ثقة ٩٥٪ (CIs) وفحص الأهمية التنبؤية لـ نسبة الصفائح الدموية إلى الخلايا الليمفاوية على البقاء على قيد الحياة بشكل عام ، والبقاء الخالي من التقدم ، ومجموعة متنوعة من الخصائص الإكلينيكية المرضية.

البقاء على قيد الحياة ضعيف لمدة ٥ سنوات (OR، ٠.٥٩؛ ٩٥٪ CI، ٠.٣٦–٠.٩٨ ، p <٠.٠٠٠١) ، موضوعات البقاء على قيد الحياة الفقيرة الخالية من التقدم لمدة عامين (OR، ٠.٤٢ ؛ ٩٥٪ CI، ٠.٢٧–٠.٦٧ ، p <٠.٠٠٠١) ، و البقاء على قيد الحياة دون تقدم لمدة ٥ سنوات (OR، ٠.٥٠ ؛ ٩٥٪ CI، ٠.٣٤–٠.٧٢ ، p <٠.٠٠٠١) كلها مرتبطة بشكل كبير مع ارتفاع معدل النمو. وبطريقة مماثلة ، ارتبط ارتفاع نسبة الصفائح الدموية إلى الخلايا الليمفاوية ارتباطًا وثيقًا بوجود أعراض B (OR، ٢.٢٢ ؛ ٩٥٪ CI، ١.٦٩–٢.٩٣ ، p <٠.٠٠٠١) ، مستوى نازعة هيدروجين اللاكتات مرتفع (OR، ٢.٩٨ ؛ ٩٥٪ CI، ٢.١٩–٤.٠٦ ، p <٠.٠٠٠١) ، مرحلة ورم أعلى (OR، ١.٨٤ ؛ ٩٥٪ CI، ١.٠٨–٣.١٣ ، p = ٠.٠٠٣).

ومع ذلك ، لم يكن هناك ارتباط كبير بين نسبة الصفائح الدموية إلى الخلايا الليمفاوية المرتفع وحالة أداء مجموعة الأورام التعاونية الشرقية ≤٢ (OR، ١.٤٤ ؛ ٩٥٪ CI، ٠.٦٩–٣.٠٢ ، P=٠.٣٣) تسلل مرتفع لنخاع العظام (OR، ١.٠٢؛ ٩٥٪ CI، ٠.٦٠–١.٧٤، P= ٠.٩٤) ، جنس الشخص (OR، ١.٢٠ ؛ ٩٥٪ CI، ٠.٩٣–١.٥٥ ، p = ٠.١٧) ؛ العمر (OR، ٠.٨٩؛ ٩٥٪ CI، ٠.٦٩–١.١٥، P = ٠.٣٧) ؛ وخلية المنشأ (OR، ١.٠٠؛ ٩٥٪ CI، ٠.٧١–١.٣٩، P= ٠.٩٨).

قد يكون تأثير نسبة الصفائح الدموية إلى الخلايا الليمفاوية على سرطان الغدد الليمفاوية B-CELL الكبيرة المنتشر جوهريًا كأسلوب لتحسين التشخيص. قد يكون المرضى الذين يعانون من سرطان الغدد الليمفاوية B-CELL الكبيرة المنتشر الذين لديهم ارتفاع في نسبة الصفائح الدموية إلى الخلايا الليمفاوية

معرضين لخطر مستقل لسوء التشخيص. لمنع حدوث مشاكل محتملة ، ننصح بمتابعة المرضى الـــذين يعانون من ارتفاع نسبة الصفائح الدموية إلى الخلايا الليمفاوية.