Int J Clin Exp Med 2015;8(3):3992-3999
www.ijcem.com /ISSN:1940-5901/IJCEM0003697

Original Article

Association of β2-microglobulin with the prognosis of non-Hodgkin's lymphoma: a meta analysis

Xiao-Liang Wang[1*], Xiao-Li Wang[1*], Shuo He[2], Hong-Li Zhai[3]

[1]Department of Paediatrics, Yuhuangding Hospital Affiliated to Qingdao University, Yantai 264000, China; [2]Department of Paediatrics, Maternal and Child Health Hospital, Jiangshan 324100, China; [3]Department of Gastroenterology, Regenerative Medicine Research Center, Shandong International Biotechnology Park, Yantai 264000, China. [*]Equal contributors.

Received November 8, 2014; Accepted January 9, 2015; Epub March 15, 2015; Published March 30, 2015

Abstract: Objective: The influence of β2-microglobulin (β2-MG) on the prognosis of non-Hodgkin's lymphoma (NHL) remains controversial. This study performed meta-analyses to evaluate the prognostic value of β2-MG on the overall survival (OS) of NHL. Methods: Through a search of relevant literature in PubMed, EMbase, Science Direct, OVID and Wanfang databases from 1980-2013, the hazard ratios (HRs) of OS between the normal β2-MG group and the increased β2-MG group were retrieved, and the results were combined using a fixed effect model and a random effect model. Subgroup analyses were performed based on univariate and multivariate analysis results, and sensitivity analyses were performed to estimate the changes of the combined HRs. In addition, funnel plots and fail-safe numbers were used to estimate publication bias. Results: A total of 17 qualified publications were included, with a cumulative total of 2,479 cases. The result of heterogeneity examination showed that there was heterogeneity among all studies ($P < 0.001$, $I^2 = 87\%$). In the random effect model, the combined HR was 2.71 (95% confidence interval [CI]: 1.91-3.85). The result of the total effect examination was statistically significant ($Z = 5.59$, $P < 0.001$). Conclusion: The increased β2-MG level was an independent risk factor for the prognosis of NHL.

Keywords: β2-microglobulin, non-Hodgkin's lymphoma, meta-analysis

Introduction

Non-Hodgkin's lymphoma (NHL) is a group of highly heterogeneous malignant tumors of the lymphatic system. NHL accounts for almost 5% of human malignant tumors, and its incidence has gradually increased in recent years. Because the clonally proliferated lymphocytes have different functions and are distributed extensively in the body, they can involve any organs and can display different clinical manifestations, histological types, natural disease courses, and prognoses [1]. The tendency of NHL to invade extranodal tissues is significant, and the disease usually results from multiple foci; therefore, the treatment efficacy is poor, the clinical courses vary, and the therapeutic responses are also significantly different. Thus, studies on prognosis-related factors of NHL have attracted researchers' attention [2].

β2-microglobulin (β2-MG) is a type of low-molecular-weight protein. β2-MG is a light chain structure in human leukocyte antigens (HLAs) that is released into blood after dissociation from HLA during the normal metabolic process in the body [3, 4]. Many published studies have demonstrated that serum β2-MG levels are associated with the prognosis of most types of NHL, mainly including chronic lymphocytic leukemia (CLL) [5-8], follicular lymphoma (FL) [9-11], mantle cell lymphoma (MCL) [12, 13], and diffuse large cell lymphoma (DLBCL) [14, 15]. Although domestic and international scholars have performed studies using β2-MG as a prognostic factor for NHL patients, the presence of differences in the experimental methods, sample contents, populations, and statistical analysis methods made the individual study results difficult to promote, and the conclusions were controversial [16-19]. Some studies reported that the increase of β2-MG was a risk factor for the prognosis of NHL patients; while other studies indicated that the increase of β2-MG had limited effects on the prognosis of

NHL patients. To scientifically evaluate the association between β2-MG and the prognosis of NHL and to reduce the bias and differences among the studies, the present study performed meta-analyses on previous study results to comprehensively evaluate the association between the increase of β2-MG and the prognosis of NHL to provide bases for the formulation of clinical therapeutic strategies.

Materials and methods

Retrieval strategy

The PubMed, Science Direct, OVID, and Wanfang databases were searched. The search terms were "lymphoma", "microglobulin", and "survival", "prognostic' or "prognosis". The retrieval period was from January 1, 1980 to December 31, 2013. During the retrieval, publications with titles containing Hodgkin's lymphoma or Hodgkin lymphoma were excluded. For the same authors with multiple publications, only the newest or the most comprehensive publication was included. Publications included in this study were all full articles.

Inclusion criteria

(1) Prospective studies; (2) publically published studies on the association between binary variables of β2-MG levels (increased group and normal group) and the prognosis of NHL; (3) the endpoint event was overall survival (OS); if both univariate and multivariate analyses of β2-MG were reported, the multivariate analyses were used whenever possible; (4) with a clear threshold β2-MG value; (5) all publications were full articles; and (6) publications were able to provide enough information [19, 20] to acquire indicators of NHL prognosis, such as relative risks and survival curves, to ensure that the hazard ratio (HR) or risk ratio (RR) could be estimated.

Exclusion criteria

(1) Retrospective studies; (2) studies irrelevant to β2-MG and to the prognosis of NHL; (3) omission of survival information data, such as HR, RR, and survival curves; (4) repetitive reports or reports with poor quality that could not be used; and (5) letters, reviews, conference records, abstracts, and commentaries.

Evaluation of literature quality

The quality evaluation of the included literature was performed according to the prognostic literature evaluation principles: (1) representative of samples and randomness of patient selection; (2) whether the study start point was clear; i.e., whether all patient follow-up started on d1 after surgery and the follow-up time was long enough; (3) whether all patients were followed up; the dropout rate did not exceed 20%; (4) whether objective prognostic indicators were used; i.e., death was the standard to determine the outcome.

Quality control

(1) Data were collected based on the literature inclusion criteria; (2) publications with small sample sizes, poor quality, and repetitive reports and publications without raw data or the original text could not be obtained were excluded; and (3) publications were input into computers to establish a database; statistical analyses were performed after verification.

Information collection

There are 3 major indicators for prognosis evaluation: survival rate, survival curve, and HR. This study used the HR as effect statistic to investigate the association between β2-MG levels and the prognosis of NHL. Two evaluators independently performed the literature screening and information retrieval. After completion, the consistency of the results was examined; if there were inconsistent opinions, the inconsistency was resolved by discussing with clinical specialists in the study group. Based on Parmar et al [21], there were 3 ways to acquire HR values: (1) HR values, 95% confidence intervals (CIs), or regression coefficients reported in the literature were used directly, of which regression coefficient b was converted into HR using exp (b); (2) if an HR value was not directly provided in the literature but there were clear P values, numbers of patients in the increased β2-MG and normal groups, and numbers of all observed deaths at the end of the study, then the HR value was estimated using the formula proposed by Parmar et al; (3) if only the Kaplan-Meier (K-M) curve was provided, then the numbers of patients in the increased β2-MG and control groups were extracted, and the survival rate at each time point in the curve was also extracted using the Engauge Digitizer V4.1 screenshot tool to estimate HR values and variances using formulas. The HR values and variances were acquired using the above 3 methods. After sorting, the logarithm value of HR [ln

Table 1. Characteristics of included studies

Authors	Publication Year	Median follow-up Time (years)	Numbers		HR	Adjusted HR	Cut-off of β2-MG (mg/L)
			High level	Normal level			
Albitar et al.	2007	-	63	-	2.88	Yes	4.16
Aviles et al.	1991	-	28	40	4.67	No	3.5
Benboubker et al.	2000	2.9	23	82	3.763	No	3.0
Dhodapkar et al.	2009	9.7	106	74	1.8	Yes	3.0
Gui et al.	2008	1.7	221	194	1.784	Yes	2.5
Ibrahim et al.	2001	-	150	-	1.027	Yes	2.5
Inamdar et al.	2009	4.3	38	31	3.3	Yes	3.0
Khouri et al.	2003	4.	9	18	40.06	No	3.0
Lopez-Guillermo et al.	2005	6.5	169	213	1.8	Yes	2.5
Maffei et al.	2010	4	249	-	17.73	No	2.2
Molica et al.	1999	3.	68	38	6.25	No	3.0
Perez-Encinas et al.	1999	2.2	63	-	2.84	Yes	3.5
Romaguera et al.	2010	8	53	44	1.77	Yes	3.0
Seymour et al.	2003	10	20	43	2	No	2.0
Stilgenbauer et al.	2009	3.2	38	57	2	No	4.41
XIE et al.	2013	3.4	157	95	2.19	No	2.2
Xu et al.	2008	-	14	81	23.73	No	3.0

(HR)] and its standard error [SE (ln (HR)] were obtained.

Meta-analyses

The generic inverse variance was selected, and ln (HR) and SE (1n (HR)) were input to perform OS analysis using RevMan 5.2 software. Heterogeneity examination was performed using the Q test; when $P > 0.05$, all studies had homogeneity; if $P \leq 0.05$, there was heterogeneity among all studies. In addition, the heterogeneity degree among all studies was measured statistically. If there was good homogeneity among all studies, the fixed effect model was used; otherwise, the random effect model was used. Subgroup analyses were conducted based on the univariate and multivariate analyses of the included literature to investigate the effects of different subgroups. Finally, sensitivity analyses were performed on the results. The publication bias of the meta-analysis was evaluated using funnel plots. Asymmetric or incomplete funnel plots suggest the presence of publication bias.

Results and analyses

Characteristics of the literature

A total of 187 publications were obtained based on the retrieval strategy. According to the inclusion and exclusion criteria, 77 irrelevant publications were initially excluded after reading the abstracts. The full texts of the 110 publications that might be included were downloaded. After reading the full texts, 93 publications that did not meet the requirement were excluded. Finally, a total of 17 publications [7-9, 16, 17, 19, 22-32] were included in this study, with a total of 2,479 observation subjects. Of these 17 publications, the HRs and 95% CIs for 11 publications were provided directly; determining these values required the use of clear P value calculation methods in 3 publications, and the values needed to be extracted from the K-M curves in 3 publications. In the combined HR analyses, because multivariate analyses considered confounding factors, they were more accurate than univariate analyses; therefore, if publications provided the HR values from both the multivariate and univariate analyses, the HR values from the multivariate analyses were chosen. The basic information regarding the publications that were included in the analyses is shown in **Table 1**. In these 17 publications, there were 8 studies provided the adjusted HR values which adjusted for age, gender, therapy methods, and other confounders. The cut-off of β2-MG is varied from 2.0 to 4.41 mg/L. The median follow-up time ranged from 1.7 to 10 years.

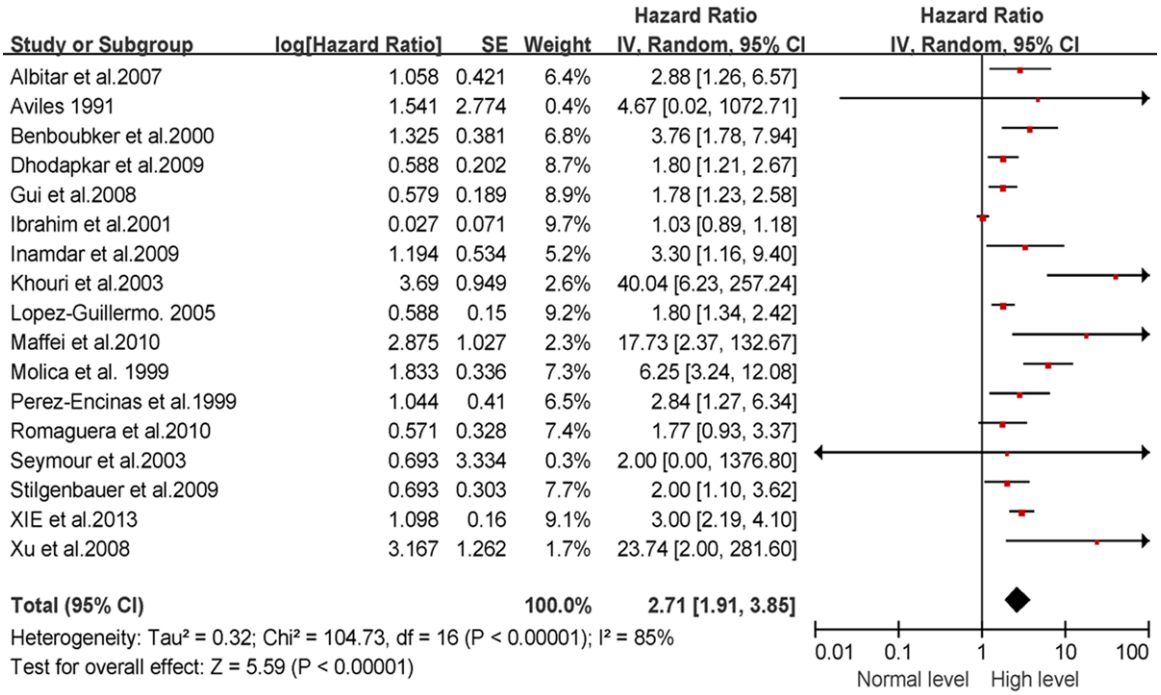

Figure 1. Forest plot of NHL and β2-MG by meta-analysis of included univariate study, the horizontal lines correspond to the study-specific OR and 95% CI, respectively. The area of the squares reflects the study-specific weight. The diamond represents the pooled results of OR and 95% CI.

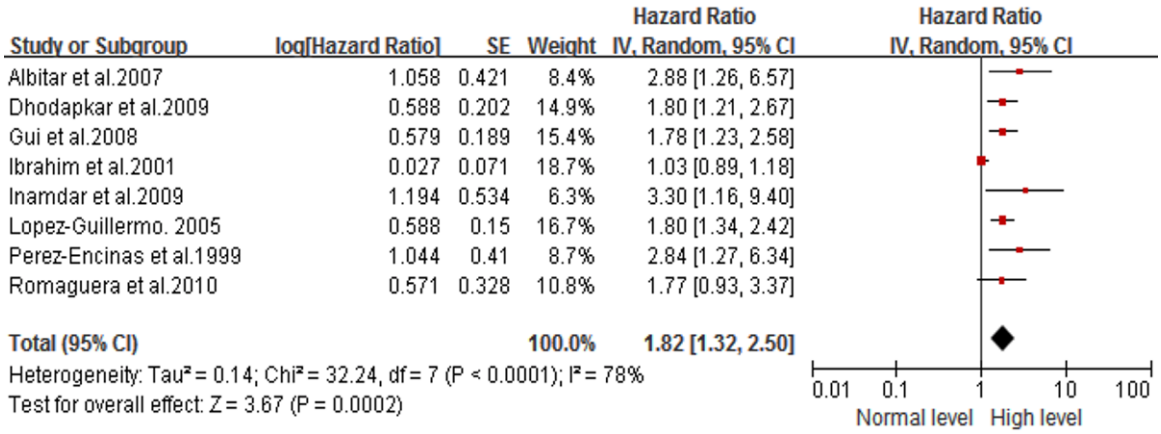

Figure 2. Forest plot of NHL and β2-MG by meta-analysis of included multivariate analyses study, the horizontal lines correspond to the study-specific OR and 95% CI, respectively. The area of the squares reflects the study-specific weight. The diamond represents the pooled results of OR and 95% CI.

β2-MG levels and the prognosis of NH

A heterogeneity examination was conducted on the 17 included publications. The results of this examination indicated that there was significant heterogeneity among all studies; therefore, quantitative and comprehensive analysis of literature needed to be performed using the random effect model. The total effect of these 17 publications was statistically significant (Z=5.59, $P < 0.001$). The combined HR value of OS for the normal β2-MG and increased groups was 2.71 (95% CI 1.91-3.85), indicating that the risk of death in patients with increased β2-MG levels increased 1.71-fold (**Figure 1**). This result suggested that increased β2-MG

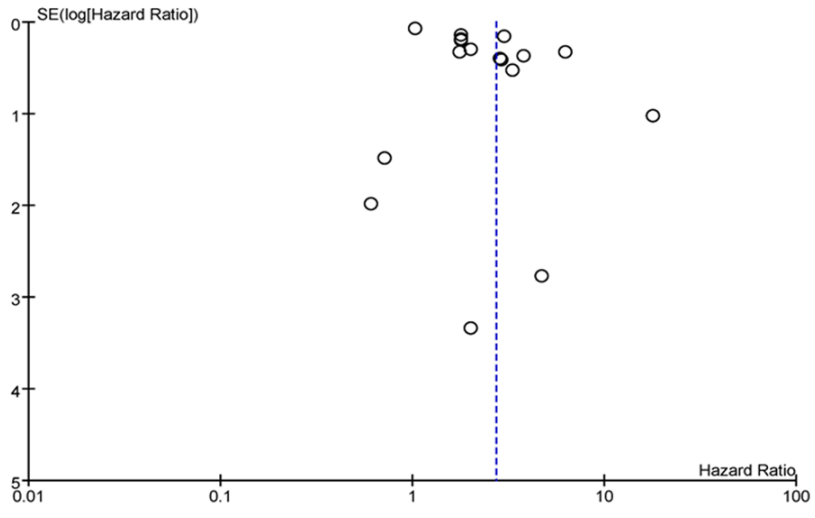

Figure 3. Funnel plot for publication bias test. Each point represents a separate study for the indicated association. Log HR represents the natural logarithm of HR. The vertical line represents the mean effects size.

levels may be a risk factor of NHL. Considering that the information regarding β2-MG in included publications was from univariate and multivariate analyses, publications that provided multivariate analysis data were used for subgroup analyses. The results showed that the combined HR value in multivariate analyses was 1.82 (95% CI 1.32-2.50) (**Figure 2**).

Publication bias and sensitivity analyses

The funnel plots of these 17 publications are shown in **Figure 3**. **Figure 3** shows that, excluding some individual abnormal dots, the distribution of the other dots is concentrated and symmetric, indicating that the influence of publication bias on this study was small and that its conclusion was reliable. To further explain the reliability of the meta-analysis, sensitivity analyses were performed, and the results showed that when individual publications were excluded one by one, the effect on the result was limited. Therefore, this study's conclusion was reliable.

Discussion

This study included a total of 17 relevant publications for meta-analysis. The results indicated that an increased β2-MG level was an independent risk factor for the prognosis of the survival of NHL. This study used a random effect model to comprehensively evaluate the prognostic value of β2-MG in the OS of NHL; therefore, the analytic results are representative, which is helpful for resolving the inconsistencies among many previous independent studies.

It has been reported that people with significantly increased β2-MG levels mostly had advanced disease and poor prognoses, while people with low concentrations had better prognosis and longer survival periods. After the improvement or remission of disease cases with surgery, chemotherapy, or other therapies, the majority of patients experienced different degrees of decreased β2-MG levels. This study showed that among NHL patients, patients with increased β2-MG levels had higher risk of death, with an HR of 2.71 (95% CI: 1.91~3.85), than patients with normal β2-MG levels. Thus, an increased β2-MG level is an independent risk factor for the prognostic survival of NHL patients and could be an important indicator for determining NHL prognosis. In addition, sensitivity analyses indicated that the results had good stability and reliability.

Furthermore, the HR values extracted in this meta-analysis were drawn from multivariate analyses whenever possible, which eliminated the confounding effects of other prognostic factors on β2-MG. Meta-analysis is a quantitative analysis method based on previous study results and is greatly influenced by the quality of the referenced studies. This study already excluded poor-quality literature that had limited amounts of information. However, due to its own limitations, the meta-analysis still has various biases. The most common bias is publication bias. However, the influence of publication bias in this study is limited, and the conclusions are reliable. Technique bias is another important bias in this study. The different detection methods and evaluation standards for measuring β2-MG might result in large differences in threshold values. Therefore, a uniform criterion is needed for standardizing β2-MG studies to reduce bias caused by technique.

The latest lymphoma classification, the 2008 WHO classification, lists over 80 different forms of lymphomas in four broad groups, most of the literatures included in the present study have been published before 2008, which did not provided the classification data. Therefore, in the present study, we did not analyze the prognosis value of β2-MG in different classification. This is a limitation of our study.

In summary, the influence of β2-MG on the prognosis of NHL still requires more information, more detailed data, and more standardized experimental techniques to further evaluate and confirm our results. If more detailed clinical staging and therapeutic regimen data could be made available for stratified analyses, then the results would be more credible and more convincing.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Hong-Li Zhai, Department of Gastroenterology, Regenerative Medicine Research Center, Shandong International Biotechnology Park, 39 Keji Avenue, Yantai High-Tech Zone, China. E-mail: xdyindx@163.com; zhaihonglii@yeah.net

References

[1] van der Poel MW, Mulder WJ, Ossenkoppele GJ, Maartense E, Wijermans P, Hoogendoorn M, Schouten HC. Comorbidity and treatment decision-making in elderly non-Hodgkin's lymphoma patients: a survey among haematologists. Neth J Med 2014; 72: 165-169.

[2] Yang F, Zhu HL, He C, Li JJ, Xiang B, Cui X, Huang J, Ji J, Ma HB, Liu T. Effect of Antiviral Prophylaxis Strategy for Chemotherapy-Associated Hepatitis B Reactivation in Non-Hodgkin's Lymphoma Patients with Hepatitis B Virus Infection: A Retrospective Cohort Study. Indian J Hematol Blood Transfus 2014; 30: 97-104.

[3] Berggard I, Beam AG. Isolation and properties of a low molecular weight beta-2-globulin occurring in human biological fluids. J Biol Chem 1968; 243: 4095-4103.

[4] Ma SP, Lin M, Liu HN, Yu JX. Lymphangiogenesis in non-Hodgkin's lymphoma and its correlation with cyclooxygenase-2 and vascular endothelial growth factor-C. Oncol Lett 2012; 4: 695-700.

[5] Peterson PA, Cunningham BA, Berggard I, Edelman GM. 2-Microglobu-lin--a free immunoglobulin domain. Proc Natl Acad Sci U S A 1972; 69: 1697-1701.

[6] Grey HM, Kubo RT, Colon SM, Poulik MD, Cresswell P, Springer T, Turner M, Strominger JL. The small subunit of HL-A antigens is beta 2-microglobulin. J Exp Med 1973; 138: 1608-1612.

[7] Stilgenbauer S, Zenz T, Winkler D, Bühler A, Schlenk RF, Groner S, Busch R, Hensel M, Dührsen U, Finke J, Dreger P, Jäger U, Lengfelder E, Hohloch K, Söling U, Schlag R, Kneba M, Hallek M, Döhner H; German Chronic Lymphocytic Leukemia Study Group. Subcutaneous alemtuzumab in fludarabine -refractory chronic lymphocytic leukemia; clinical results and prognostic marker analyses from the CLL2H study of the German Chronic Lymphocytic Leukemia Study Group. J Clin Oncol 2009; 27: 3994-4001.

[8] Xu W, Li JY, Wu YJ, Yu H, Shen QD, Li L, Fan L, Qiu HX. Prognostic significance of ATM and TP53 deletions in Chinese patients with chronic lymphocytic leukemia. Leuk Res 2008; 32: 1071-1077.

[9] Gui W, Wang T, Wang J, Wang L, He J, Yang B, Zhao Z, Zhang H, Zhang Q. An improved prognostic parameter for non-Hodgkin's lymphoma based on the combination of three serum tumor markers. Int J Biol Markers 2008; 23: 207-213.

[10] Wierda WG, O'Brien S, Wang X, Faderl S, Ferrajoli A, Do KA, Cortes J, Thomas D, Garcia-Manero G, Koller C, Beran M, Giles F, Ravandi F, Lerner S, Kantarjian H, Keating M. Prognostic nomogram and index for overall survival in previously untreated patients with chronic lymphocytic leukemia. Blood 2007; 109: 4679-85.

[11] Federico M, Guglielmi C, Luminari S, Mammi C, Marcheselli L, Gianelli U, Maiorana A, Merli F, Bellei M, Pozzi S, Stelitano C, Lazzaro A, Gobbi PG, Baldini L, Bergantini S, Fregoni V, Brugiatelli M. Prognostic relevance of serum beta2 microglobulin in patients with follicular lymphoma treated with anthracycline-containing regimens. A GISL study. Haematologica 2007; 92: 1482-1488.

[12] Gins E, Montoto S, Bosch F, Arenillas L, Mercadal S, Villamor N, Martínez A, Colomo L, Campo E, Montserrat E, López-Guillermo A. The follicular lymphoma international prognostic index (FLIPI) and the histological subtype are the most important factors to predict histological transformation in follicular lymphoma. Ann Oncol 2006; 17: 1539-1545.

[13] Montoto S, Lbpez-Guillermo A, Ferrer A, Camós M, Alvarez-Larrán A, Bosch F, Bladé J, Cervantes F, Esteve J, Cobo F, Colomer D, Campo E, Montserrat E. Survival after progression in

patients with follicular lymphoma: analysis of prognostic factors. Ann Oncol 2002; 13: 523-530.
[14] Zelenetz AD. Guidelines for NHL: Updates to the Management of Diffuse Large B-Cell Lymphoma and New Guidelines for Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders and T-Cell Large Granular Lymphocytic Leukemia. J Natl Compr Canc Netw 2014; 12 Suppl 5: 797-800.
[15] Bismar MM, Alasadi M, Hendawy BS, Waness A. A case of successful remission of extensive primary gastric diffuse large B cell lymphoma: radiologic, endoscopic and pathologic evidence. Case Rep Gastroenterol 2014; 8: 134-140.
[16] Romaguera JE, Fayad LE, Feng L, Hartig K, Weaver P, Rodriguez MA, Hagemeister FB, Pro B, McLaughlin P, Younes A, Samaniego F, Goy A, Cabanillas F, Kantarjian H, Kwak L, Wang M. Ten-year follow-up after intense chemoimmunotherapy with Rituximab-HyperCVAD alternating with Rituximab-high dose methotrexate/cytarabine (RMA) and without stem cell transplantation in patients with untreated aggressive mantle cell lymphoma. Br J Haematol 2010; 150: 200-208.
[17] Inamdar KV, Romaguera JE, Drakos E, Knoblock RJ, Garcia M, Leventaki V, Medeiros LJ, Rassidakis GZ. Expression of eukaryotic initiation factor 4E predicts clinical outcome in patients with mantle cell lymphoma treated with hyper-CVAD and rituximab, alternating with rituximab, high-dose methotrexate, and cytarabine. Cancer 2009; 115: 4727-4736.
[18] Duletic-Nacinovic A, Stifter S, Marijic B, Lucin K, Valković T, Petranović D, Jonjić N. Serum IL-6, IL-8, IL-10 and beta2-microglobulin in association with International Prognostic Index in diffuse large B cell lymphoma. Tumori 2008; 94: 511-517.
[19] Khouri IF, Saliba RM, Okoroji GJ, Acholonu SA, Champlin RE. Long-term follow-up of autologous stem cell transplantation in patients with diffuse mantle cell lymphoma in first disease remission: the prognostic value of beta2-microglobulin and the tumor score. Cancer 2003; 98: 2630-2635.
[20] Conconi A, Zucca E, Roggero E, Bertoni F, Bernasconi A, Mingrone W, Pedrinis E, Cavalli F. Prognostic models for diffuse large B-cell lymphoma. Hematol Oncol 2000; 18: 61-73.
[21] Parmar MK, Torri V, Stewart L. Extracting summary statistics to perform mete-analyses of the published literature for survival endpoints. Stet Med 1998; 17: 2815-2834.
[22] Ibrahim S, Keating M, Do KA, O'Brien S, Huh YO, Jilani I, Lerner S, Kantarjian HM, Albitar M. CD38 expression as an important prognostic factor in B-cell chronic lymphocytic leukemia. Blood 2001; 98: 181-186
[23] Maffei R, Martinelli S, Santachiara R, Rossi D, Guarnotta C, Sozzi E, Zucchetto A, Rigolin GM, Fiorcari S, Castelli I, Fontana M, Coluccio V, Leonardi G, Zucchini P, Tripodo C, Cuneo A, Gattei V, Del Poeta G, Forconi F, Gaidano G, Torelli G, Marasca R. Angiopoietin-2 plasma dosage predicts time to first treatment and overall survival in chronic lymphocytic leukemia. Blood 2010; 116: 584-592.
[24] Dhodapkar MV, Hoering A, Gertz MA, Rivkin S, Szymonifka J, Crowley J, Barlogie B. Long-term survival in Waldenstrom macroglobulinemia: 10-year follow-up of South west Oncology Group-directed intergroup trial 59003. Blood 2009; 113: 793-796.
[25] Lbpez-Guillermo A, Colomo L, Jiménez M, Bosch F, Villamor N, Arenillas L, Muntañola A, Montoto S, Giné E, Colomer D, Beà S, Campo E, Montserrat E. Diffuse large B-cell lymphoma: clinical and biological characterization and outcome according to the nodal or extranodal primary origin. J Clin Oncol 2005; 23: 2797-2804
[26] Seymour JF, Pro B, Fuller LM, Manning JT, Hagemeister FB, Romaguera J, Rodriguez MA, Ha CS, Smith TL, Ayala A, Hess M, Cox JD, Cabanillas F, McLaughlin P. Long-term follow-up of a prospective study of combined modality therapy for stage I-II indolent non-Hodgkin's lymphoma. J Clin Oncol 2003; 21: 2115-2122.
[27] Benboubker L, Valat C, Linassier C, Cartron G, Delain M, Bout M, Fetissof F, Lefranq T, Lamagnere JP, Colombat P. A new serologic index for low-grade non-Hodgkin's lymphoma based on initial CA125 and LDH serum levels. Ann Oncol 2000; 11: 1485-1491.
[28] Pérez-Encinas M, Quintas A, Bendaña A, Rabuñal MJ, Bello JL. Correlation and prognostic value of serum soluble ICAM-1, beta-2 microglobulin, and IL-2alphaR levels in non-Hodgkin's lymphoma. Leuk Lymphoma 1999; 33: 551-8.
[29] Molica S, Levato D, Cascavilla N, Levato L, Musto P. Clinico-prognostic implications of simultaneous increased serum levels of soluble CD23 and beta2 -microglobulin in B -cell chronic lymphocytic leukemia C. Eur J Haematol 1999; 62: 117-122.
[30] Avilés A1, Díaz-Maqueo JC, Rodriguez L, García EL, Guzmán R, Talavera A. Prognostic value of serum beta 2 microglobulin in primary gastric lymphoma. Author information Hematol Oncol 1991; 9: 115-21.
[31] Albitar M, Vose JM, Johnson MM, Do KA, Day A, Jilani I, Kantarjian H, Keating M, O'Brien SM, Verstovsek S, Armitage JO, Giles FJ. Clinical relevance of soluble HLA-I and beta2-microglobu-

lin levels in non-Hodgkin's lymphoma and Hodgkin's disease. Leuk Res 2007; 31: 139-145.

[32] Xie W, Hu K, Xu F, Zhou D, Huang W, He J, Shi J, Luo Y, Zhang J, Lin M, Ye X, Cai Z, Huang H. Significance of clinical factors as prognostic indicators for patients with peripheral T-cell non-Hodgkin lymphoma: A retrospective analysis of 252 cases. Mol Clin Oncol 2013; 1: 911-917.