Innovative analysis of predictors for overall survival from systemic non-Hodgkin T cell lymphoma using quantile regression analysis

Da-Yong Huang1, Yi-Fei Hu2, Na Wei1, Li Fu1, Lin Wu1, Jing Shen1, Jing-Shi Wang1, Zhao Wang1

1Department of Hematology, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China; 2Department of Child, Adolescent and Maternal Health, School of Public Health, Capital Medical University, Beijing 100069, China.

Abstract

Background: Non-Hodgkin T/NK cell lymphoma is a rare and widely variable type of lymphoma with the most dismal prognosis. This study aimed to investigate varied impact of the clinical indicators to the overall survival (OS).

Methods: We conducted a retrospective study to identify the non-invasive clinical features of T cell lymphoma that can predict prognosis with an innovative analysis method using quantile regression. A total of 183 patients who visited a top-tier hospital in Beijing, China, were enrolled from January 2006 to December 2015. Demographic information and main clinical indicators were collected including age, erythrocyte sedimentation rate (ESR), survival status, and international prognostic index (IPI) score.

Results: The median age of the patients at diagnosis was 45 years. Approximately 80% of patients were at an advanced stage, and the median survival time after diagnosis was 5.1 months. Multivariable analysis of the prognostic factors for inferior OS associated with advanced clinical staging [HR = 3.16, 95%CI (1.39–7.2)], lower platelet count [HR = 2.57, 95%CI (1.57–4.19), P < 0.001] and higher IPI score [HR = 1.29, 95%CI (1.01–1.66), P = 0.043]. Meanwhile, T cell lymphoblastic lymphoma [HR = 0.40, 95%CI (0.20–0.80), P = 0.010], higher white blood cell counts [HR = 0.57, 95%CI (0.34–0.96), P = 0.033], higher serum albumin level [HR = 0.6, 95%CI (0.37–0.97), P = 0.039], and higher ESR [HR = 0.53, 95%CI (0.33–0.87), P = 0.011] were protective factors for OS when stratified by hemophagocytic lymphohistiocytosis (HLH). Multivariable quantile regression between the OS rate and each predictor at quartiles 0.25, 0.5, 0.75, and 0.95 showed that the coefficients of serum β2-microglobulin level and serum ESR were statistically significant in the middle of the coefficient curve (quartile 0.25–0.75). The coefficient of IPI was negatively associated with OS. The coefficients of hematopoietic stem cell transplantation (HSCT) and no clinical symptoms were higher at the middle of the quartile level curve but were not statistically significant.

Conclusions: The IPI score is a comparatively robust indicator of prognosis at 3 quartiles, and serum ESR is stable at the middle 2 quartiles section when adjusted for HLH. Quantile regression can be used to observe detailed impacts of the predictors on OS.

Keywords: Systemic non-Hodgkin T cell lymphoma; Overall survival; Quantile regression analysis

Introduction

Non-Hodgkin T/NK cell lymphoma is a comparatively rare and widely variable type of lymphoma that has the most dismal prognosis due to different histological subgroups with durable remission and fatal outcome once disseminated.[1,2] Most studies have evaluated prognosis with the international prognostic index (IPI), which is considered the most powerful prediction tool.[3] We propose that the variant clinicopathological features (or clinical characteristics) of these patients, as indicated in clinical observations and records, can be used to predict prognosis, particularly overall survival (OS), but not invasive characteristics. For example, an elevated level of serum β2-microglobulin (β2MG) is a dismal prognostic factor in some patients with Hodgkin lymphoma,[4,5] B cell lymphoma[6,7] and NK/T cell lymphoma.[5] Several studies have shown that higher serum β2MG and lower albumin are predictive of a lower OS rate among patients with Hodgkin lymphoma who are receiving treatment.[4] Among patients with peripheral T cell lymphoma—not otherwise specified (PTCL-NOS), lower hemoglobin, lower albumin and elevated lactate dehydrogenase (LDH) levels are associated with a shorter OS duration.[5,10] Additionally, a higher erythrocyte sedimentation rate (ESR),[11] lower white blood cell (WBC) count[12] and lower platelet count[13] may be associated with the prognosis of B cell lymphoma.[14] However, the above clinical features have rarely been explored in patients with T cell lymphoma. ESR has been reported to be associated with
with Hodgkin lymphoma in children[14] but is seldom reported to be associated with non-Hodgkin T/NK cell lymphoma.

Several previous studies[16–18] have sought to identify such predictors of prognosis and have used general regression methods that may be invalid given some unmet assumptions. Other studies using linear regression, requires a normal distribution of the residuals, as well as homoscedastic. To date, the significant predictive factors for T cell lymphoma have not yet been established. Linear regression is used to model the relationship between a response variable and several predictor variables to estimate the mean value of the response variable for given range of the predictor variables.[19] Other studies have used logistic or Cox regression based on outcome indicator categorization, which may cause categories for the determination of cutoff values arbitrarily. Such methods often miss measuring the effect of covariates from the perspective of the whole distribution of the dependent variable.

Compared with logistic or linear regression, quantile regression enables studies of changing directional effects of a covariate on any section of the distribution.[19] Unlike logistic regression, quantile regression considers all the data, thereby avoiding information loss due to arbitrary categorization of response variables. Moreover, quantile regression has more benefits. It’s helpful to measure statistical dispersion for a more comprehensive understanding of the relationship between variables, as well the central tendency.[23] Quantile regression has been used to identify predictive relationships between variables, while possible there is a weak association between the means of those variables. Ecologically, quantile regression has the advantage of identifying the complexity of interactions in reality, and it could disentangle the relationship of the data with unequal variation for different ranges of other variables.[24]

Therefore, we aimed to achieve two goals: first, to identify the non-invasive clinical features for T cell lymphoma prognosis prediction; and second, to explore the potential impact of most predictors using an interval of the variant curve with quantile regression, suggesting a comparatively new method in this research area.

Methods

Ethical approval

The study was performed in accordance with the ethical requirement of the Beijing Friendship Hospital Institutional Review Boards (No. 2018-P2-006-01) and complied with the Declaration of Helsinki. Patient consent was waived by the Ethics Committee due to the retrospective nature of this study.

Patients

A total of 183 patients with systemic non-Hodgkin T/NK cell lymphoma who were admitted to the Beijing Friendship Hospital from January 2006 to December 2015 and received first-line chemotherapy were enrolled in the study. Among them, 14 angioimmunoblastic T cell lymphoma (AITL) received bortezomib+CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) regimen, all NK/T cell lymphoma received an aspargase+CHOP regimen and ten cases of NK/T lymphoma, nasal administrated additionally with radiology. The left cases were given a CHOP regimen. The median of chemotherapy cycles is six in our hospital. There were 87 (47.5%) cases of death.

Among these patients, there were 68 cases of NK/T cell lymphoma (37.2%), 40 cases of AITL, (21.9%), 34 cases of peripheral T cell lymphoma-not otherwise unspecified (PTCL-NOS 18.6%), 20 cases of T cell lymphoblastic lymphoma (T-LBL) (10.9%), eight cases of ALK- (4.4%) anaplastic large cell lymphoma (ALCL), seven cases of ALK+(3.8%) ALCL, and six cases of subcutaneous panniculitisis-like T cell lymphoma (SPTL) (3.3%). Among all patients, 128 patients presented with B symptoms (69.95%). The OS of peripheral T/NK-cell lymphoma and precursor T-cell lymphoma (T-LBL) of the included cases showed no different though two diseases differ in terms of biology and treatment strategy. That justifies our decision to observe the predictors to survival in the same cohort.

Data collection

Three physicians of the research team extracted the clinical information for each patient from medical records and entered the data into a standard clinical datasheet for computerization. Each record included admission No., record No., sex, date of birth, date of last follow-up, living or not, Ann Arbor stage and symptoms at diagnosis. Additional data and laboratory data were recorded, including hemoglobin (Hb), platelet count, WBC count, ESR, serum lactate dehydrogenase, β2MG, serum Ca²⁺ level, initial therapy and response, survival status and cause of death. In a few cases, some clinical information was missing due to the condition deteriorated quickly and no further testing.

The diagnosis was established according to the World Health Organization (WHO) 2003 classification (the WHO updated the classification in 2008, but there was no revision or update on T cell lymphoma). It was consistent with the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) as well.

The personally identifiable patient information was removed, and informed consent for possible academic research purpose was obtained from all patients upon admittance.

The OS time was the main outcome indicator and was measured from the date of diagnosis to the date of death or last follow-up. Surviving patients at the last contact date of follow-up were classified as censored.

The continuous variables, such as serum albumin, β2MG, ESR, and WBC, were primarily categorized by median value; Hb was categorized with a normal range, and Ca²⁺ was categorized by 20th percentile values at a statistically significant cutoff value (Supplementary File 1, http://links.lww.com/CMJ/A12).
Statistical analysis

The data were analyzed with SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA). Non-normally distributed continuous data were presented as the median, interquartile range (IQR), and range. The OS rate was compared between groups using Pearson χ²-test. The univariate life-test analysis was calculated by the Kaplan-Meier method to generate the product-limit survival. Multiple Cox regression was performed to identify prognostic factors for OS, and the hazard ratio (HR) was stratified by hemophagocytic lymphohistiocytosis (HLH). We calculated the HR and its 95% confidence interval (CI) with Cox regression. Significant variables in the univariate analyses were considered for inclusion in the multivariable Cox regression model. These values were selected by a stepwise regression with an entry criterion of P ≤ 0.05 and exit criterion of P ≥ 0.10.

We computed the regression models and made statistical inferences on the parameters estimation by PROC QUANTREG in SAS 9.4. Quantile regression is a robust method with which to estimate either the conditional median or other quantiles of the response variable. This method does not make a distributional assumption for the errors in modeling and is more robust against outliers in the measurements of dependent variable. The CI estimation employed the inversion of a rank test with QReg.[19] The regression coefficients of each variable changed over the range of the curve based on other covariates, indicating the different impact on OS. The most clinically relevant impact in different sections of the distribution on OS was detected by a significance testing of the coefficients variation over the different quartiles of the QReg. The response variable OS for each individual was considered over the study period. We also considered the quartiles of OS values, and the 25th, 50th, 75th, and 95th percentiles.

Results

The demographic characteristics of the patients are presented in Table 1. Among 183 participants, the median age was 45 years with a range of 12 to 85 years; 127 (69.4%) individuals were male; 163 (89.1%) individuals were diagnosed with peripheral T cell lymphoma; 38 (20.8%) had HLH; 128 (70.0%) patients presented with clinical symptoms at diagnosis; 87 (47.5%) showed that higher serum albumin level, serum Ca level, and platelet count at diagnosis and patients free of HLH were associated with a higher survival rate, whereas lower serum LDH level, lower IPI score and earlier Ann Arbor clinical stage were associated with a higher survival rate. The median duration of survival after diagnosis was 5.1 months (Q1–Q3 = 1.1–24.5). No significant differences presented in sex, age (below or above 60 years) and serum β2MG level between 2 groups classified by median values and HSCT [Table 2]. The OS rate based on the product-limit survival distribution was significantly associated with the Ann Arbor clinical stage (stage=I-II, P < 0.001), having HLH or not (P < 0.001), the IPI score (IPI=0–1, P < 0.001), and having B symptoms or not (P < 0.001); however, OS was not associated with age above 60 years or sex [Figure 1].

Table 1: Clinical characteristics of the patients with systemic non-Hodgkin T/NK cell lymphoma (n=183)

| Characteristics                  | Values |
|----------------------------------|--------|
| Age (years)                      | 45 (28–61) |
| Sex                              |        |
| Male                             | 127 (69.4) |
| Female                           | 56 (30.6)  |
| Diagnosed with                   |        |
| PTCL                             | 163 (89.1) |
| Non-PTCL                         | 20 (10.9)  |
| Had HLH                          |        |
| Yes                              | 38 (20.8)  |
| No                               | 145 (79.2) |
| Clinical staging with symptoms   |        |
| Yes                              | 55 (30.0)  |
| No                               | 128 (70.0) |
| Underwent stem cell transplantation|      |
| Yes                              | 14 (7.7)   |
| No                               | 169 (92.3) |
| Death                            |        |
| Yes                              | 87 (47.5)  |
| No                               | 96 (52.5)  |

Values were shown as median (Q1–Q3) or n (%). HLH: Hemophagocytic lymphohistiocytosis; PTCL: Peripheral T cell lymphoma.

After adjustments for other variables, multivariable analysis of prognostic factors for OS showed that patients with advanced clinical stage and symptoms have a 3.16-times greater HR compared to those without symptoms (the adjusted HR is 3.16, 95% CI: 1.39–7.20); this value is based on stratification by HLH. The HR for patients with a lower platelet count was 2.57 (95% CI: 1.57–4.19), and the HR for patients with a higher IPI score was 1.29 (95% CI: 1.01–1.66), suggesting that with each unit increasing in IPI score, the HR increase by approximately 1.3 times. Additionally, T-LBL (HR = 0.40, 95% CI: 0.20–0.80), higher white cell counts at diagnosis (HR = 0.57, 95% CI: 0.34–0.96), higher levels of serum albumin at diagnosis (HR = 0.6, 95% CI: 0.37–0.97; ref = “≥34 g/L”) and a higher ESR (HR = 0.53, 95% CI: 0.33–0.87; ref = “≥23 mm/h”) were protective factors for OS (Table 3).
were statistically significant. The coefficients of serum β2MG level and serum ESR were statistically significant at the middle of the coefficient curve. The coefficient of IPI was consistently negatively associated with OS (IPI ≥2), suggesting that higher IPI scores had a greater impact on the OS time than lower IPI scores; however, these values were not significant at Q3. To obtain a more detailed understanding of the impacts of the coefficient variation for each variable on OS, we could, for example, observe the effects of every 5 percent change in each quartile on OS [Figure 2]. The coefficient of IPI (IPI ≥2) was negatively associated with quartile level, which suggests that higher IPI scores have a greater impact on the OS time than lower IPI scores. The same trend was observed in the coefficients of platelet count, serum Ca+ level, and serum β2MG level; while the coefficient of serum Ca+

Table 2: Overall survival rate stratified by sociodemographic and clinical characteristics (n=183)

| Factors                       | Values | Survival cases at the last follow-up (n) | Total cases of the subgroup (N) | OS rate (%) | χ2        | P        |
|-------------------------------|--------|----------------------------------------|---------------------------------|------------|-----------|----------|
| Sex                           |        |                                        |                                 |            |           |          |
| Male                          | 68     | 127                                    | 53.5                            | 0.20       | 0.658     |          |
| Female                        | 28     | 56                                     | 50.0                            |            |           |          |
| Age (years), median (Q1–Q3)   | 45 (28–61) | 65                                    | 133                            | 48.9       | 2.50      | 0.113    |
| <60                           |        |                                        |                                 |            |           |          |
| ≥60                           |        |                                        |                                 |            |           |          |
| Serum albumin levels (g/dL), median (Q1–Q3) | 34.4 (28.6–38.8) | 35                                    | 93                                             | 37.6       | 16.7      | <0.0001  |
| <34                           |        |                                        |                                 |            |           |          |
| ≥34                           |        |                                        |                                 |            |           |          |
| Serum β2MG levels (mg/L), median (Q1–Q3) | 2.9 (2.1–4.2) | 59                                    | 111                                           | 53.2       | 0.05      | 0.815    |
| <2.9                          |        |                                        |                                 |            |           |          |
| ≥2.9                          |        |                                        |                                 |            |           |          |
| Serum Ca levels at diagnosis (g/dL), median (Q1–Q3) | 2.14 (1.99–2.24) | 8                                     | 27                                             | 29.6       | 6.62      | 0.010    |
| <1.9                          |        |                                        |                                 |            |           |          |
| ≥1.9                          |        |                                        |                                 |            |           |          |
| ESR at diagnosis (g/dL), median (Q1–Q3) | 23 (9–46) | 47                                    | 106                                           | 44.3       | 6.62      | 0.010    |
| <23                           |        |                                        |                                 |            |           |          |
| ≥23                           |        |                                        |                                 |            |           |          |
| Hemoglobin levels at diagnosis (g/dL), median (Q1–Q3) | 110 (87–132) | 43                                    | 111                                           | 38.7       | 21.3      | <0.0001  |
| <120                          |        |                                        |                                 |            |           |          |
| ≥120                          |        |                                        |                                 |            |           |          |
| LDH levels at diagnosis (g/dL), median (Q1–Q3) | 233 (150–469) | 62                                    | 93                                             | 66.7       | 15.2      | <0.0001  |
| <233                          |        |                                        |                                 |            |           |          |
| ≥233                          |        |                                        |                                 |            |           |          |
| Platelet levels at diagnosis (g/dL), median (Q1–Q3) | 157 (64–234) | 4                                     | 40                                             | 10.0       | Fisher    | <0.000   |
| <53                           |        |                                        |                                 |            |           |          |
| ≥53                           |        |                                        |                                 |            |           |          |
| White cell count at diagnosis (/L), median (Q1–Q3) | 5.05 (2.96–7.80) | 34                                    | 91                                             | 37.4       | 16.5      | <0.0001  |
| <5                            |        |                                        |                                 |            |           |          |
| ≥5                            |        |                                        |                                 |            |           |          |
| International prognostic index (IPI)† |        |                                        |                                 |            |           |          |
| 0/1                           |        |                                        |                                 |            |           |          |
| 2/3                           |        |                                        |                                 |            |           |          |
| 4/5                           |        |                                        |                                 |            |           |          |
| Ann Arbor clinical stage      |        |                                        |                                 |            |           |          |
| I&II                          | 32     | 37                                     | 86.5                            | 21.5       | <0.0001   |          |
| III&IV                        | 64     | 146                                    | 43.8                            |            |           |          |
| Underwent stem cell transplantation |        |                                        |                                 |            |           |          |
| Yes                           | 7      | 14                                     | 50.0                            | 0.04       | 0.850     |          |
| No                            | 89     | 169                                    | 52.7                            |            |           |          |
| Had HLH                       |        |                                        |                                 |            |           |          |
| Yes                           | 4      | 38                                     | 10.5                            | 33.81      | <0.0001   |          |
| No                            | 92     | 145                                    | 63.5                            |            |           |          |
| Survival time after diagnosis (months) | 5.1 (1.1–24.5) |                                        |                                 |            |           |          |

β2MG: Beta-2 microglobulin; HLH: Hemophagocytic lymphohistocytosis; IPI: International prognostic index; LDH: Lactate dehydrogenase; OS: Overall survival. Stem cell transplantation includes autologous and allogeneic transplantation without further classification due to limited cases. *OS rate (%) = Survival cases at the last follow-up (n) / Total cases of the subgroup (N) × 100. †Two cases missed IPI score.
level was significantly and negatively associated with OS above the 85th percentile, a high serum Ca+ level had a negative impact on the OS time when controlled for other factors. The coefficients of serum ESR and diagnosis with PTCL increased with the OS time but were statistically significant only at higher quartiles. The coefficients of HSCT and no clinical symptoms were greater at the middle of the quartile curve, showing a greater impact on the central quartile when controlled for other factors.
Discussion

To our knowledge, this study added evidence to explore the predictors of survival time in patients with non-Hodgkin T/NK lymphoma and presenting their varied impact over different percentile levels using a quantile regression model rather than linear or logistic regression. Our main findings were that the IPI has a consistent negative association with OS (IPI ≥ 2) and that higher IPI score showed more impact on the survival time. The quantile regression also showed that the IPI score is a highly robust prognostic indicator after adjusting for other factors and statistically significant at 3 quartiles of the curve. In addition, serum ESR is also comparatively stable at the middle 2 quartiles of the curve as a prognostic indicator. The same trend was observed in the coefficients of platelet count, serum Ca+ level, and serum β2MG level, while HSCT and clinical stage without clinical symptoms impacted the survival time only in the middle section of the curve; the lower and upper concentration levels had no significant impact on the survival time. These findings are interesting and are worthy of further observation. Most of the prognostic indicators were validated with Federico et al[25] and Xu et al[26], but we presented with a more specified way in term of concrete section of the distribution of the curve.

There is no consensus on the efficacy of HSCT in the treatment of non-Hodgkin T/NK lymphoma. Some studies have focused on small populations characterized by mixed histology, varying disease status at transplantation, and treatments with diverse regimens. Other studies have excluded patients with chemo-refractory or poor-risk disease who were not eligible for HSCT, which may incur selection bias.[1] Studies[27-29] have also shown that HSCT could improve the prognosis of peripheral T cell lymphoma. However, the results of the present study did not show that HSCT could increase the OS rate in the multivariable analysis. These results were consistent with those of Tse[30,31] showing that allogeneic HSCT should be reserved for patients who are at high risk of relapse; moreover, the role of allogeneic HSCT in NK/T cell
lymphoma must be strictly evaluated. These findings might be true or might be due to the limited number of selected research participants, the aggressive nature of these diseases or the frequency at which the disease relapses. However, HSCT might have an impact on OS among the average patients at the central quantile.

The findings of the present study on the correlation between serum ESR and OS are consistent with those of Bien et al\cite{19}; moreover, these results may be attributed to quantile regression. The correlation of ESR with OS does not present a linear prediction, central 2 quartiles have good predicting roles in OS. In addition, platelet count was an independent prognostic indicator in patients with diffuse large B cell lymphoma, which was consistent with the others’ findings,\cite{26,32} but the impact of platelet count was more significant at extremely low levels according to the percentage curve.

Gui et al and Bien et al\cite{15,27} found that serum β2MG levels could predict the OS of patients with peripheral T cell lymphoma or Hodgkin lymphoma. We, however, observed a statistically significant impact from serum β2MG on OS only in the middle section, although the impact of serum β2MG on OS seemed to increase with increasing quartile level.

According to our multiple Cox proportional hazards regression analysis and quantile regression analysis, absolute WBC count might be a promising predictor for OS, though significant only in the lower boundary of the quantile regression curve. But the predicting power of WBC count is validated by a European study named “T cell score” for modeling PTCL-NOS prognosis based on 4 covariates (serum albumin, performance status, stage and absolute neutrophil count).\cite{33} In most occasions, absolute neutrophil count is consistent with WBC count of patients with non-Hodgkin T/NK cell lymphoma.

The strength of this study included: We used quantile regression and revealed some interesting findings on the impact of different indicators on the prediction of OS over a quartile distribution. These effects might be underestimated by least squares regression. There were paucity of researches focus on predictors of OS in B cell lymphoma patients, while few studies conducted among non-Hodgkin T/NK cell lymphoma patients. As the largest study center for HLH in China, our hospital admits quite high proportion of HLH patients. In the present study, we included 30 HLH patients. Most HLH patients have really poor prognosis\cite{18}; therefore, to control for the potential confounding factor of HLH, we stratified patients based on HLH status for a clearer understanding of the predictive values of clinical manifestations/indicators on OS than other studies that might mix HLH patients with other participants.

This study had also some limitations. As a retrospective study, we collected data on OS time and prognostic factors but no other information on survival, such as progress-free survival (PFS) or disease-free survival (DFS), in a single institution. There might be bias during patient selection, data collection and even data analysis. These findings may not be generalizable throughout China. Most patients who sought treatment in Beijing, a comparatively megakropolitan city, had advanced disease stages or better economic conditions. Discharged patients who did not live in Beijing presented challenges in the follow-up. In addition, patients with different disease types or stages and received heterogeneous treatment undoubtedly had different clinical outcomes and treatment responses; thus, the serum indicators may vary. Therefore, we reported whether the lower bound, middle bound or upper bound of the indicators had greater impact on survival. Furthermore, considering the number of systemic lymphoma patients, the impact of prognostic factors may not be generalizable. However, 183 patients could shed some light on the prediction of prognostic outcomes. We did not consider the impact of the histological subtype on autologous stem cell transplantation (ASCT), and as the DFS or PFS time is much shorter for patients with diseases such as NK/T cell lymphoma, we selected the OS rate as the only indicator to compare with more conventional risk factors, such as the IPI.

In summary, we used an innovative statistical method, quantile regression, to explore the prognostic predictors of OS among systemic lymphoma patients. The IPI score was determined to be a robust indicator of prognosis at 3 quartiles, and serum ESR is stable at the middle 2 quartiles section when adjusted for HLH. In addition, platelet count, and serum β2MG level could predict OS among non-Hodgkin’s T/NK cell lymphoma patients at different percentage levels.

**Funding**

This work was supported by grants from the National Natural Science Foundation of China (No. 81673232), the Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding (No. ZYLYX201702), the Beijing Municipal Science and Technology Plan of Capital Characteristics Project (No. Z151100004015172), and the Capital Health Research and Medical Development Foundation (No. 2016-2-2027).

**Conflicts of interest**

None.

**References**

1. Dhawale TM, Shustov AR. Autologous and allogeneic hematopoietic cell transplantation in peripheral T/NK-cell Lymphomas: a histology-specific review. Hematol Oncol Clin North Am 2017;31:335–357. doi: 10.1016/j.hoc.2016.11.003.
2. Xu B, Liu P. No survival improvement for patients with angioimmunoblastic T-cell lymphoma over the past two decades: a population-based study of 1207 cases. PloS One 2014;9:e92385. doi: 10.1371/journal.pone.0092385.
3. Kao HW, Lin TL, Shih LY, Dunn P, Kuo MC, Hung YS, et al. Clinical features, outcome and prognostic factors of 87 patients with angioimmunoblastic T cell lymphoma in Taiwan. Int J Hematol 2016;104:256–265. doi: 10.1007/s12185-016-2010-6.
4. Nakajima Y, Tomita N, Watanabe R, Ishiyama Y, Yamamoto E, Ishihashi D, et al. Prognostic significance of serum beta2 microglobulin level in Hodgkin lymphoma treated with ABVD-based therapy. Med Oncol 2014;31:185. doi: 10.1007/s12032-014-0185-3.
