

Clinical characteristics and prognostic factors of primary gastric lymphoma

A retrospective study with 165 cases

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Abstract

Primary gastric lymphoma (PGL) is the most common extranodal non-Hodgkin lymphoma. This retrospective study aimed to analyze the clinical characteristics, prognostic factors, and roles of different treatment modalities in patients with PGL.

From January 2003 to November 2014, 165 patients who were diagnosed with PGL at West China Hospital were enrolled in this study. The clinical features, treatment, and follow-up information were analyzed.

In this study, diffuse large B-cell lymphoma (DLBCL) (108, 65.5%) and mucosa-associated lymphoid tissue (MALT) lymphoma (52, 31.5%) were two predominant histological subtypes. One-year and 5-year overall survival (OS) rates of all patients were 95.2% and 79.5%, respectively; in whom 110 (66.7%) underwent surgery, 110 (66.7%) received chemotherapy, 12 (7.3%) received radiotherapy, and 10 (6.1%) received *Helicobacter pylori* eradication. And 75 patients (45.5%) were treated with at least 2 different types of therapies. Elevated lactic dehydrogenase (LDH) levels, poor performance status (PS), advanced stage, International Prognostic Index (IPI) score ≥ 3 , conservative treatment, and high-grade histological subtype were associated with worse prognosis in univariate analysis. Cox regression analysis showed that LDH levels, PS, staging, and histological subtype were independent predictors of survival outcomes. In the DLBCL type, 5-year OS was significantly better in the surgically treated group (80.1%) than that of patients conservatively treated (49.8%) ($P=0.001$). Surgical treatment had almost no impact on OS in the MALT type than conservative treatment ($P=0.597$). The proportion of patients received conservative treatment increased from 4.5% in period 1 to 51.7% in period 4.

High LDH levels, poor PS, advanced staging, and malignant pathological type at diagnosis are significantly associated with poor OS. Our data suggest that surgery is superior in prognosis over conservative treatment in the DLBCL type, but not in the MALT type. Recently, conservative treatment is becoming more preferred approach in patients with PGL.

Abbreviations: CI = confidence interval, DLBCL = diffuse large B-cell lymphoma, ECOG = Eastern Cooperative Oncology Group, EUS = endoscopic ultrasonography, HE = hematoxylin eosin, HR = hazard ratio, IPI = International Prognostic Index, JGCA = Japanese Gastric Cancer Association, LDH = lactic dehydrogenase, MALT = mucosa-associated lymphoid tissue, MST = mean survival time, NHL = non-Hodgkin lymphoma, OS = overall survival, PGL = primary gastric lymphoma, PS = performance status, WHO = World Health Organization.

Keywords: conservative treatment, primary gastric lymphomas, prognosis, surgical treatment

1. Introduction

Primary gastric lymphoma (PGL) is a rare tumor, accounting for 4% to 20% of all non-Hodgkin lymphomas (NHL) and for 5% of primary gastric neoplasms.^[1] The stomach is the most common extranodal site of NHL presentation, representing

30% to 40% of all extranodal lymphomas and 55% to 65% of all gastrointestinal lymphomas.^[2,3]

According to World Health Organization (WHO) classification, the predominant histological subtypes of PGL are marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue

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(MALT) and diffuse large B-cell lymphoma (DLBCL).^[4] MALT lymphomas are low-grade lesions, which are usually secondary to *Helicobacter pylori* infection. So H pylori (+) MALT lymphomas were regularly treated with *H pylori* eradication therapy.^[5] As for DLBCL, it is high-grade type gastric lymphoma and more common than low-grade type. The most common symptoms at presentation include epigastric pain, nausea, vomiting, weight loss, and gastrointestinal bleeding.^[6] Regarding therapies of PGL, the role of gastrectomy is still controversial. Although there are many options in treatment approach, including surgical resection, antibiotic therapy, chemotherapy, and radiotherapy, they can be simply divided into 2 kinds of treatments by whether taking surgery. Surgery was used to be the front-line treatment for PGL. However, recent studies have shown that radical gastrectomy is disputed and considered unnecessary.^[7] Surgery is recommended as urgent treatment of patients presenting severe perforation or bleeding, and as palliative treatment.^[8] In previous researches, general prognosis of PGL involved tumor characteristics and host-related factors, such as histological subtype, age, performance status (PS), and so on.^[9]

The aim of this retrospective research was to analyze the clinical characteristics, prognostic factors, and roles of different treatment modalities in patients with PGL.

2. Materials and methods

2.1. Patients

This retrospective study included 165 patients who were diagnosed with PGL from January 2003 to November 2014 in West China Hospital, Sichuan University, China. The pathological specimens were obtained from endoscopic biopsies and surgical resections. All the cases were diagnosed with PGL based on hematoxylin eosin (HE) and immunohistochemical methods according to the criteria of Isaacson.^[10] CD20, UCHL, and LCA staining were routinely carried out before 2006; after 2006, CD3, CD10, phosphoenolpyruvate carboxykinase, and Bcl-6 were conducted routinely; for some cases, CD30, CD56, CD79, epithelial membrane antigen, and CyclinD1⁺ were also performed. In addition, detection of clonal IgH rearrangements was routinely carried out after 2004. Details of history, physical examination, blood tests, staging, treatment, and outcome were obtained from medical records. The characteristics or results were recorded for each patient including age, sex, presenting symptoms, PS, lactic dehydrogenase (LDH) level, tumor stage, pathological subtype, grade, International Prognostic Index (IPI) score, and treatment modality.

According to the Lugano staging system, staging procedure was based on physical examination, blood tests, imaging examination for patients with conservative treatment. As for patients with surgical treatment, intraoperative exploration, and pathology results were further included. Besides, advances in imaging techniques, including endoscopic ultrasonography (EUS), have offered better preoperative diagnostic evaluation and more accurate staging. Performance status was evaluated according to the Eastern Cooperative Oncology Group (ECOG) scale.^[11] Changing trends of treatment modalities to PGL were analyzed in 4 consecutive time periods: from 2003 to 2005 (period 1), from 2006 to 2008 (period 2), from 2009 to 2011 (period 3), and from 2012 to 2014 (period 4). Regular outpatient visit was the first choice and follow-up information was updated until November 2015. Telephones and mails were adopted as 2 main supplementary follow-up methods.

2.2. Statistics

SPSS 19.0 (SPSS, Chicago, IL) was used for all statistical analyses. Kaplan–Meier curves (log-rank test) were used for the analyses of survival outcome, and the log-rank test was performed to test the statistical significance. The prognostic value of different variables for clinical outcome was estimated by multivariate analysis using the Cox regression model with the backward stepwise method. Hazard ratio (HR) with 95% confidence interval (CI) was calculated. Potential prognostic factors were included in the Cox regression model as *P* < 0.05 in the univariate analysis. A 2-sided *P* value of <0.05 was considered statistically significant.

The West China Hospital research ethics committee approved retrospective analysis of anonymous data. Signed patient informed consent was waived per the committee approval, because it was a retrospective analysis.

3. Results

3.1. Clinical and histological characteristics

Patients' characteristics are detailed in Table 1. The group of patients included in the study consisted of 90 men and 75 women. The median age was 56 years (range 21 to 78 years) for the whole group. The most common symptoms were epigastric pain in 133 patients (80.6%), gastrointestinal bleeding in 59 (35.8%), and weight loss in 29 (17.8%). Most frequent histological subtype of PGL in our study was DLBCL in 108 patients (65.5%), followed by MALT lymphoma in 52 patients (31.5%). Using the Lugano staging system, 136 patients (82.4%) were diagnosed with Stage I

Table 1
Clinical characteristics of the patients.

Characteristics	Number of assessable patients (%)
Age, y	
Median	56
Range	21–78
Sex	
Male	90 (54.5)
Female	75 (45.5)
LDH	
Normal	128 (77.6)
Elevated	37 (22.4)
WHO PS	
0–1	113 (68.5)
2	52 (31.5)
Lugano staging	
I	67 (40.6)
II1	43 (26.1)
II2	26 (15.7)
IIE	15 (9.1)
IV b	14 (8.5)
IPI score	
0–2	146 (88.5)
≥3	19 (11.5)
Histology	
DLCL	108 (65.5)
MALT	52 (31.5)
Burkitt lymphoma	3 (1.8)
PTCL	1 (0.1)
ALCL	1 (0.1)

ALCL = anaplastic large cell lymphoma, DLBCL = diffuse large B-cell lymphoma, IPI = International Prognostic Index, LDH = lactic dehydrogenase, MALT = mucosa-associated lymphoid tissue, PS = performance status, PTCL = peripheral T-cell lymphoma, WHO = World Health Organization.

Table 2**Various treatment modalities according to histological subtypes.**

Treatment modality	DLBCL	MALT	Burkitt lymphoma	PTCL	ALCL
Surgical treatment					
SUR alone	22	17			1
SUR+CT	51	13	3	1	
SUR+CT+RT	2				
Conservative treatment					
CT alone	29	6			
RT alone		5			
CT+RT	4	1			
HP eradication only		10			

ALCL = anaplastic large cell lymphoma, CT = chemotherapy, DLBCL = diffuse large B-cell lymphoma, HP = *Helicobacter pylori*, MALT = mucosa-associated lymphoid tissue, PTCL = peripheral T-cell lymphoma, RT = radiotherapy, SUR = surgical treatment.

and II disease, 15 (9.1%) and 14 (8.5%) patients were diagnosed with stage IIE and IV disease, respectively.

3.2. Treatment modalities

Table 2 shows the treatment modalities applied to patients with respect to histological subtype. Surgical treatment either combined or as single therapy was performed in 110 patients (66.7%). The most common type of surgical treatment procedure was total gastrectomy and lymph node dissection. Gastrojejunostomy was performed as palliative care in 3 patients with pyloric obstruction. Among the 110 patients (66.7%) who received chemotherapy, 35 patients received only chemotherapy and 75 patients received chemotherapy combined with other treatment modalities. The most common chemotherapy regimen was CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone). It was first-line treatment in 108 patients (86 patients with DLBCL, 19 patients with MALT lymphoma, 2 patients with Burkitt lymphoma, and 1 patient with peripheral T-cell lymphoma). Twenty-six patients treated with rituximab (ranged from 1 to 8 cycles), with a median of 6 cycles. Other regimens included FC (fludarabine and cyclophosphamide) (1 case with MALT) and Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone, methotrexate, and cytarabine) (1 case with Burkitt lymphoma). Of the 12 patients (7.3%) who received radiotherapy, 7 received it as adjuvant treatment, while 5 patients with MALT lymphoma received only radiotherapy for *H. pylori* (−). Ten patients (6.1%) underwent treatment for *H. pylori* eradication as they were diagnosed with *H. pylori* (+) MALT lymphomas.

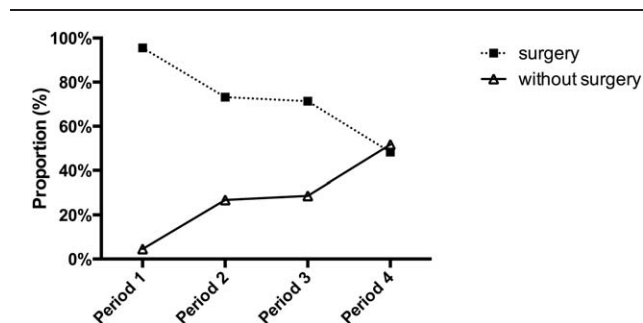


Figure 1. Trend of treatment modalities to primary gastric lymphoma (PGL) over the 12-year period from 2003 to 2014.

Figure 1 shows the changing trend of treatment modalities to PGL. The proportion of patients who received conservative treatment increased from 4.5% in period 1 to 51.7% in period 4, whereas patients who received surgical treatment gradually decreased from 95.5% in period 1 to 48.3% in period 4.

3.3. Survival and prognostic factors

As of November 2015, 30 patients in this study had died. All 165 patients were enrolled into survival analysis study. The median follow-up was 45 (3–155) months and the follow-up rate was 97.6%. The 1-year and 5-year overall survival (OS) rates, which were estimated by using the Kaplan–Meier method, were 95.2% and 79.5%, respectively, with mean survival time (MST) of 127 months (95% CI 118–136). In patients with elevated serum LDH level, the 5-year OS was 47.2% versus 89.0% for those with normal serum LDH level ($P < 0.001$).

In univariate analysis among all potential prognostic factors, elevated LDH levels (>245 U/L), poor PS (ECOG ≥ 2), advanced Lugano staging ($\geq$ stage IIE), IPI ≥ 3 , conservative treatment, and high-grade histological subtype were associated with poor survival. In multivariate analysis of OS, the results showed that LDH levels (>245 U/L) (HR = 2.42, 95% CI 1.05–5.59, $P = 0.039$), PS (ECOG ≥ 2) (HR = 8.57, 95% CI 3.78–19.44, $P < 0.001$), Lugano staging ($\geq$ stage IIE) (HR = 5.67, 95% CI 2.36–13.62, $P < 0.001$), and histological subtype (HR = 5.04, 95% CI 1.58–16.03, $P = 0.006$) remained as significant predictors. Table 3 summarizes univariate and multivariate analyses of the factors considered as predictors of OS.

We also evaluated OS separately for patients with DLBCL and MALT lymphoma, but not in other histological types of gastric lymphomas, due to a rather small number of patients in each group. In the 108 DLBCL patients, 75 patients treated with surgery had 5-year OS 80.1% versus 49.8% for patients treated conservatively ($P = 0.001$) (Fig. 2). Meanwhile, in the 52 MALT lymphoma patients, 30 patients treated with surgery had 5-year OS 86.4% versus 95.5% for patients treated conservatively ($P = 0.597$) (Fig. 3).

4. Discussion

In this series, there are 165 patients with PGL, 54.5% of which were men and 45.5% women. The male predominance result corresponds to previous observations.^[12,13] Epigastric pain, gastrointestinal bleeding, weight loss, vomiting, and nausea were the most common symptoms in our study, as reported in other series.^[12,14,15]

Table 3
Risk factors associated with overall survival in patients.

Variable	Univariate analysis		Multivariate analysis	
	Five-year OS (%)	P	HR (95% CI)	P
Age				
≤60 y	83.2	0.175		
>60 y	73.0			
Sex				
Female	76.7	0.436		
Male	83.4			
LDH				
Normal	89.0	<0.001	2.42	0.039
Elevated	47.2		(1.05–5.59)	
WHO PS				
0–1	89.2	<0.001	8.57	<0.001
2	56.6		(3.78–19.44)	
Lugano staging				
I–II2	87.5	<0.001	5.67	<0.001
≥II2	43.8		(2.36–13.62)	
IPI score				
0–2	87.0	<0.001	—*	—
≥3	26.3			
Treatment				
Surgery	84.3	0.014	Not significant	
Conservative	69.4			
Histological subtypes				
MALT	73.3	0.018	5.04	0.006
Non-MALT	92.8		(1.58–16.03)	

IPI=International Prognostic Index, LDH=lactic dehydrogenase, MALT=mucosa-associated lymphoid tissue, PS=performance status, WHO=World Health Organization.

*IPI score was not included in multivariate analysis, considering it covers LDH levels, PS, and Lugano staging.

According to histological types, PGLs include low-grade MALT lymphoma and high-grade DLBCL.^[4] In this retrospective study, the proportions of the DLBCL (65.5%) and MALT lymphoma (31.5%) were similar to the 59.9% and 37.9%, respectively, reported by Koch et al.^[15] The distribution of the rare subtypes (Burkitt lymphoma 1.8%, anaplastic large cell lymphoma 0.1%, peripheral T-cell lymphoma 0.1%) was similar in both researches.

There are multiple factors that contribute to survival. In previous studies, female, low-grade histology, good PS, and surgical resection have been reported to be associated with high OS. Age >60 years, advanced stage, poor PS, and elevated LDH were associated with poor outcome.^[12,13,16–18] Based on our results, variables associated with decreased survival were elevated LDH levels, poor PS, advanced stage, IPI score ≥3, conservative treatment, and high-grade histological subtype. This study did not show a relationship between age and survival rate. The relatively small sample size may cause this outcome. Only LDH levels, PS, staging, and histological subtype retained their significance in the multivariate analysis.

LDH level was considered as a prognostic factor, and its level higher than the upper limit of the normal range implied poor prognosis.^[9,19] Our study was in agreement with previous research. IPI is a commonly used clinical predictive system for patients with NHL. It is comprised of 5 factors including age >60 years, elevated serum LDH level, poor PS, advanced disease stage, and involvement of multiple extranodal sites. This index was shown to be an effective prognostic model to predict long-term survival in NHL.^[20] Given that IPI score covers LDH levels, PS, and Lugano staging, it was not included in multivariate analysis. Since these 3 factors were proved to be independent predictors of survival outcomes in multivariate analysis, our data

revealed that IPI had a prognostic value in predicting survival in PGL and they were also consistent with a recently published report by Hosseini et al.^[21] In addition, some researches suggested that a modified IPI could be more accurate than the initial IPI to predict prognosis in PGL.^[22,23]

Infection with *H pylori* appears to be a vital causal factor in the development of MALT lymphomas. Thus, the treatment of low-grade MALT lymphoma included *H pylori* eradication. Previous studies have showed that eradication of *H pylori* can lead to lymphoma regression. Other therapeutic approaches, like radiotherapy and surgery are used for patients who are unresponsive to antibiotics or relapse after the first remission.^[24,25] In the present study, all 10 patients who underwent treatment for *H pylori* eradication were still alive. As for 30 patients treated with surgery of the 52 MALT lymphoma patients, we found that there was no significant difference when we compared the OS of patients treated either with surgery alone

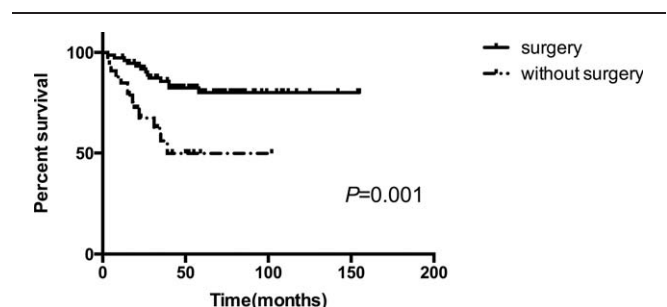


Figure 2. Effect of surgery on survival in the diffuse large B-cell lymphoma (DLBCL) patients.

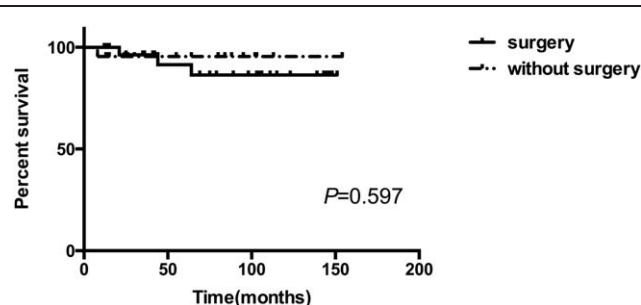


Figure 3. Effect of surgery on survival in the mucosa-associated lymphoid tissue (MALT) lymphoma patients.

or with combination therapy. Our data suggested that conservative treatment modalities should be preferred in MALT lymphoma patients.

Traditionally, radical gastrectomy was regarded as the front-line treatment for PGL. In recent years, however, surgery has gradually been replaced by chemotherapy and radiotherapy in the treatment of PGL. Huang et al^[26] reported a prospective study of 83 patients. There was no statistically significant difference between surgery and conservative groups. Our results were different from some other studies suggesting stomach-conserving therapies for PGL,^[26,27] which showed that surgical group had a statistically significant survival advantage compared with the conservative group in the DLBCL patients. The results were biased, as some inoperable patients treated with conservative treatment were in a worse PS or presented with a more extensive disease. Nearly 90.0% of the DLBCL patients recruited in the surgery group presented at an early Lugano stage (I-II2), and the proportion in conservative group was 66.7%. Furthermore, based on multivariate analysis of OS, treatment modality was not associated with OS. Considering the acceptable tolerance and promoted quality of life conservative treatment should be recommended.

Actually, conservative approach to treatment of PGL has gradually been front-line treatment in our hospital, since 2011 after the guideline for lymphoma published by Japanese Gastric Cancer Association (JGCA).^[28] Treatment modality to PGL changed from surgery predominantly to conservative treatment preferred initially.

The main limitations of this study were its retrospective design with a relatively small sample size. And the data come from a single hospital, so the results may not represent the Chinese population well. Further randomized prospective studies with a large sample size are needed to establish the optimal management for patients with PGL.

5. Conclusion

In this study, high LDH levels, poor PS, advanced staging, and malignant pathological type at diagnosis were associated with poor OS. Our data suggest that surgery is superior in prognosis over conservative treatment in the DLBCL type, but not in the MALT type. Recently, conservative treatment is becoming more preferred approach in patients with PGL.

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References

- [1] Al-Akwaa AM, Al-Mofleh SIA. Primary gastric lymphoma. *World J Gastroenterol* 2004;195:1199.
- [2] Prasanna , Ghimire , Guang-Yao , et al. Primary gastrointestinal lymphoma. *World J Gastroenterol* 2011;17:697–707.
- [3] Newton R, Ferlay J, Beral V, et al. The epidemiology of non-Hodgkin's lymphoma: comparison of nodal and extra-nodal sites. *Int J Cancer* 1997;72:923–30.
- [4] Doglioni C, Ponzoni M, Ferreri AJM, et al. Gastric lymphoma: the histology report. *Dig Liver Dis* 2011;43:S310–8.
- [5] Koch P, Probst A, Berdel WE, et al. Treatment results in localized primary gastric lymphoma: data of patients registered within the German multicenter study (GIT NHL 02/96). *J Clin Oncol* 2005;23:7050–9.
- [6] Medina-Franco H, Germes SS, Maldonado CL. Prognostic factors in primary gastric lymphoma. *Ann Surg Oncol* 2007;14:2239–45.
- [7] O'Malley DP, Goldstein NS, Banks PM. The recognition and classification of lymphoproliferative disorders of the gut. *Hum Pathol* 2013;45:899–916.
- [8] Avilés A, Nambo MJ, Neri N, et al. The role of surgery in primary gastric lymphoma - Results of a controlled clinical trial. *Ann Surg* 2004;240:44–50.
- [9] Dai C, Oki Y, Ine S, et al. Primary gastric diffuse large B-cell lymphoma (DLBCL): analyses of prognostic factors and value of pretreatment FDG-PET scan. *Eur J Haematol* 2010;84:493–8.
- [10] Isaacson PG. Gastrointestinal lymphoma. *Hum Pathol* 1994;25:1020–9.
- [11] Rohatiner A, Damore F, Coiffier B, et al. Report on a workshop convened to discuss the pathological and staging classifications of gastrointestinal tract lymphoma. *Ann Oncol* 1994;5:397–400.
- [12] Koch P, Valle F, Del , et al. Primary gastrointestinal non-Hodgkin's lymphoma: I. Anatomic and histologic distribution, clinical features, and survival data of 371 patients registered in the German multicenter study GIT NHL 01/92. *J Clin Oncol* 2001;19:3861–73.
- [13] Koch P, Valle F, Del , et al. Primary gastrointestinal non-Hodgkin's lymphoma: II. Combined surgical and conservative or conservative management only in localized gastric lymphoma—results of the prospective German multicenter study GIT NHL 01/92. *J Clin Oncol* 2001;19:3874–83.
- [14] Schmidt WP, Schmitz N, Sonnen R. Conservative management of gastric lymphoma: the treatment option of choice. *Leuk Lymphoma* 2004;45:1847–52.
- [15] Li M, Zhang S, Gu F, et al. Clinicopathological characteristics and prognostic factors of primary gastrointestinal lymphoma: a 22-year experience from South China. *Int J Clin Exp Pathol* 2014;7:2718–28.
- [16] Nakamura S, Matsumoto T, Iida M, et al. Primary gastrointestinal lymphoma in Japan. *Cancer* 2003;97:2462–73.
- [17] Yoon SS, Coit DG, Portlock CS, et al. The diminishing role of surgery in the treatment of gastric lymphoma. *Ann Surg* 2004;240:28–37.
- [18] Ding D, Pei W, Chen W, et al. Analysis of clinical characteristics, diagnosis, treatment and prognosis of 46 patients with primary gastrointestinal non-Hodgkin lymphoma. *Mol Clin Oncol* 2014;2:259–64.
- [19] Rotaru I, Găman GD, Stănescu C, et al. Evaluation of parameters with potential prognosis impact in patients with primary gastric diffuse large B-cell lymphoma (PG-DLBCL). *Rom J Morphol Embryol* 2014;55:15–21.
- [20] Binn M, Ruskoné-Fourmestreaux A, Lepage E, et al. Surgical resection plus chemotherapy versus chemotherapy alone: comparison of two strategies to treat diffuse large B-cell gastric lymphoma. *Ann Oncol* 2003;14:1751–7.
- [21] Hosseini S, Dehghan P. Primary non-hodgkin lymphoma of the stomach: clinicopathological characteristics and prognostic factors in Iranian patients. *Iran J Cancer Prev* 2014;7:219–24.
- [22] Miller TP, Dahlberg S, Cassady JR, et al. Chemotherapy alone compared with chemotherapy plus radiotherapy for localized intermediate- and high-grade non-Hodgkin's lymphoma. *N Engl J Med* 1998;339:21–6.
- [23] Cortelazzo S, Rossi A, Roggero F, et al. Stage-modified international prognostic index effectively predicts clinical outcome of localized primary gastric diffuse large B-cell lymphoma. *Ann Oncol* 1999;10:1433–40.

- [24] Shotaro N, Toshiro S, Takayuki M, et al. Long-term clinical outcome of gastric MALT lymphoma after eradication of *Helicobacter pylori*: a multicentre cohort follow-up study of 420 patients in Japan. *Gut* 2012;61:507–13.
- [25] Stathis A, Chini C, Bertoni F, et al. Long-term outcome following *Helicobacter pylori* eradication in a retrospective study of 105 patients with localized gastric marginal zone B-cell lymphoma of MALT type. *Annals of Oncology* 2009;20:1086–93.
- [26] Huang JJ, Jiang WQ, Xu RH, et al. Primary gastric non-Hodgkin's lymphoma in Chinese patients: clinical characteristics and prognostic factors. *BMC Cancer* 2010;10:358.
- [27] Selc Ukbiricik F, Tural D, Elicin O, et al. Primary gastric lymphoma: conservative treatment modality is not inferior to surgery for early-stage disease. *ISRN Oncol* 2012;2012:951816–1951816.
- [28] Japanese Gastric Cancer Association Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer* 2011;14:113–23.