RESEARCH ARTICLE
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Prognostic Significance of Paraproteinemia in Marginal Zone Lymphoma

Marjinal Zon Lenfomada Paraproteineminin Prognostik Önemi

Burak Karakaya[1], Boran Yavuz[2], Fatih Demirkan[2]

[1]Dokuz Eylül University Faculty of Medicine, Department of Internal Medicine, İzmir, Türkiye
[2]Dokuz Eylül University Faculty of Medicine, Division of Hematology, İzmir, Türkiye
[2]Dokuz Eylül University Faculty of Medicine, Division of Hematology, İzmir, Türkiye

Burak Karakaya, M.D., Dokuz Eylül University Faculty of Medicine, Department of Internal Medicine, İzmir, Türkiye
drburakkarakaya@gmail.com
https://orcid.org/0000-0002-6184-7876

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ABSTRACT

Objective: The prognostic significance of paraproteinemia in marginal zone lymphoma (MZL) is underexplored. We aimed to investigate the clinical and biological impact of paraproteinemia and its association with survival outcomes in patients with MZL.

Materials and Methods: We retrospectively evaluated 73 patients diagnosed with MZL between 2000 and 2022 at a single center. Baseline clinical characteristics and survival outcomes were compared according to paraproteinemia status.

Results: Paraproteinemia was present in 27.3% (20/73) of patients, predominantly of the IgM subtype. Paraproteinemia was significantly associated with older age ($p<0.001$), advanced disease stage ($p=0.023$), elevated β2-microglobulin ($p=0.001$), bone marrow involvement ($p=0.026$), and lower hemoglobin ($p=0.002$) and albumin levels ($p<0.001$). Patients with paraproteinemia had significantly shorter overall survival (OS) and progression-free survival (PFS) compared to those without paraproteinemia (mean OS: 73.8 vs. 178.8 months, $p=0.046$; mean PFS: 63.5 vs. 159.7 months, $p=0.049$). The negative prognostic impact was more pronounced among patients with IgM paraproteinemia (OS: 58.8 vs. 178.2 months, $p=0.006$; PFS: 45.2 vs. 157.4 months, $p=0.004$). In histologic subtypes analysis, only MALT lymphoma patients with IgM paraproteinemia showed significantly shorter OS (70.5 vs. 152.6 months, $p=0.010$). Patients with IgM paraproteinemia treated with R-CHOP-like regimens experienced significantly shorter PFS and OS.

Conclusion: Paraproteinemia, particularly of the IgM subtype, is associated with adverse clinical and biological features and predicts inferior survival in patients with MZL. Evaluating paraproteinemia status at diagnosis as a potential prognostic marker may guide treatment strategies. Prospective studies are needed to confirm the prognostic utility of paraproteinemia and support its incorporation into MZL treatment management.

Keywords: Lymphoma, B-Cell, Marginal Zone; Paraproteinemias; Immunoglobulins, Monoclonal; Retrospective Studies; Prognosis; Survival Analysis

ÖZET

Amaç: Paraproteineminin marjinal zon lenfoma (MZL)'daki prognostik önemi yeterince araştırılmamıştır. Bu çalışmada MZL tanılı hastalarda paraproteinemi varlığının klinik ve biyolojik etkilerinin hastaların sağkalımı ile ilişkisini değerlendirmeyi amaçladık.
Gereç ve Yöntem: 2000–2022 yılları arasında tek merkezde MZL tanısı almış 73 hasta retrospektif olarak değerlendirildi. Temel klinik özellikler ve sağkalım sonuçları paraproteinemi durumuna göre karşılaştırıldı.
Bulgular: Paraproteinemi, hastaların %27,3'ünde (20/73) saptandı ve çoğunlukla IgM alt tipindeydi. Paraproteinemi varlığı ile ileri yaş ($p<0.001$), ileri evre hastalık ($p=0.023$), yüksek β2-mikroglobulin düzeyi ($p=0.001$), kemik iliği tutulumu ($p=0.026$), düşük hemoglobin ($p=0.002$) ve albümin düzeyleriyle ($p<0.001$) anlamlı ilişkiliydi. Paraproteinemisi olan hastaların genel sağkalım (OS) ve progresyonsuz sağkalım (PFS) süreleri olmayanlara anlamlı derecede daha kısaydı (ortalama OS: 73,8 vs. 178,8 ay, p=0,046; ortalama PFS: 63,5 vs. 159,7 ay, p=0,049). Bu olumsuz etki IgM paraproteinemisi olan hasta grubunda daha belirgindi (OS: 58,8 vs. 178,2 ay, p=0,006; PFS: 45,2 vs. 157,4 ay, p=0,004). Histolojik alt gruplar analiz edildiğinde, yalnızca IgM paraproteinemisi olan MALT lenfomalı hastalarda OS anlamlı olarak daha kısaydı (70,5 vs. 152,6 ay, p=0,010). IgM paraproteinemili ve R-CHOP benzeri rejimlerle tedavi edilen hastalarda OS ve PFS belirgin olarak daha kısa saptandı.
Sonuç: Paraproteinemi, özellikle IgM alt tipi, MZL hastalarında olumsuz klinik ve biyolojik özelliklerle ilişkili olup azalmış sağkalımı öngördürmektedir. Tanı anında potansiyel bir prognostik belirteç olarak paraproteinemi durumunun değerlendirilmesi tedavi stratejilerine yol gösterebilir. Paraproteineminin prognostik yararını doğrulamak ve MZL tedavisinin yönetimine dahil edilmesini desteklemek için prospektif çalışmalara ihtiyaç vardır.
Anahtar Kelimeler: Lenfoma, B-Hücre, Marjinal Bölge; Paraproteinemiler; İmmünoglobulinler, Monoklonal; Retrospektif Çalışmalar; Prognoz; Sağkalım Analizi

Introduction

Marginal zone lymphomas (MZLs) are B-cell lymphomas derived from post-germinal center marginal zone B cells [1]. MZL accounts for 7–8% of all non-Hodgkin lymphoma (NHL) cases. It is the third most common type of lymphoma among all NHLs. There are three distinct subtypes: mucosa-associated lymphoid tissue (MALT) lymphoma (50-70%), splenic MZL (SMZL) (10-20%), and nodal MZL (NMZL) (10-20%) [2].
Unlike Diffuse Large B-cell lymphoma (DLBCL), which is aggressive and requires immediate treatment, or Follicular Lymphoma (FL), which is indolent but clinically predictable, MZL shows clinical and prognostic heterogeneity [3,4]. MALT lymphoma is often localized with a favorable prognosis, while SMZL and NMZL are more commonly disseminated at diagnosis and may follow a more progressive course [5]. Moreover, aggressive transformation is less frequent than FL, though it remains a clinical concern [6].
Given this heterogeneity, treatment of MZL must be individualized based on clinical presentation and disease progression. Management strategies include watchful waiting, antibiotic therapy, surgical resection, radiotherapy, chemoimmunotherapy, and targeted therapies [7,8]. Despite the generally favorable outcomes, the risk of progression with relapses and aggressive lymphoma transformation emphasizes the need for additional prognostic factors to guide individualized treatment. Therefore, prognosis assessment is essential for the selecting optimal treatment strategy [1,7].
The ability of B cells to secrete immunoglobulins is a regulated process acquired during terminal differentiation into plasma cells or long-lived memory B cells. In B-cell lymphomas, malignant clones may retain or acquire this secretory function, resulting in the production of monoclonal immunoglobulins, detectable as serum paraproteins. Paraproteinemia (PP) is classically associated with monoclonal gammopathy of undetermined significance, multiple myeloma, Waldenström macroglobulinemia/lymphoplasmacytic lymphoma, and light chain amyloidosis. However, nearly all types of B-cell lymphomas can secrete paraproteins. PP reflects the capacity of the malignant B-cell clone to undergo plasmacytic differentiation, which has been linked with high-risk biological features and poor outcomes in certain lymphomas [8–11]. Few studies have assessed its impact on survival in MZL. The frequency of monoclonal gammopathy in MZL subtypes ranges from 5-46% [12–19] and has been correlated with plasmacytic differentiation, advanced disease, and bone marrow involvement in MALT lymphoma [15,20]. However, current prognostic models do not include biological features such as PP, which may carry additional prognostic value [21–23].
In this study, we evaluated the clinical characteristics associated with PP in MZL patients and assessed its impact on survival.

Materials and Methods

Study Design and Patient Selection

Between January 2000 and June 2022, 73 patients diagnosed with MZL and followed at our center were included. Diagnoses were made according to the WHO classification of Tumours of Haematopoietic and Lymphoid Tissues, which was valid at the time of diagnosis (2008 and 2016 editions). We included only patients evaluated for monoclonal gammopathy via serum immunofixation electrophoresis (SIFE) and serum protein electrophoresis (SPEP). Patients under 18 years of age, those with <1-month follow-up, insufficient clinical data, or a second solid organ malignancy

were excluded. The study was approved by the Dokuz Eylül University Faculty of Medicine's Local Ethics Committee (Protocol Code: 2022/15-11, April 20, 2022). This study was conducted in accordance with the Declaration of Helsinki.

Definition of Paraproteinemia

PP was defined as a monoclonal band detected on SIFE and demonstrated an M-spike on SPEP. Free light chain (FLC) testing was not routinely available and was excluded from the definition. We included only patients who were evaluated with both SPEP and SIFE. We excluded patients with FLC results alone, without confirmatory SIFE, to avoid potential diagnostic bias.

Staging and Baseline Assessments

Staging evaluation consisted of a complete physical examination; imaging of the neck, thorax, abdomen, and pelvis with computed tomography (CT); and positron emission tomography/CT (PET/CT). Magnetic resonance imaging, endoscopy, and bone marrow biopsy were performed in the selected cases. Assessment of bone marrow involvement was defined exclusively by bone marrow biopsy with histopathologic ± immunohistochemical confirmation. All cases were retrospectively reassessed with the modified Ann Arbor staging system. Treatment response was retrospectively evaluated based on clinical records and imaging, according to IWG criteria[24], and categorized as complete response, partial response, stable disease, or progressive disease.

Data Collection

Baseline clinical characteristics collected from the medical record system included age, gender, comorbidities, Eastern Cooperative Oncology Group (ECOG) performance status, primary disease site, extranodal involvement, lymph node status, B symptoms, laboratory workup at the initial evaluation (hemoglobin, leucocyte, and platelet count, lactate dehydrogenase (LDH), serum β2-microglobulin (β2-MG), calcium levels), Hepatitis B, Hepatitis C, HIV status, and serum immunoglobulins (IgG, IgA and IgM) levels. None of the patients tested positive for hepatitis C or HIV.

Statistical Analysis

We used IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA) for statistical analysis. Descriptive statistics were generated for categorical variables using frequencies and percentages and for continuous variables using mean, median, standard deviation, and range. The chi-square test or Fisher's exact test was used for comparisons of categorical data.

Overall survival (OS) was defined as the time from diagnosis to death from any cause. Progression-free survival (PFS) was defined as the time from the start of first-line therapy to relapse/progression or death from any cause. OS and PFS were calculated with the Kaplan-Meier method and compared with the log-rank test. All estimates were reported with 95% confidence intervals; p-values ≤ 0.05 were considered statistically significant.

Results

Baseline Characteristics

A total of 73 patients were analyzed in this study. The baseline characteristics are summarized in Table 1. PP was detected in 20 out of 73 patients (27.3%). PP was most frequently observed in patients with NMZL. PP was present in 11 (55%) patients with NMZL, 7 (35%) with MALT lymphoma, and 2 (10%) with SMZL. IgM was the most common paraprotein found in the study (Table 2).

PP was ascertained in 20 patients, of whom 11 were IgM type. PP was detected in 20 of 73 patients (27.3%), mostly IgM-κ (9, 45%), followed by IgG-κ (7, 35%), IgM-λ (2, 10%), IgA-λ (1, 5%), and IgA-κ (1, 5%). The presence of PP was significantly associated with advanced age ($p<0.001$), advanced disease stage (III-IV) ($p=0.023$), elevated ß2-MG level ($p=0.001$), decreased hemoglobin level ($p=0.002$), decreased albumin level ($p<0.001$), and bone marrow involvement ($p=.026$). Gender, elevated LDH levels, and elevated Ki-67 levels were not associated with PP.

Survival Analysis

The prognostic value of PP and other clinical outcomes is summarized in Table 3. The median follow-up was 58 (range: 3-200) months, during which 18 patients experienced relapse or refractory cases and 10 patients died. Among the deaths, three were attributed to sepsis. Four patients died due to lymphoma-related causes: 2 from aggressive lymphoma transformation and 2 from disease progression. For the remaining 3 patients, the exact causes of death could not be determined due to the deaths occurring outside the hospital.

Median OS and PFS were not reached. The mean OS and PFS were 169.9±8.5 and 146.4±10.6 months, respectively. The OS rates at 5 and 10 years were 87.2% and 81.9%, while the PFS rates were 71.5% and 68.3%, respectively.

Patients with PP had a significantly shorter survival. The mean OS rates were 73.8 months versus 178.8 months ($p=0.046$), and the 5-year OS rates were 69.7% and 93.0%, respectively. Similarly, mean PFS was 63.5 months in the patients with PP versus 159.7 months without ($p=0.049$), with 5-year PFS rates of 56.8% and 76.8%, respectively. (Figure 1)

This effect was more pronounced among patients with IgM-type PP (IgM-PP). These patients had shorter OS (58.8 months vs. 178.2 months, p = 0.006; 5-year OS: 48.5% vs. 92.8%) and PFS (45.2 months vs. 157.4 months, p = 0.004; 5-year PFS: 25.3% vs. 78.5%) (Figure 2)

We further examined the impact of PP within each histological subtype. However, when analyzing subtypes individually, the effect of PP on survival was not statistically significant. In MALT lymphoma, the IgM-PP group was very small (n=3), but showed a significantly shorter OS than those without (70.5 months vs. 152.6 months, p=0.010); this result should be interpreted with caution due to the limited sample size (Table 2). There was no significant difference in OS or PFS among PP subtypes (p=0.553 and p=0.476, respectively).

The overall response rate (ORR) of patients who were treated with chemoimmunotherapy and having PP were 12/14 (86%) and 27/29 (93%) those without (p>0.05), respectively, whereas the complete response (CR) of those patients having PP were 7/14 (50%) and 12/29 (59%) those without (p>0.05), respectively. The ORR in patients treated with an R-CHOP-like regimen and having PP were 8/9 (89%) and 17/18 (94%) those without (p>0.05), respectively. The CR in patients treated with an R-CHOP-like regimen and having PP were 4/9 (44%) and 11/18 (61%) those without (p>0.05), respectively.

We further analyzed patients who required systemic therapy as first-line treatment. OS and PFS did not differ with the presence or absence of PP and IgM-PP at diagnosis. Patients with IgM-PP who received chemoimmunotherapy had shorter PFS (mean: 39.1 months vs. 96.2 months, p = 0.036). Within the specific subgroup of patients with IgM-PP receiving R-CHOP-like regimen (the most common systemic therapy), it was associated with significantly shorter OS (mean: 33 months vs. 112.5 months, p<0.001) and PFS (mean: 13.9 months vs. 101.9 months, p=0.001) , compared to those without IgM-PP (Figure 3). Due to the limited number of patients and the small number of patients receiving other systemic therapies, further survival analyses for other systemic regimens were not feasible.

Discussion

Although MZL is an indolent lymphoma, but may present with relapsed/refractory disease or histological transformation over time. Identifying prognostic factors is therefore crucial. In our study, the presence of PP was significantly associated with advanced age (≥65), advanced stage disease, elevated ß2MG, decreased hemoglobin and albumin levels, and bone marrow infiltration. Importantly, the presence of PP significantly shortened OS and PFS. When we analyzed MZL subtypes, we observed that only IgM-PP significantly shortened OS in patients with MALT lymphoma.

Previous studies reported the PP incidence in MZL ranging from 5% to 46% [12–14,16–19,25]. In our cohort, PP was detected in 20 out of 73 patients (27.3%), consistent with previous studies. Notably, the incidence of PP in NMZL has been previously reported, ranging from 5% to 40% [16,18,19]. Fifty-five percent of NMZL patients had PP, which is higher than previously reported cohorts in the literature [12,13,16,18,26], possibly due to limited sample size or institutional differences in patient profiles.

There is growing evidence showing that the presence of PP is linked with poor prognosis in MZL and other lymphoma subtypes [8,10,11,15,27,28]. FL with PP were associated with decreased PFS and OS, and PP was an independent risk factor in patients over 60 [11]. Similarly, Chronic lymphocytic leukemia patients with IgM-PP were associated with more advanced stage, del(17p)/TP53 mutation, and shortened survival [8]. Several studies have investigated the prognostic impact of PP in MZL. PP has been correlated with decreased survival, especially among patients with non-gastric MALT lymphoma and those with multiple mucosal sites involved. [16,28,29] . Another study demonstrated that MALT lymphoma patients with Ig and IgM-PP had shortened OS and PFS; PP was identified as an independent prognostic factor. The authors suggested that incorporating PP into the MALT-lymphoma International Prognostic Index (MALT-IPI) score could help to select optimal treatment and predict prognosis [14].

Consistent with previous findings, our study demonstrated that PP, particularly the IgM subtype, was significantly shortened in both OS and PFS.. While this effect was observed across MZL subtypes, it reached statistical significance only in MALT lymphoma. Although PP is commonly linked with advanced stage, bone marrow involvement, and multiple extranodal sites, our data suggest that it reflects more than the overall tumor burden. Notably, some patients with early-stage disease also presented with PP despite the absence of a significant tumor burden. This suggests that PP may serve as an independent prognostic marker rather than merely indicating disease extent and may provide insight into the underlying biological nature of the tumor.

Our findings, together with prior studies, indicate that PP, especially the IgM subtype, may reflect a more aggressive biological behavior in MZL, even in early-stage disease. These findings highlight the importance of thorough staging and may justify the consideration of systemic therapy instead of relying solely on localized treatment approaches in selected cases.

Several studies have shown that IgM-PP has been linked with adverse biological features and poor outcomes under R-CHOP [10,30]. Some studies suggested that bendamustine-rituximab (BR) and chemoimmunotherapies may be preferred over R monotherapy in patients with PP [16]. In our cohort, patients with IgM-PP treated with R-CHOP-like

regimens had significantly shorter OS and PFS. Similarly, among patients who received chemoimmunotherapy, inferior PFS was associated. These findings suggest that R-CHOP-like regimens could be associated with shorter survival in this subgroup, and it may be reasonable to prioritize BR treatment in this patient group. Nevertheless, further investigation is required to confirm.

Histological transformation to aggressive lymphoma remains a concern in MZL. Some studies determined that the presence of M-protein may increase the risk [16]. In our study, during a median 58-month follow-up period, aggressive lymphoma transformation was observed in 2 of 73 patients (2.7%), both of whom did not have PP. The cumulative incidence of transformation did not significantly differ between groups in our study (p=0.402), though the number of events was too small to draw definitive conclusions. Clarifying the potential association will require studies with greater sample sizes and longer observation periods.

Recently, Arcaini et al. [21] established the MZL International Prognostic Index (MZL-IPI), which applies to all MZL patients and incorporates hemoglobin level, lymphocyte count, the presence of NMZL or disseminated disease, LDH level, and platelet count. In our cohort, PP was more frequent in NMZL patients and was associated with decreased hemoglobin level and inferior survival. Given increasing evidence, we propose that PP be evaluated for incorporation into future prognostic models.

Study Limitations

Our study has several limitations. First, its retrospective, single-center design and relatively small sample size may introduce selection biases and limit generalizability. Second, because the quantitative **values** of immunoglobulin levels were not collected, which limited our ability to assess their prognostic relevance. Third, the number of histologic transformations was limited to only two cases in the entire cohort, which reduces the ability to draw definitive conclusions regarding the relationship between paraproteinemia and transformation risk. Lastly, the variety of treatment protocols limited the generalizability of our results. Considering the limited sample size of our study and heterogeneity in the literature, future studies concentrating specifically on MZL patients are necessary. These new analyses could help resolve or clarify the prognostic role of PP in MZL. As more data accumulate, researchers will be able to perform meta-analyses to definitively clarify the prognostic role of PP in MZL and better guide clinical practice.

Conclusion

In conclusion, our study provides evidence that PP, particularly of the IgM subtype, is an adverse prognostic factor in MZL. We found that IgM-PP has markedly shortened PFS and OS in patients with MZL. To our knowledge, this study is the first to demonstrate a survival disadvantage for MZL patients with IgM-PP specifically, emphasizing the importance of assessing paraprotein status at diagnosis. Evaluating all MZL patients for paraproteinemia as part of the initial workup may help stratify the patients and choose the optimal treatment modalities. We recommend investigating PP in all patients, regardless of histological subtype and stage, which could help clinicians choose a more aggressive and appropriate treatment strategy from the outset. Further studies are needed to validate these findings and explore personalized treatment strategies for patients with PP.

Ethics: The study was approved by the Dokuz Eylül University Faculty of Medicine's Local Ethics Committee (Protocol Code: 2022/15-11, April 20, 2022). This study was conducted in accordance with the Declaration of Helsinki.

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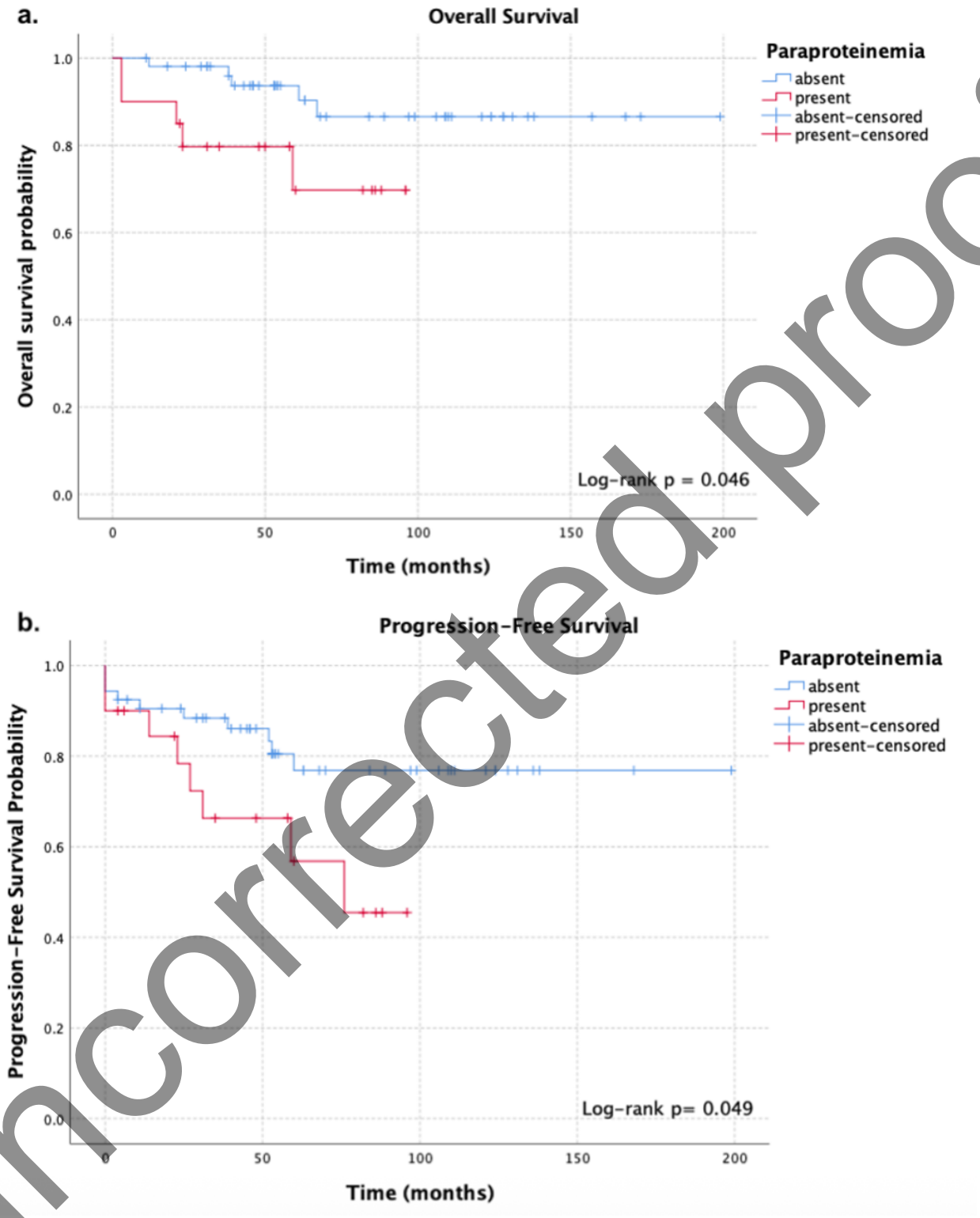

Figure 1. Kaplan–Meier curves for **(a)** overall survival and **(b)** progression-free survival according to paraproteinemia status.

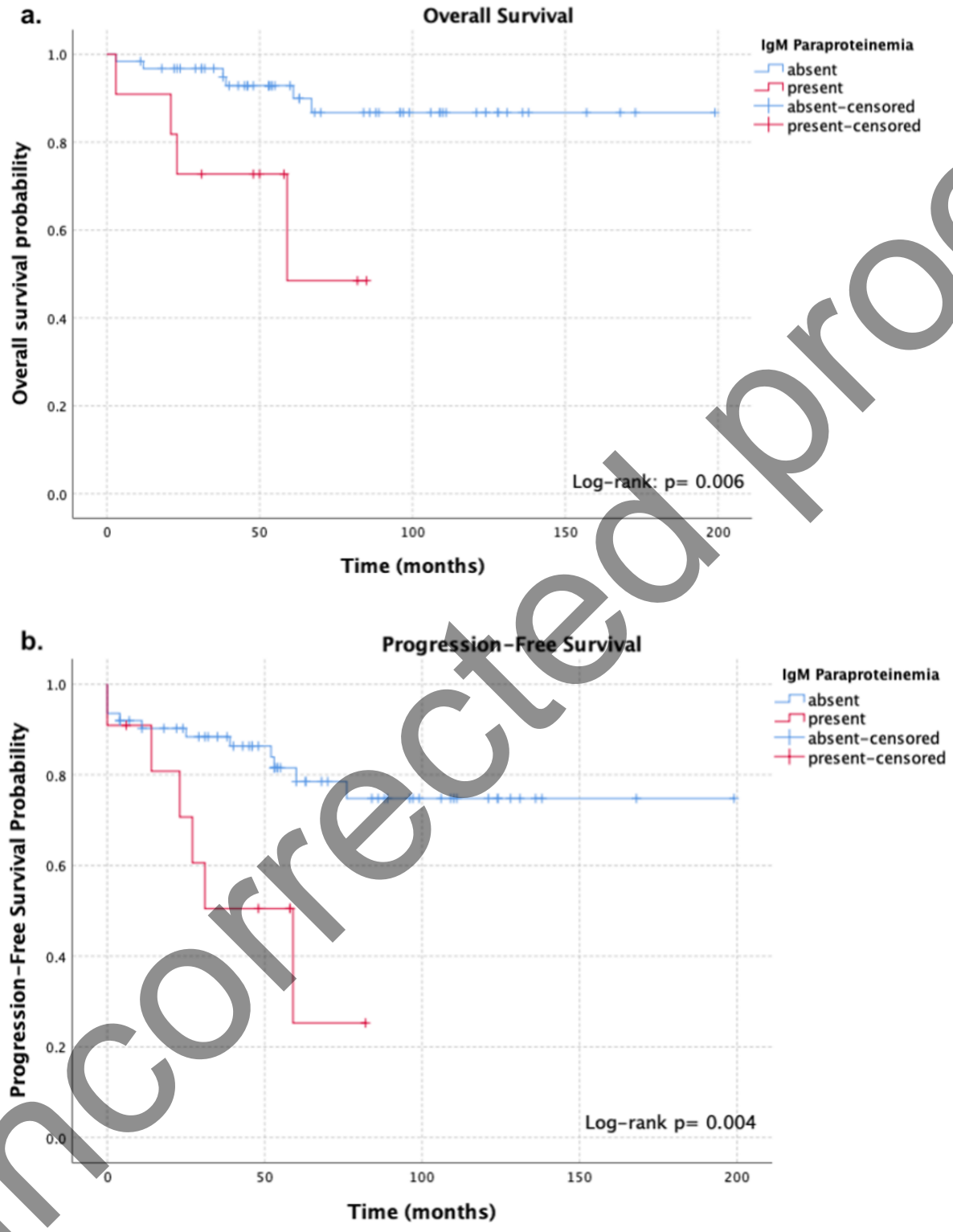

Figure 2. Kaplan–Meier curves for **(a)** overall survival and **(b)** progression-free survival according to IgM paraproteinemia status.

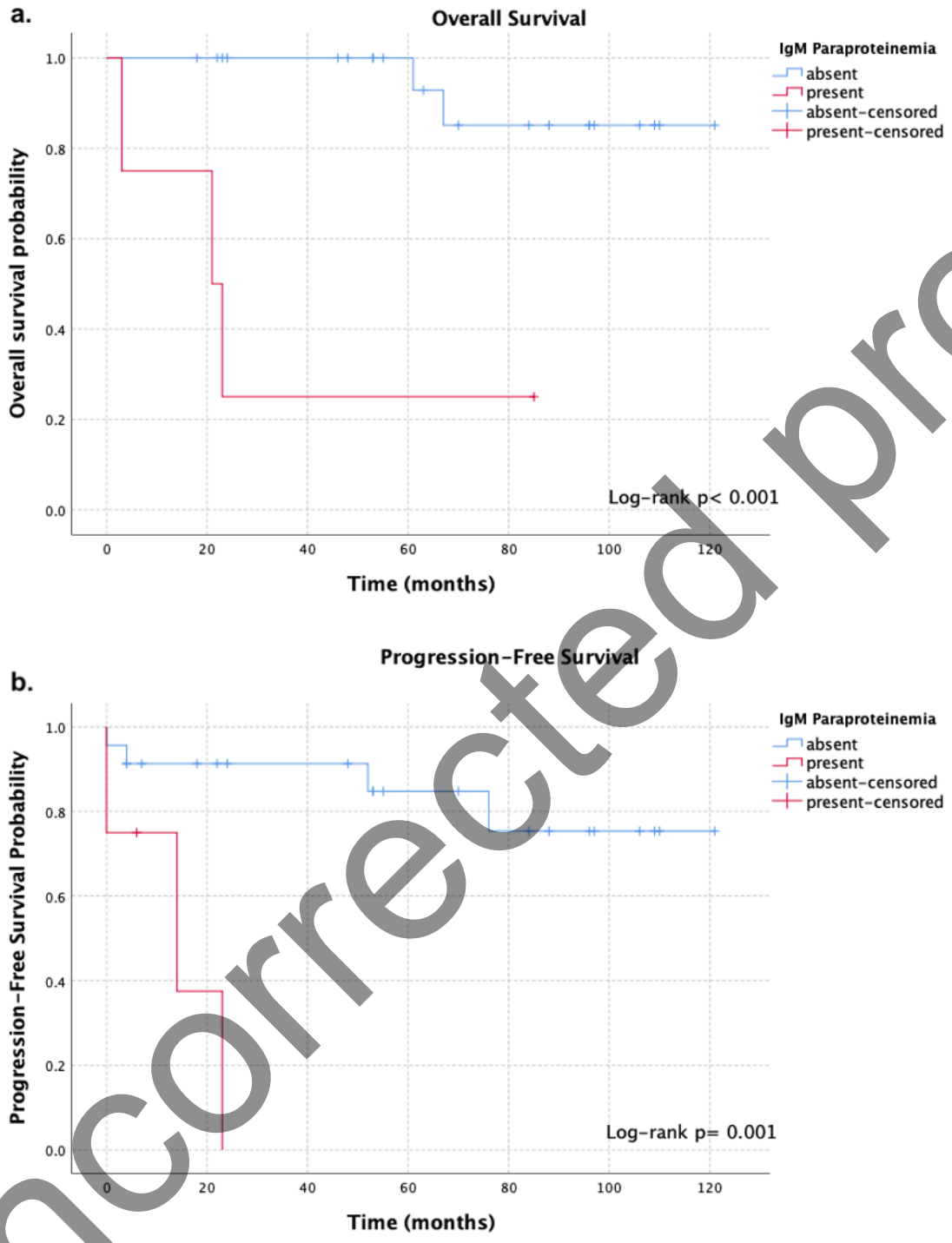

Figure 3. Kaplan–Meier curves for **(a)** overall survival and **(b)** progression-free survival in patients treated with R-CHOP–like regimens, stratified by IgM paraproteinemia status.

Table 1. Baseline clinical characteristics of patients

	All patients n=73 (%)	PP (–) n=53 (%)	PP (+) n=20 (%)	p-value
Median age, years (range)	59 (31-83)	56 (31-80)	66 (43-83)	**<0.001***
Sex, male (%)	38 (52%)	25 (47%)	13 (65%)	0.174
Hemoglobin (g/dL)	12.5 (6.6-15.7)	13.1 (9.2-15.7)	11.8 (6.6-14.9)	***0.002****
Albumin (g/dL)	4.13 (2.17-5.1)	4.28 (3.3-5.1)	3.73 (2.17-4.6)	***<0.001****
LDH (U/L)	193 (98-551)	196 (98-551)	177 (109-513)	0.790
B_2MG (ng/mL)	2.92 (0.8-11.5)	2.52 (0.8-6.3)	4.72 (1.89-11.5)	***0.001****
Ki-67 (%)	20 (1-40)	20 (7-40)	20 (1-25)	0.955
EMZL (%)	38 (52)	31 (58)	7 (35)	
SMZL (%)	14 (19)	12 (23)	2 (10)	***0.009****
NMZL (%)	21 (29)	10 (19)	11 (55)	
Stage, III-IV (%)	39 (53)	24 (46)	15 (71)	***0.023****
ECOG-PS, ≥2 (%)	3 (4)	0 (0)	3 (15)	***0.018****
Bone marrow involvement, n (%)	32 (49)	18 (34)	14 (70)	***0.026****
B symptoms (%)	12 (16)	6 (11)	6 (30)	0.077
Systemic therapy (%)	44 (60)	30 (68)	14 (70)	0.297
Median follow-up in months	58	63	54	

PP: paraproteinemia; LDH: lactate dehydrogenase; B2MG: beta-2 microglobulin; MZL: marginal zone lymphoma; EMZL: extranodal MZL; SMZL: splenic MZL; NMZL: nodal MZL; ECOG-PS: Eastern Cooperative Oncology Group Performance Score.
p-values < 0.05 are considered statistically significant and shown in bold.

Table 2. Distribution of the Paraprotein Subtypes by MZL subtypes

Subtype	IgG K	IgM L	IgM K	IgA L	IgA K	Total
MALT Lymphoma	3	1	2	0	1	7
SMZL	2	0	0	0	0	2
NMZL	2	1	7	1	0	11
Total	7	2	9	1	1	20

MZL: marginal zone lymphoma; MALT: mucosa-associated lymphoid tissue; SMZL: splenic marginal zone lymphoma; NMZL: nodal marginal zone lymphoma.

Table 3. Prognostic Value of Paraproteinemia and Clinical Factors on Survival Outcomes

	All patients n=73, (%)	Exitus n=10, (%)	OS p-value	Relapsed or Refractory disease n=18, (%)	PFS p-value
Sex, male	38 (52)	7 (70)	0.191	12 (67)	0.128
EMZL	38 (52)	2 (20)		6 (33)	
SMZL	14 (19)	2 (20)	***0.017****	3 (17)	***0.009****
NMZL	21 (29)	6 (60)		9 (50)	
PP	20 (27)	5 (50)	***0.046****	8 (44)	***0.049****
IgM-PP	11 (15)	6 (60)	***0.006****	6 (33)	***0.004****
Autoimmune disesase	22 (30)	1 (10)	0.143	6 (33)	0.920
ECOG-PS ≥ 2	3 (4)	3 (30)	***<0.001****	3 (17)	***<0.001****
Stage III-IV disease	39 (53)	8 (80)	0.059	13 (72)	***0.035****
Bulky disease (>5 cm)	5 (7)	1 (10)	0.910	3 (17)	0.051
Bone marrow infiltration	32 (44)	7 (70)	0.083	10 (56)	0.297
B symptoms	12 (16)	3 (30)	0.202	6 (33)	***0.009****
Systemic therapy	44 (60)	7 (70)	0.466	14 (78)	***0.035****

PP: paraproteinemia; IgM-PP: Immunoglobulin M paraproteinemia; MZL: marginal zone lymphoma; EMZL: extranodal MZL; SMZL: splenic MZL; NMZL: nodal MZL; ECOG-PS: Eastern Cooperative Oncology Group Performance Score; OS: overall survival; PFS: progression-free survival.
p-values < 0.05 are considered statistically significant and shown in bold.