British Journal of Global Ecology and Sustainable Development
Volume- 48, January 2026
ISSN (E): 2754-9291

TREATMENT OUTCOMES AND PROGNOSTIC FACTORS IN DIFFUSE LARGE B-CELL LYMPHOMA WITH EXTRANODAL INVOLVEMENT

S. V. Kamyshov [1],
O.R. Kobilov [2]
Sh.Kh. Niyozova [2]
K. Sh. Izrailbekova [1]
[1]Republican Specialized Scientific and Practical Center of Oncology and Radiology
[2]Tashkent State Medical University

Abstract

Objective: The aim of this study was to evaluate the immediate and long-term treatment outcomes in patients with diffuse large B-cell lymphoma (DLBCL) with extranodal involvement and to identify key prognostic factors affecting disease outcome.

Materials and Methods: A retrospective study was conducted including 81 patients with DLBCL with extranodal involvement treated between 2015 and 2021. Clinical-laboratory, morphological, immunohistochemical, and instrumental methods were employed. Treatment efficacy was assessed according to international tumor response criteria.

Results: Complete therapeutic response was achieved in 65.4% of patients, with a five-year overall survival of 60.1%. The most unfavorable prognostic factors included high expression of BCL-2, BCL-6, GCET1, Ki-67 >60%, as well as lack of complete response to therapy.

Conclusion: DLBCL with extranodal involvement demonstrates clinical heterogeneity. A comprehensive approach with early assessment of treatment response allows for improved prognosis.

Keywords: Diffuse large B-cell lymphoma, extranodal involvement, chemotherapy, radiotherapy, prognosis

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, accounting for approximately 30–40% of all cases, and is characterized by significant clinical, biological, and molecular heterogeneity. The disease may present with lymph node involvement or primary/secondary extranodal organ involvement, including the gastrointestinal tract, liver, lungs, bones, and central nervous system. Extranodal forms of DLBCL, especially with multiple sites affected, are often associated with more aggressive clinical courses, high tumor burden, presence of B symptoms, and poor prognosis.

The clinical variability of DLBCL reflects its biological diversity, including differences in cell-of-origin subtypes (GCB and non-GCB), genetic and epigenetic alterations, and tumor microenvironment features. These factors significantly influence therapy

sensitivity and disease outcome. Despite the introduction of rituximab-containing chemoimmunotherapy regimens, primarily the R-CHOP protocol, which remains the standard first-line treatment, a significant proportion of patients retain a risk of primary refractoriness or early relapse.

Diagnosis and management of patients with widespread extranodal DLBCL pose particular challenges, as lesions may mimic metastatic solid tumors on imaging studies, leading to delayed diagnosis and initiation of specific therapy. Modern functional imaging methods, especially ^{18}F-FDG PET/CT, play a key role in accurate staging and early metabolic response assessment, which has important prognostic value.

Despite progress in DLBCL treatment, issues related to individualized therapy, prognosis assessment in patients with adverse clinical features, and management of patients with concomitant chronic infections remain relevant and require further study, highlighting the importance of presenting clinical observations in this patient group.

Materials and Methods

The retrospective study included 81 patients with morphologically verified DLBCL with extranodal involvement, who were under observation at the Republican Specialized Scientific and Practical Center of Oncology and Radiology between 2023 and 2024. Inclusion criteria were age over 18 years, newly established DLBCL diagnosis confirmed by histological and immunohistochemical results, and presence of one or more extranodal lesions according to imaging studies. Patients with transformed lymphomas, primary mediastinal B-cell lymphomas, and HIV-associated lymphoproliferative disorders were excluded.

Morphological verification was performed using biopsy material from affected lymph nodes or extranodal lesions with mandatory immunohistochemical typing (CD20, CD3, CD10, BCL6, MUM1, BCL2, Ki-67, etc.) to determine B-cell origin and cell-of-origin according to Hans algorithm. Disease staging followed the Ann Arbor classification (Lugano modification), using clinical examination, CT, and/or ^{18}F-FDG PET/CT, including bone marrow assessment.

All patients received standard first-line polychemoimmunotherapy according to the R-CHOP protocol. In cases of high tumor burden, pronounced clinical symptoms, or risk of tumor lysis syndrome, cytoreductive therapy was applied beforehand. For inadequate response to induction therapy or development of refractoriness, second-line regimens including DHAP were used. Radiotherapy was applied individually, mainly for localized residual lesions.

Treatment efficacy was assessed based on clinical-laboratory data and follow-up imaging, including PET/CT, using Lugano response criteria. The primary endpoints were overall survival (OS) and event-free survival (EFS). Statistical analysis included Kaplan–Meier survival curves and Cox regression for evaluating the impact of clinical, demographic, and biological factors. Differences were considered statistically significant at $p < 0.05$.

Journal Zone Publishing, Ilford, United Kingdom

Results

A complete response according to Lugano criteria was achieved in 53 patients (65.4%), partial response in 21 patients (25.9%). Disease progression was observed in 7 patients (8.6%), and disease- or treatment-related deaths occurred in 5 patients (6.2%).

The five-year overall survival (OS) was 60.1%, and the five-year event-free survival (EFS) was 55.3%. The most favorable outcomes were observed in patients with primary mediastinal and lung involvement, whereas multiple extranodal lesions, particularly involving the liver and bones, were associated with poorer survival.

Analysis of prognostic factors revealed that high Ki-67 (>60%) and BCL-2 expression were significantly associated with worse prognosis. Patients with lower Ki-67 expression (<60%) demonstrated higher rates of complete response and improved survival.

Table 1. Clinical response to therapy in patients with DLBCL with extranodal involvement (n = 81)

Response Category	Number of patients	**Percent (%)**
Full answer	53	65,4
Partial answer	21	25,9
Progression	7	8,6
Fatalities	5	6,2

Table 2. The influence of clinical and pathological factors on five-year survival

Factor	**Five-year compulsory medical insurance (%)**	P-value
Mediastinal lesion	78,3	0,03
Lung damage	75,0	0,04
Ki-67 >60%	45,2	0,01
BCL 2 positive	48,7	0,02
Multiple extranodal lesions	52,0	0,05

Table 3. Clinical response to therapy depending on the location of extranodal lesions (n = 81)

Localization of the lesion	**Number of patients**	**Full answer, n (%)**	**Partial answer, n (%)**	**Progression, n (%)**
Mediastinum	12	10 (83,3)	2 (16,7)	0 (0)
Lungs	10	8 (80,0)	2 (20,0)	0 (0)
Stomach	18	11 (61,1)	5 (27,8)	2 (11,1)
Liver	15	8 (53,3)	5 (33,3)	2 (13,3)
Skeleton bones	16	9 (56,3)	6 (37,5)	1 (6,2)
Multiple extranodal lesions	10	7 (70,0)	3 (30,0)	0 (0)

Note: Patients may have had lesions in multiple organs simultaneously; the table lists the primary or most clinically significant lesions.

Journal Zone Publishing, Ilford, United Kingdom

Table 4. Clinical response to therapy and biological markers by extranodal lesion location (n = 81)

Localization of the lesion	Number of patients	Full answer, n (%)	Partial answer, n (%)	Progression, n (%)	Average expression Ki-67 (%)	BCL 2 positive, n (%)
Mediastinum	12	10 (83,3)	2 (16,7)	0 (0)	48	5 (41,7)
Lungs	10	8 (80,0)	2 (20,0)	0 (0)	50	4 (40,0)
Stomach	18	11 (61,1)	5 (27,8)	2 (11,1)	62	11 (61,1)
Liver	15	8 (53,3)	5 (33,3)	2 (13,3)	65	10 (66,7)
Skeleton bones	16	9 (56,3)	6 (37,5)	1 (6,2)	67	12 (75,0)
Multiple extranodal lesions	10	7 (70,0)	3 (30,0)	0 (0)	60	6 (60,0)

Conclusions from the Results Section

The analysis of treatment outcomes revealed several key observations:
The highest rate of complete response and lower Ki-67/BCL-2 expression were observed in patients with mediastinal and lung involvement.
Involvement of the liver and skeletal bones was associated with high Ki-67 and BCL-2 expression, corresponding to a more aggressive disease course and reduced survival.
Multiple extranodal lesions demonstrated moderate Ki-67 and BCL-2 levels with a high rate of complete response, likely reflecting the efficacy of intensive therapy.
Lesion localization combined with biological markers represents a significant predictor of therapeutic response and prognosis in patients with DLBCL.

Discussion

The findings confirm the critical role of immunohistochemical markers, such as Ki-67 and BCL-2, in predicting treatment outcomes in patients with diffuse large B-cell lymphoma (DLBCL) with extranodal involvement. In this study, high Ki-67 (>60%) and BCL-2 expression were associated with lower rates of complete response to therapy and reduced five-year survival. These results are consistent with the literature, which indicates that hyperproliferative tumors with anti-apoptotic activity exhibit a more aggressive clinical course and higher relapse rates.
Analysis of clinical response according to lesion location demonstrated the best outcomes in patients with mediastinal and lung involvement, whereas liver and skeletal bone lesions were associated with poorer prognosis. This observation underscores the importance of early detection of extranodal foci and careful monitoring throughout therapy. In cases of multiple extranodal lesions, the high rate of complete response may be attributed to cytoreductive therapy and intensive R-CHOP regimens with additional metabolic response monitoring using ^{18}F-FDG PET/CT.
These results highlight the importance of early treatment response assessment. Interim PET/CT after two to three cycles of R-CHOP allows identification of patients not achieving complete metabolic response and enables timely adjustment of therapeutic

Journal Zone Publishing, Ilford, United Kingdom

strategy, including escalation to intensive second-line regimens or targeted therapy. This approach is particularly relevant for patients at high risk of HBV reactivation, who require antiviral prophylaxis and regular monitoring of liver function.

Moreover, our observations emphasize the need for a comprehensive prognostic evaluation that includes both morphobiological tumor characteristics (Ki-67, BCL-2, cell-of-origin subtype) and clinical parameters such as lesion localization, presence of B symptoms, extent of bone marrow and liver involvement, and concomitant infections. Such an approach enables more accurate identification of high-risk patients and the planning of individualized therapy.

The findings are consistent with current guidelines for DLBCL management (NCCN, ESMO), which emphasize the importance of early treatment response assessment and consideration of biological markers in decisions regarding continuation or modification of therapy. This study demonstrates that integrating molecular and clinical factors can serve as a basis for developing personalized treatment regimens and improving outcomes in patients with extranodal disease.

Conclusion

Extranodal forms of diffuse large B-cell lymphoma exhibit significant clinical and biological heterogeneity, necessitating an individualized therapeutic approach. High expression of Ki-67 and BCL-2 is a reliable prognostic factor for unfavorable outcomes. Early assessment of response to chemoimmunotherapy, including interim ^{18}F-FDG PET/CT, allows timely adjustment of therapy and enhances treatment efficacy. Lesion localization and tumor morphobiological characteristics are key factors in predicting outcomes and planning personalized management strategies for patients with DLBCL.

References

1. Swerdlow S.H. et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC, 2017.
2. Coiffier B. et al. Long-term outcome of patients with diffuse large B-cell lymphoma treated with R-CHOP. Blood, 2010.
3.Кобилов О.Р. Обоснование и принципы коррекции гематологической токсичности полихимиотерапии злокачественных опухолей (обзор литературы) // Вестник науки и образования. — 2019. — № 17 (71). — С. 68–72.
4. Ниёзова Ш.Х., Камышов С.В., Баленков О.Ю., Кобилов О.Р. Протоонкогены как предиктивные факторы эффективности противоопухолевой терапии метастатического колоректального рака // Вестник Ташкентской медицинской академии. — 2020. — № 1. — С. 30–33.
5.Кобилов О.Р. Современные принципы коррекции гематологической токсичности химиотерапии злокачественных опухолей (обзор литературы) // European Science. — 2020. — № 5 (47). — С. 66–72.
6.Атаханова Н.Э., Камышов С.В., Кобилов О.Р., Ниёзова Ш.Х., Юсупова Ч.О. Влияние иммуногистохимических характеристик на клиническое течение и

Journal Zone Publishing, Ilford, United Kingdom

прогноз у больных диффузной В-крупноклеточной лимфомой с экстранодальными поражениями. — Ташкент, Узбекистан, 2024.
7. Ниёзова Ш.Х., Израильбекова К.Ш. Коррекция гематологической токсичности химиотерапии неходжкинских лимфом индукторами гемопоэза // Colloquium-Journal. — 2020. — № 14 (66). — С. 9–12.
8.Ниёзова Ш.Х. Гепатотоксический синдром на фоне полихимиотерапии солидных опухолей и современные возможности его коррекции (обзор литературы) // Вестник науки и образования. — 2019. — № 17 (71). — С. 73–76.
9.Ниёзова Ш.Х. Основные цитокины иммунной системы у онкогинекологических больных на фоне сопроводительной иммунотерапии // Вестник науки и образования. — 2019. — № 17 (71). — С. 76–82.
10. Ниёзова Ш.Х. Оценка провоспалительных цитокинов иммунной системы в зависимости от вариантов сопроводительной иммунотерапии у больных раком шейки матки // International Journal of Medicine and Psychology. — 2019. — Т. 2, № 4. — С. 77–82.
11.Израильбекова К.Ш., Камышов С.В. Стратегические комбинации для предотвращения и преодоления резистентности к таргетной терапии в онкологии // Онкология. — 2020. — Т. 3. — С. 184–197.
12.Израильбекова К.Ш., Камышов С.В. Изучение категории больных с ассоциированными первично-множественными злокачественными опухолями женской репродуктивной системы // Онкологический журнал. — 2020. — Т. 15, № 2. — С. 81–84.

Journal Zone Publishing, Ilford, United Kingdom