

Original article

Pretreatment hyperuricemia and hypoalbuminemia as predictors for one-year mortality in diffuse large B-cell lymphoma beyond the international prognostic index

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Abstract:

Background: Diffuse large B-cell lymphoma (DLBCL) is prevalent in Thailand; however, real-world data identifying risk factors for mortality in local practice remain limited. **Objective:** This study aimed to evaluate the one-year mortality rate and identify risk factors for early death among patients with DLBCL treated with chemotherapy.

Methods: This single-center retrospective study analyzed data from medical records of patients newly diagnosed with DLBCL between 2019 and 2025 at a provincial hospital in Thailand. Patients who received palliative or end-of-life care shortly after diagnosis were excluded. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of mortality within the first year of treatment. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were reported. **Results:** Of 97 eligible patients (54% male; mean age±standard deviation, 63.1±12.2 years), the one-year mortality rate was 24%. Univariate analysis demonstrated significant associations between one-year mortality and age ≥ 60 years, poor performance status, Ann Arbor stage III-IV, anemia, chronic kidney disease stages 3-5, a low prognostic nutritional index, B-symptoms, serum albumin < 3.0 g/dL, serum uric acid ≥ 6.8 mg/dL and an international prognostic index (IPI) ≥ 3. Multivariate analysis identified three independent predictors of mortality: high IPI (aOR, 11.80; 95%CI: 1.36-91.88; p = 0.03), hypoalbuminemia (aOR, 5.92; 95%CI: 1.59-22.06; p = 0.008) and hyperuricemia (aOR, 3.74; 95%CI: 1.19-11.78; p = 0.02). **Conclusions:** The one-year mortality rate among patients with DLBCL in rural Thailand was 24%. In addition to the standard IPI, pretreatment hypoalbuminemia and hyperuricemia were identified as independent predictors of early mortality in DLBCL.

Keywords : ● Albumin ● Diffuse large B-cell lymphoma ● Mortality ● Uric acid ● Thailand

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นิพนธ์ต้นฉบับ

ภาวะกรดยูริกในโลหิตสูงและอัลบูมินในโลหิตต่ำก่อนการรักษาเป็นปัจจัยเสี่ยงนอกเหนือดัชนียาการณโรคสากต่อการเสียชีวิตในปีแรกของผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองชนิดบีเซลล์ขนาดใหญ่

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บทคัดย่อ

บทนำ โรคมะเร็งต่อมน้ำเหลืองชนิดบีเซลล์ขนาดใหญ่พบได้บ่อยในประเทศไทย แต่ข้อมูลจากเวชปฏิบัติจริงในระดับท้องถิ่นที่แสดงถึงปัจจัยเสี่ยงต่อการเสียชีวิตมีจำกัด **วัตถุประสงค์** เพื่อศึกษาอัตราการตายในระยะเวลา 1 ปี และปัจจัยเสี่ยงต่อการเสียชีวิตในผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองชนิดบีเซลล์ขนาดใหญ่ที่รักษาด้วยยาเคมีบำบัด **วิธีการศึกษา** การศึกษาวิเคราะห์ข้อมูลย้อนหลังผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองชนิดบีเซลล์ขนาดใหญ่ที่วินิจฉัยใหม่ อายุ 15 ปีขึ้นไป และรักษาด้วยยาเคมีบำบัด ระหว่างปี พ.ศ. 2562 ถึง พ.ศ. 2568 ณ โรงพยาบาลจังหวัดแห่งหนึ่งในประเทศไทย โดยคัดผู้ป่วยที่รักษาเฉพาะเพื่อประคับประคองระยะสุดท้ายของชีวิตออก วิเคราะห์สถิติถดถอยโลจิสติกเพื่อประเมินปัจจัยทำนายอิสระที่ส่งผลต่อการเสียชีวิตในปีแรก และรายงานอัตราส่วนออดที่ปรับปัจจัยกวนพร้อมช่วงความเชื่อมั่นร้อยละ 95 **ผลการศึกษา** ในผู้ป่วย 97 ราย (ร้อยละ 54 เป็นเพศชาย; อายุเฉลี่ย $\pm$ ส่วนเบี่ยงเบนมาตรฐาน, 63.1 ± 12.2 ปี) พบอัตราการตายในปีแรกร้อยละ 24 จากการวิเคราะห์แบบตัวแปรเดียว อัตราตายสัมพันธ์อย่างมีนัยสำคัญทางสถิติกับอายุ 60 ปีขึ้นไป ECOG 2 คะแนนขึ้นไป ระยะของโรคโลหิตสูง (ระยะที่ III-IV) โลหิตจาง โรคไตเรื้อรังระยะที่ 3-5 ดัชนีพยากรณ์ทางโภชนาการต่ำ มี B-symptoms ระดับอัลบูมินในโลหิตน้อยกว่า 3.0 ก./ดล. ระดับกรดยูริกในโลหิต 6.8 มก./ดล. ขึ้นไป และดัชนียาการณโรคสาก 3 คะแนนขึ้นไป ซึ่งการวิเคราะห์แบบพหุตัวแปรยืนยันว่ามี 3 ปัจจัยเป็นปัจจัยทำนายอิสระต่อการเสียชีวิต ได้แก่ ค่าดัชนียาการณโรคสากสูง (อัตราส่วนออด 11.80; ช่วงความเชื่อมั่นร้อยละ 95: 1.36-91.88; $p = 0.03$), ภาวะอัลบูมินในโลหิตต่ำ (อัตราส่วนออด, 5.92; ช่วงความเชื่อมั่นร้อยละ 95: 1.59-22.06; $p = 0.008$) และภาวะกรดยูริกในโลหิตสูง (อัตราส่วนออด 3.74; ช่วงความเชื่อมั่นร้อยละ 95: 1.19-11.78; $p = 0.02$) **สรุป** อัตราตายภายในปีแรกของผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองชนิดบีเซลล์ขนาดใหญ่ในพื้นที่ชนบทของประเทศไทยอยู่ที่ร้อยละ 24 นอกเหนือจากดัชนียาการณโรคสาก ภาวะอัลบูมินในโลหิตต่ำและกรดยูริกในโลหิตสูงก่อนการรักษา เป็นปัจจัยทำนายอิสระต่อการเสียชีวิตในระยะแรกของโรคมะเร็งต่อมน้ำเหลืองชนิดบีเซลล์ขนาดใหญ่

คำสำคัญ : ● อัลบูมิน ● โรคมะเร็งต่อมน้ำเหลืองชนิดบีเซลล์ขนาดใหญ่ ● อัตราตาย ● กรดยูริก ● ประเทศไทย

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2569;36:283-94.

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL), arising from a heterogeneous spectrum of molecular alterations. Clinically, DLBCL is characterized by aggressive behavior, with variable manifestations and responses to treatments. Although the introduction of the R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) as the standard first-line immunochemotherapy has significantly improved survival outcomes for patients with DLBCL, a subset of patients still experiences early treatment failure associated with high mortality.

In Thailand, NHL represents a major public health concern as the sixth most common malignancy, with DLBCL accounting for approximately 64% of all cases.¹ The disease affects a wide demographic range; however, more than 40% of cases occur in individuals aged 60 years or older.^{1,2} Thai patients with DLBCL frequently present with advanced disease features, including multiple sites of lymphadenopathy, extranodal involvement and constitutional symptoms. Notably, nearly 60% of patients are diagnosed at an advanced stage (Ann Arbor stage III-IV), which is strongly associated with a poor prognosis.

Currently, risk stratification for DLBCL relies heavily on the international prognostic index (IPI). Although advanced molecular techniques have enhanced risk assessment in developed healthcare settings, access to these tools remains limited in resource-constrained countries. Consequently, there is a critical need to identify readily available clinical and laboratory markers that can predict outcomes beyond the standard IPI. Despite the high prevalence of DLBCL in Thailand, data specifically addressing risk factors for early (one-year) mortality in the local setting remain scarce. Identifying the determinants of early mortality is essential for optimizing management strategies and improve outcomes in high-risk patient groups.

Therefore, this study aimed to identify potential factors independently associated with early mortality among patients with DLBCL treated with chemotherapy. In addition, it sought to determine the one-year mortality rate in this population, thereby providing evidence to support improved pretreatment risk assessment and clinical management of Thai patients with DLBCL.

Methods

Study design and population

This single-center retrospective study analyzed medical records of patients newly diagnosed with DLBCL at Phichit Hospital, Phichit, Thailand, between January 1, 2019 and December 31, 2025. Eligible participants were adults aged ≥ 15 years with a pathologically confirmed diagnosis of DLBCL who consented to and received chemotherapy.

Patients were initially identified from the medical records database using the diagnosis code C83.3 according to the International Classification of Diseases, Tenth Revision (ICD-10) and the morphology code 9680/3 according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3). Patients were excluded if they did not receive chemotherapy for any reasons, including those who received palliative, or end-of-life care shortly after diagnosis. Additional exclusion criteria included treatment at another institution and incomplete medical records lacking essential clinical or laboratory datavariabes (Figure 1). Patients who did not received chemotherapy were excluded to minimize confounding bias and ensure that survival analyses reflected the therapeutic effects of chemotherapy rather than the natural progression of the disease.

The primary objective of this study was to identify clinical and laboratory factors associated with mortality. The secondary objective was to determine the mortality rate within the first year after initiation of chemotherapy. The study protocol was approved by the Institutional Review Board of Phichit Hospital.

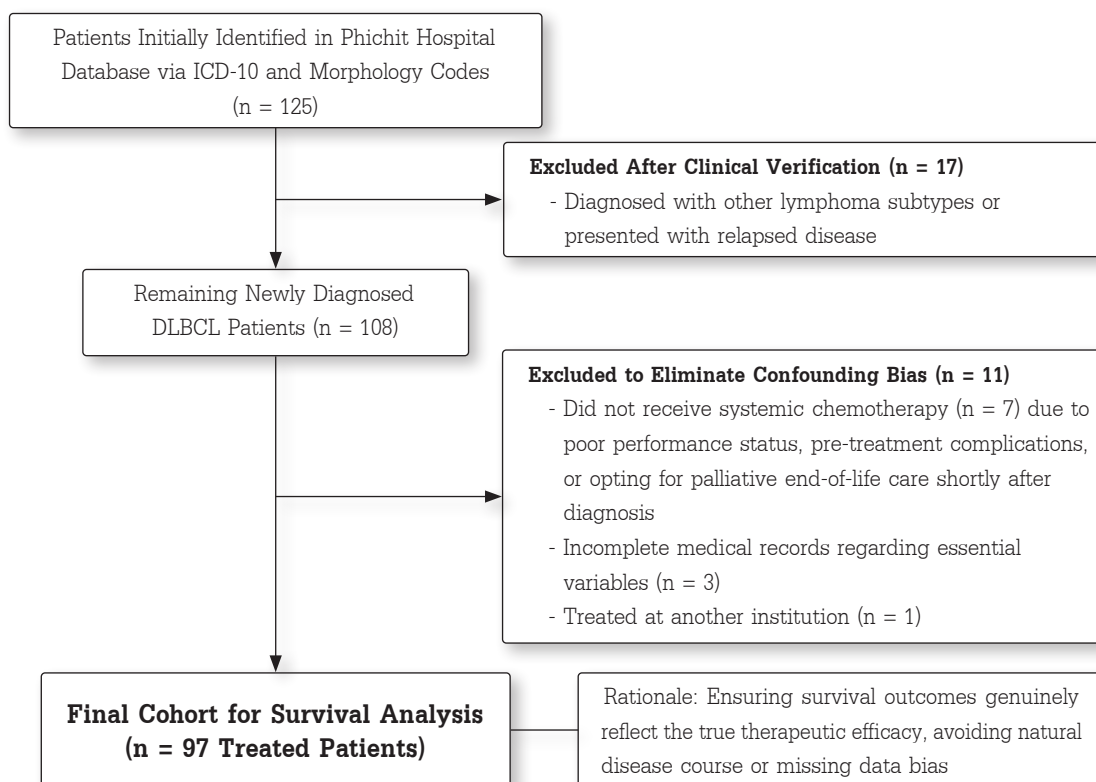


Figure 1 Patient selection flow diagram. From an initial identification of 125 patients via ICD-10 codes for DLBCL, 17 were excluded following diagnostic verification (due to non-DLBCL histology or relapsed disease). Among the remaining 108 eligible subjects with newly diagnosed DLBCL, 11 patients were additionally excluded from the survival analysis to minimize confounding bias, including those who did not receive systemic chemotherapy ($n = 7$), had incomplete medical records ($n = 3$), or were treated at another institution ($n = 1$). The final analytical cohort comprised 97 treated patients with DLBCL.

Data collection and definitions

The diagnosis of DLBCL was established according to ICD-O-3 histological criteria, while disease staging was based on the Ann Arbor staging system for NHL. A comprehensive review of medical records was conducted to collect baseline demographic data, including sex, age, performance status based upon the Eastern Cooperative Oncology Group (ECOG) score and comorbidities. The main disease-related characteristics recorded included the presence of B symptoms, (defined as unexplained fever $> 38^{\circ}\text{C}$, unexplained weight loss $> 10\%$ of body weight during the preceding 6 months and drenching night sweats), extranodal involvement, bulky disease (≥ 10 cm in maximum diameter) and Ann Arbor staging (I-IV).

Relevant pretreatment laboratory parameters were also collected, including hemoglobin level, absolute lym-

phocyte count (ALC), neutrophil-to-lymphocyte ratio (NLR), platelet count, serum albumin, serum uric acid, serum lactate dehydrogenase (LDH), creatinine clearance and prognostic nutritional index (PNI). For statistical analyses, continuous laboratory variables were dichotomized according to established clinical and physiological thresholds. Hyperuricemia was defined as a serum uric acid level of ≥ 6.8 mg/dL, corresponding to the physiological limit of urate solubility in serum at normal body temperature. This threshold has been associated with increased tumor burden and tumor lysis syndrome in hematological malignancies.³ Hypoalbuminemia was defined as a serum albumin level of < 3.0 g/dL. Although mild hypoalbuminemia is conventionally defined as < 3.5 g/dL, a more stringent cutoff of < 3.0 g/dL was used in this study to identify patients with moderate-to-severe baseline malnutrition and systemic inflammation.⁴ The

PNI, which reflects both nutritional and immunological status, was calculated using the formula: serum albumin (g/L) + 5 × absolute lymphocyte count (10^9 /L). A PNI score < 42 was considered low, based on previous evidence demonstrating an association with inferior overall survival (OS) among patients with DLBCL receiving rituximab-based chemotherapy.⁵

The primary outcome was all-cause mortality occurring within one year after initiation of chemotherapy. Other clinical and surrogate outcomes were considered secondary outcomes.

Statistical analysis

Descriptive statistics were used to summarize baseline characteristics. Categorical variables were presented as frequencies and percentages, whereas continuous variables were expressed as means ± standard deviations (SD) or medians with ranges, as appropriate based on data distribution.

Univariate logistic regression analyses were performed to evaluate associations between clinical and laboratory variables and one-year mortality, with results reported as unadjusted odds ratios (ORs) and 95% confidence intervals (CIs). Variable identified in univariate analyses were subsequently entered into a multivariate logistic regression model to adjust for potential confounders and identify independent predictors of mortality within the first year of treatment. Results were reported as adjusted OR (aOR) with 95% CIs.

Survival analyses were conducted using the Kaplan-Meier method, and survival curves were compared using the log-rank test.

All statistical tests were two-sided, and a *p*-value < 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, Version 31.0 (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

Between January 1, 2019 and December 31, 2025, a total of 125 patients recorded as DLBCL based on ICD-10

and ICD-O-3 codes were identified. Of these, 97 patients with newly diagnosed, pathologically confirmed DLBCL who underwent chemotherapy and did not meet any exclusion criteria were ultimately included in the study. The majority of patients were male (*n* = 52, 53.6%) and aged ≥ 60 years (*n* = 66, 68.0%). Regarding disease severity, 51 patients (52.6%) presented with Ann Arbor stage III-IV disease, while 42 (43.3%) and 4 (4.1%) had stage I and stage II disease, respectively. Poor performance status (ECOG ≥ 2) was observed in 58 patients (59.8%). Other notable clinical features included bulky disease (37.1%), extranodal involvement (53.6%) and the presence of B-symptoms (33.0%). Detailed patient characteristics are presented in Table 1.

Baseline laboratory assessments (Table 1) revealed elevated LDH levels in 71.1% of patients and hyperuricemia (serum uric acid ≥ 6.8 mg/dL) in 34.0%. Hypoalbuminemia (serum albumin < 3.0 g/dL) was observed in 16.5% of patients. Hematologic abnormalities included anemia (hemoglobin < 10 g/dL) in 24.7% and thrombocytopenia (platelet count < 150,000/mm³) in 14.4%. Renal function was largely preserved, with 85.6% of patients demonstrating a creatinine clearance ≥ 60 mL/min, as calculated using the Cockcroft-Gault formula. Overall, comorbidities were present in 46.4% of the cohort.

Treatment response and survival outcomes

All patients with Ann Arbor stage II-IV disease (*n* = 93, 95.9%) received standard R-CHOP chemotherapy for 6-8 cycles, based on evidence from the landmark GELA and MInT trials and reimbursement regulations of the National Health Security Office. In contrast, patients with Ann Arbor stage I disease were treated with CHOP or CHOP-like chemotherapy without rituximab because of the lack of phase III evidence demonstrating a survival benefit in this subgroup.

Overall, 23 patients (23.7%) died within the first year of follow-up. Infectious complications were the leading cause of death, accounting for 52.2% (*n* = 12) of all early deaths. These patients were predominantly older individuals (mean age ± SD, 72.5 ± 5.5 years) with

Table 1 Baseline characteristics of 97 patients with DLBCL treated with chemotherapy

Baseline characteristics	Statistical value (n = 97)
Demographics	
Male, n (%)	52 (53.6)
Mean age, year $\pm$ SD	63.1 $\pm$ 12.2
Age $\geq$ 60 years, n (%)	66 (68.0)
Clinical features	
ECOG performance status, n (%)	
0-1	39 (40.2)
2-4	58 (59.8)
Ann Arbor stage, n (%)	
I-II (early stage)	46 (47.4)
III-IV (advance stage)	51 (52.6)
Extranodal involvement, n (%)	52 (53.6)
B-symptoms, n (%)	32 (33.0)
Bulky disease, n (%)	36 (37.1)
IPI, n (%)	
0-2 (low/low-intermediate risk)	37 (38.1)
3-5 (high-intermediate/high risk)	60 (61.9)
Other comorbidities, n (%)	45 (46.4)
Laboratory Findings	
Mean hemoglobin, g/dL $\pm$ SD	11.3 $\pm$ 2.1
Hemoglobin < 10 g/dL, n (%)	24 (24.7)
Mean platelet count, /mm ³ $\pm$ SD	270,600 $\pm$ 118,000
Platelet count < 150,000/mm ³ , n (%)	14 (14.4)
Mean ALC, /mm ³ $\pm$ SD	1,898 $\pm$ 1,214
ALC < 1,000/mm ³ , n (%)	16 (16.5)
NLR $\geq$ 3.5, n (%)	34 (35.0)
Mean serum albumin, g/dL $\pm$ SD	3.6 $\pm$ 0.6
Serum albumin < 3.0 g/dL, n (%)	16 (16.5)
Mean serum uric acid, mg/dL $\pm$ SD	6.3 $\pm$ 2.5
Serum uric acid $\geq$ 6.8 mg/dL, n (%)	33 (34.0)
Median serum LDH, U/L (range)	264 (122-4,375)
Serum LDH $\geq$ 224 U/L, n (%)	69 (71.1)
Mean CrCl, mL/min $\pm$ SD	82.9 $\pm$ 23.6
CrCl < 60 mL/min (CKD stage 3-5), n (%)	14 (14.4)
PNI < 42, n (%)	28 (28.9)

Abbreviations: ALC, absolute lymphocyte count; CrCl, creatinine clearance; ECOG, Eastern Cooperative Oncology Group; IPI, international prognostic index; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio; PNI, prognostic nutritional index; SD, standard deviation.

lower serum albumin levels (mean $\pm$ SD, 3.0 $\pm$ 0.7 g/dL). Refractory or progressive disease accounted for 34.7% (n = 8) of deaths. Compared with patients who died from infections, those who died from disease progression were younger (mean age $\pm$ SD, 64.4 $\pm$ 13.5 years) and higher serum uric acid levels (mean $\pm$ SD, 8.6 $\pm$ 3.6 mg/dL). Among the remaining three cases, one was attributed

to upper gastrointestinal hemorrhage, while the causes of death in the other two patients were unknown.

With a median follow-up of 31 months (range, 1-83 months), the median OS was not reached. The one-year OS rate for the entire cohort was 76.3%. When stratified according to the IPI, a clear survival difference was observed between risk groups. Patients in the low

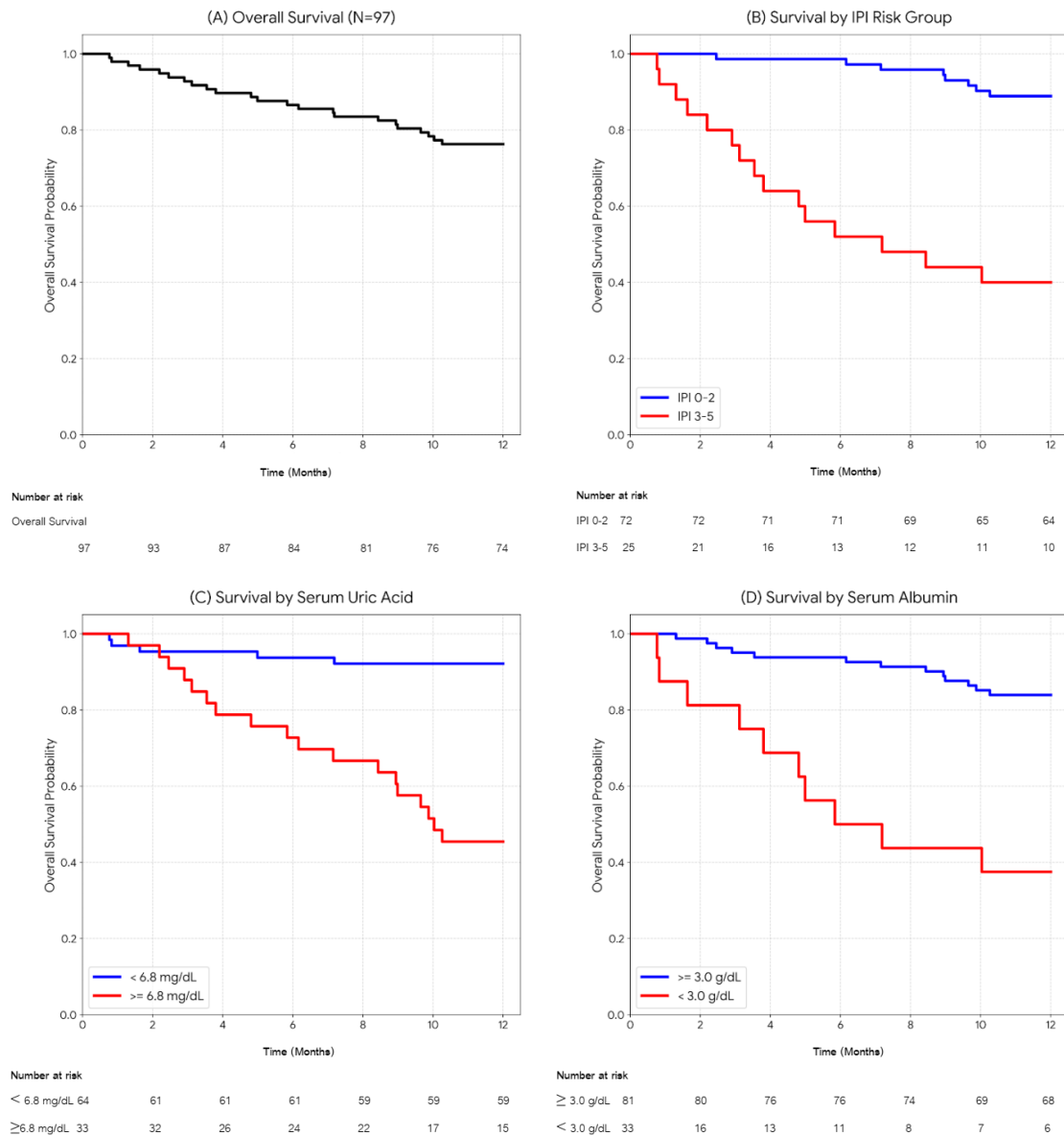


Figure 2 Kaplan-Meier curves showing one-year survival in patients with DLBCL. (A) The OS of the entire study cohort ($n = 97$). (B) Survival probability stratified by the IPI, comparing low/low-intermediate risk (IPI 0-2, blue line) vs. high/high-intermediate risk (IPI 3-5, red line). (C) Survival probability stratified by serum uric acid levels, comparing normal levels (< 6.8 mg/dL, blue line) vs. hyperuricemia (≥ 6.8 mg/dL, red line). (D) Survival probability stratified by serum albumin levels, comparing normal levels (≥ 3.0 g/dL, blue line) vs. hypoalbuminemia (< 3.0 g/dL, red line). All survival times are censored at 12 months. The red lines represent high-risk subgroups associated with significantly lower survival rates.

to low-intermediate risk group (IPI 0-2, $n = 39$) had a significantly higher one-year OS rate of 94.9%, with only two deaths occurring within the first year. In contrast, patients in the high-intermediate to high-risk group (IPI 3-5, $n = 58$) had a significantly lower one-year OS rate of 63.8%, accounting for 21 deaths during the first year of treatment (log-rank $p < 0.001$; Figure 2).

Risk factors associated with early mortality

Univariate analysis identified several clinical and laboratory factors that were associated with one-year mortality (Table 2). Among the clinical characteristics, an IPI ≥ 3 was the strongest predictor of mortality (unadjusted OR, 20.84; 95%CI: 2.67-162.75; $p < 0.001$), followed by poor performance status (unadjusted OR,

Table 2 Univariate analysis of factors associated with one-year mortality in DLBCL

Factor	No. of participants (n)	Mortality, n (%)	Unadjusted OR (95%CI)	p-value
Sex				
Female	45	8 (17.8)	1.00	-
Male	52	15 (28.8)	1.88 (0.71-4.95)	0.24
Age				
< 60 year	31	3 (9.7)	1.00	-
≥ 60 year	66	20 (30.3)	4.06 (1.10-14.91)	0.04
ECOG performance status				
0-1	39	2 (5.1)	1.00	-
2-4	58	21 (36.2)	10.50 (2.30-48.02)	<0.001
Ann Arbor stage				
I-II	46	5 (10.9)	1.00	-
III-IV	51	18 (35.3)	4.47 (1.50-13.33)	0.008
Extranodal involvement				
No	45	8 (17.8)	1.00	-
Yes	52	15 (28.8)	1.88 (0.71-4.95)	0.24
Bulky disease				
No	61	12 (19.7)	1.00	-
Yes	36	11 (30.6)	1.80 (0.70-4.64)	0.32
B-symptoms				
No	65	8 (12.3)	1.00	-
Yes	32	15 (46.9)	6.29 (2.28-17.34)	<0.001
IPI				
0-2	37	1 (2.7)	1.00	-
3-5	60	22 (36.7)	20.84 (2.67-162.75)	<0.001
Other comorbidities				
No	52	12 (23.1)	1.00	-
Yes	45	11 (24.4)	1.08 (0.42-2.75)	1.000
Hemoglobin				
≥ 10 g/dL	73	13 (17.8)	1.00	-
< 10 g/dL	24	10 (41.7)	3.30 (1.20-9.04)	0.03
Platelet count				
≥ 150,000/mm ³	83	17 (20.5)	1.00	-
< 150,000/mm ³	14	6 (42.9)	2.91 (0.89-9.53)	0.09
ALC				
≥ 1,000/mm ³	81	17 (21.0)	1.00	-
< 1,000/mm ³	16	6 (37.5)	2.26 (0.72-7.10)	0.20
NLR				
< 3.5	63	14 (22.2)	1.00	-
≥ 3.5	34	9 (26.5)	1.26 (0.48-3.31)	0.63

Table 2 Univariate analysis of factors associated with one-year mortality in DLBCL (continue)

Factor	No. of participants (n)	Mortality, n (%)	Unadjusted OR (95%CI)	p-value
Serum albumin				
≥ 3.0 g/dL	81	13 (16.0)	1.00	-
< 3.0 g/dL	16	10 (62.5)	8.72 (2.70-28.18)	<0.001
Serum uric acid				
< 6.8 mg/dL	64	9 (14.1)	1.00	-
≥ 6.8 mg/dL	33	14 (42.4)	4.50 (1.68-12.08)	0.005
Serum LDH				
< 224 U/L	28	3 (10.7)	1.00	-
≥ 224 U/L	69	20 (29.0)	3.40 (0.92-12.55)	0.07
CKD				
Stage 1-2	83	16 (19.3)	1.00	-
Stage 3-5	14	7 (50.0)	4.19 (1.29-13.64)	0.02
PNI				
≥ 42	69	12 (17.4)	1.00	-
< 42	28	11 (39.3)	3.07 (1.15-8.20)	0.03

Abbreviations: ALC, absolute lymphocyte count; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; IPI, international prognostic index; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio; OR, odds ratio; PNI, prognostic nutritional index.

Table 3 Multivariate analysis of factors associated with one-year mortality in DLBCL

Factor	aOR (95%CI)	p-value
IPI 3-5 (high-intermediate/high risk)	11.8 (1.36-91.88)	0.03
Pretreatment serum albumin < 3.0 g/dL	5.92 (1.59-22.06)	0.008
Pretreatment serum uric acid ≥ 6.8 mg/dL	3.74 (1.19-11.78)	0.02

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ECOG, IPI, international prognostic index.

10.50; 95%CI: 2.30-48.02; $p < 0.001$) and the presence of B-symptoms (unadjusted OR, 6.29; 95%CI: 2.28-17.34; $p < 0.001$). Advance-stage diseases and age ≥ 60 years were also significant risk factors.

Among biochemical markers, hypoalbuminemia emerged as the most significant predictor (unadjusted OR, 8.72; 95%CI: 2.70-28.18; $p < 0.001$). Other significant indicators included hyperuricemia (unadjusted OR, 4.50; 95%CI: 1.68-12.08; $p = 0.005$), renal impairment (chronic kidney disease stage 3-5; unadjusted OR, 4.19; 95%CI: 1.29-13.64; $p = 0.02$), anemia (unadjusted OR, 3.30; 95%CI: 1.20-9.04; $p = 0.03$) and a low PNI score

(< 42; unadjusted OR, 3.07; 95%CI: 1.15-8.20; $p = 0.03$).

After adjustment for potential confounders in the multivariate logistic regression model (Table 3), three factors remained independently associated with one-year mortality. A high IPI score (≥ 3) retained the strongest predictive value (aOR, 11.80; 95%CI: 1.36-91.88; $p = 0.03$). In addition, hypoalbuminemia and hyperuricemia remained significant independent predictors, conferring approximately 6-fold (aOR, 5.92; 95%CI: 1.59-22.06; $p = 0.008$) and 4-fold (aOR, 3.74; 95%CI: 1.19-11.78; $p = 0.02$) increased risks of death, respectively.

Discussion

Mortality in DLBCL is driven by a complex interplay of patient demographics, disease biology and treatment-related complications. Our findings corroborate that clinical status and disease burden are key determinants of short-term survival. The IPI demonstrated exceptional predictive power in our cohort. This high-risk estimate validates its utility as a composite prognostic tool that effectively integrates disease burden and patient functional reserve. These findings align with the established literature, in which advanced Ann Arbor stage (III-IV), the presence of B-symptoms and poor performance status (ECOG ≥ 2) are consistently identified as adverse prognostic factors.⁶ Furthermore, advanced age is a critical driver of mortality, early relapse and lower response rates,⁷⁻¹¹ likely due to increased susceptibility to chemotherapy-induced toxicities and a high-burden of comorbidities.

Beyond conventional prognostication, our study highlights the critical role of nutritional and metabolic markers in influencing survival among patients with DLBCL. Pretreatment hypoalbuminemia (serum albumin < 3.0 g/dL) emerged as a strong independent risk factor for early mortality in this study. Low serum albumin serves not only as a marker of malnutrition but also as a surrogate measure for systemic inflammation. Consistent with previous studies linking a low PNI to treatment failure,¹²⁻¹⁹ our data strongly suggest that poor nutritional status may compromise tolerance to chemotherapy in patients with DLBCL. This malnutrition-inflammatory complex likely contributes to an increased risk of severe infections, a major complication with reported incidence rates ranging from 10% to 63% among patients with DLBCL treated with R-CHOP.²⁰⁻²¹

In addition, metabolic dysregulation was shown to be a significant prognostic factor. Hyperuricemia (serum uric acid ≥ 6.8 mg/dL), together with elevated serum LDH, was independently associated with early mortality, reflecting high tumor proliferation and cell turnover.^{3,22} These markers, which are closely associated with

tumor lysis syndrome, may delay or complicate the early phases of lymphoma treatment through acute renal complications. Although immunological markers such as lymphopenia and NLR have been shown to stratify mortality risk in DLBCL,²³⁻²⁵ our findings from a rural Thai population underscore that, in resource-limited settings, readily available biomarkers such as serum albumin and uric acid can provide valuable prognostic information and help identify patients at the highest risk of early death.

The OS of patients with DLBCL in our cohort demonstrated a pronounced decline during the first three months, indicating a substantial burden of early mortality, followed by a subsequent plateau. Stratification according to the IPI revealed clear separation of survival curves across risk groups, confirming that a higher IPI score (≥ 3) was strongly associated with inferior survival outcomes. Notably, metabolic and nutritional disturbances were also associated with an adverse prognosis. Patients with hyperuricemia and hypoalbuminemia experienced a rapid and statistically significant decline in survival probability than those with normal baseline levels.

The strengths of this study include the evaluation of readily available clinical and laboratory parameters, particularly serum albumin and serum uric acid, which enhance the practical applicability of the findings in resource-limited settings where advanced molecular profiling is unavailable. The use of multivariate logistic regression analysis allowed adjustment for key confounders and confirmed independent associations beyond the IPI, supporting the robustness of the identified predictors. However, several limitations should be acknowledged. The retrospective single-center design may have introduced selection and information bias and limits the generalizability of the findings to other institutions or healthcare systems. The modest sample size also contributed to wide confidence intervals for some estimates. Furthermore, the lack of detailed molecular subtyping data and comprehensive information regarding supportive care may have limited further

interpretation of the findings. Therefore, these results should be considered hypothesis-generating and warrant validation in large prospective cohorts.

Conclusions

Although the IPI remains the gold standard for prognostication in patients with DLBCL, our study demonstrates that it may be insufficient on its own to identify all patients at high risk of mortality. The inclusion of serum albumin and serum uric acid levels—accessible, cost-effective and highly informative biomarkers—may improve the identification of patients at risk of death within the first year of chemotherapy. Serum albumin reflects not only nutritional status but also systemic inflammation, which is not explicitly captured by the IPI scoring system. In contrast, elevated serum uric acid is associated with aggressive lymphoma biology and an increased risk of acute kidney injury. Integrating these markers into routine clinical assessment may facilitate more precise stratification, enabling proactive nutritional interventions, closer monitoring for complications and optimization of strategies aimed at reducing short-term mortality in patients with DLBCL.

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Author contributions

N.C. designed the study, collected and interpreted data, analyzed data and wrote the manuscript draft; C.M. and S.K. interpreted data, critically reviewed, and edited the manuscript; all authors read and approved the final version of the manuscript.

Disclosures

The authors stated that they had no interests perceived as posing a conflict or bias.

Data availability statement

The corresponding author has full access to all data and takes responsibility for the integrity and accuracy

of data. The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement

The protocol of this study was reviewed and approved by the Institutional Review Board of Phichit Hospital. All research procedure in this retrospective study adhered strictly to the principles of the Declaration of Helsinki.

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