



The clinical significance of the prognostic nutritional index in very elderly patients over 80 years of age with diffuse large B-cell lymphoma

Erina Hamada¹ · Ogura Shinji¹ · Yuriko Nishiyama-Fujita¹ · Masahiro Akiimoto¹ · Tomohiko Tanigawa¹ · Chisako Ito¹ · Aki Sakurai¹ · Yoshinobu Aisa¹ · Tomonori Nakazato¹

Received: 4 March 2020 / Accepted: 27 March 2020 / Published online: 8 April 2020
© Springer-Verlag GmbH Germany, part of Springer Nature 2020

Dear Editor,

We read with interest the recently published article, “Clinical impact of prognostic nutritional index (PNI) in diffuse large B cell lymphoma” by Go et al. [1]. The authors performed a retrospective analysis of 228 newly diagnosed diffuse large B-cell lymphoma (DLBCL) patients. The median overall survival (OS) was shorter in the low PNI group than in the high PNI group (15.6 months vs. not reached; $p < 0.001$). A multivariate analysis showed that the PNI was an independent prognostic factor for OS. However, no studies have demonstrated the prognostic value of the PNI in very elderly patients with DLBCL. We therefore investigate the predictive role of PNI in very elderly patients (≥ 80 years of age) with DLBCL.

We retrospectively reviewed 84 very elderly patients who were diagnosed and treated at our hospital from 2007 to 2018. The PNI was calculated as $10 \times$ serum albumin concentration (g/dL) $+ 0.05 \times$ lymphocyte count (number/mm³). The cutoff value of the PNI was set by the receiver operator characteristic (ROC) curve. The Kaplan–Meier method, a univariate Cox proportional hazards analysis, and a multivariate analysis were used to verify the prognostic impact of each factor, including sex, stage, International Prognostic Index score (IPI), performance status (PS), extra-nodal site involvement (ESI), and soluble IL-2 receptor (SIL2R), albumin and lactate dehydrogenase (LDH) levels on overall survival (OS). Of the 84 patients, 39 were male and 45 were female. The

median age was 84 years (range: 80–94 years). The characteristics of the participants are shown in Table 1. The median observation period was 39 months. Sixty-two patients received rituximab-containing chemotherapy regimens as an initial treatment, including R-CHOP ($n = 30$), R-CVP ($n = 26$), and rituximab alone ($n = 5$). Proper dose adjustment was performed according to patients’ clinical status such as age, frailty, and comorbidity. Most patients were treated with R-miniCHOP or 70% dose R-CVP. Twenty-one patients received palliative therapy. The optimal cutoff value of the PNI for 3-year OS was set as 41.3, and 38 and 46 patients were classified into the high and low PNI groups, respectively. As shown in Fig. 1, the Kaplan–Meier curve demonstrated that the low PNI group showed significantly worse 3 year OS (3-year OS: 18.8% vs. 55.9%, $p < 0.001$). In a multivariate analysis, parameters that were independently associated with worse OS included low PNI ($p = 0.03$, HR 2.72), PS ≥ 2 ($p < 0.001$, HR 3.14) and high LDH ($p = 0.04$, HR 3.09) (Table 2).

DLBCL is the most common type of non-Hodgkin lymphoma with a median patient age of 60–70 years [2]. Especially in Japan, where the population is aging, the number of elderly DLBCL patients is increasing. As a global standard, the IPI is widely used as a prognostic score for DLBCL. It is known that age itself is associated with the life prognosis and the IPI includes ≥ 61 years of age as a poor prognostic factor [3]. For elderly patients of ≥ 80 years of age, R-CHOP therapy at a lower dose or with a reduced number of courses is described as a reasonable alternative therapy [4]. In order to reach complete remission, it is necessary to maintain an appropriate treatment intensity and minimize adverse events. Thus, physicians need to take into account multiple factors, including comorbidities, complications, cognitive deficiency, social

✉ Tomonori Nakazato
n-tomo@eurus.dti.ne.jp

¹ Department of Hematology, Yokohama Municipal Citizen’s Hospital, Yokohama, Japan

Table 1 Baseline characteristics of the study patients

Clinical factors	PNI		P value
	≤41.3(n = 46)	≥41.3(n = 38)	
Gender (male)	22 (47.8%)	17 (44.7%)	0.828
Stage ≥ III	39 (84.8%)	24 (63.1%)	0.041
B symptom plus	27 (58.7%)	4 (10.5%)	<0.001
ESI ≥ 2	12 (26.1%)	4 (10.5%)	0.095
ESI ≥ 3	40 (87.0%)	21 (55.3%)	0.001
ESI ≥ 2	39 (84.8%)	7 (18.4%)	<0.001
LDH > ULN 211 IU/l	42 (91.3%)	26 (68.4%)	0.011
Age–median	83 (80–93)	84 (80.94)	0.968

background, and nutritional status. In this study, the PNI was an independent predictor of the prognosis, while the IPI was not in a multivariate analysis that was adjusted for confounding factors. In addition, a former study revealed that a low PNI was significantly associated with more treatment-related adverse events and early treatment interruption [4]. Furthermore, the PNI can be easily calculated by blood tests at a first visit, which can be helpful for treatment selection at an earlier stage after the diagnosis. Taking these factors into consideration, this simple marker may have an important role in the provision of appropriate treatment for individuals.

Our study indicated that the PNI can be routinely used as an independent prognostic marker for DLBCL patients of ≥ 80 years of age. Additional prospective large-scale studies are needed to clarify the clinical significance of relationship between the PNI and the prognosis of elderly patients with DLBCL.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the

Fig. 1 Kaplan–Meier curves of overall survival according to the PNI

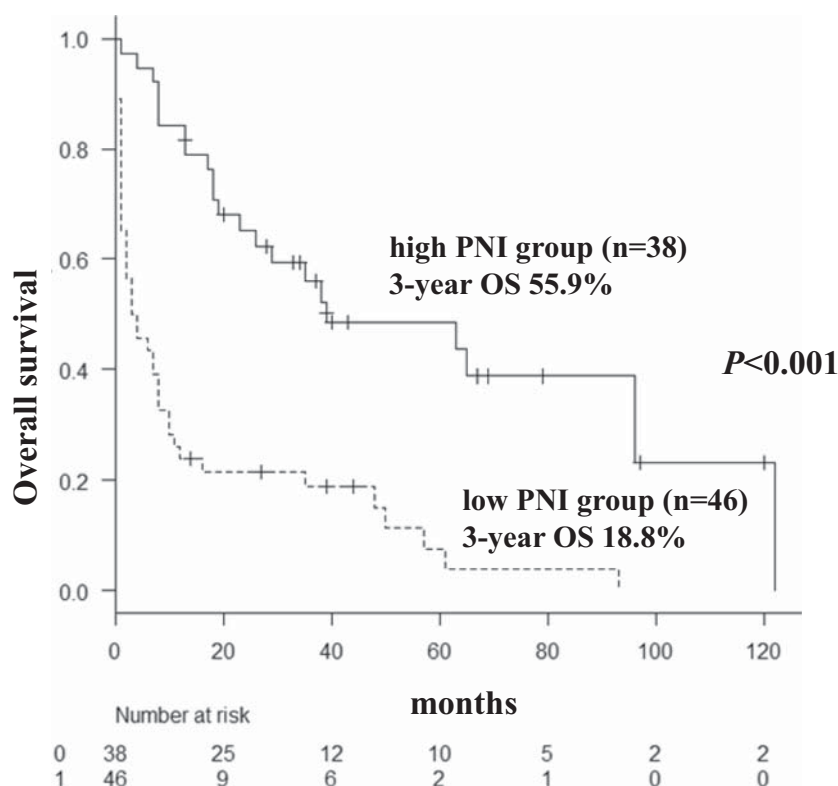


Table 2 Univariate and multivariate analysis for overall survival

Variable	Univariate analysis		Multivariate analysis	
	HR (95%CT)	<i>P</i> value	HR (95%CT)	<i>P</i> value
Alb < 3.5 g/dl	3.18 (1.86–5.44)	< 0.001		
Lymphocyte \geq 837 mm ³	1.804 (1.10–3.00)	0.02		
IPI \geq 3	2.53(1.37–4.68)	< 0.001		
ESI \geq 2	1.33(0.722–2.46)	0.36		
PS \geq 2	4.09 (2.33–7.18)	< 0.001	3.14 (1.37–7.21)	< 0.001
LDH > ULN 211 IU/l	3.11 (1.42–6.85)		3.09 (1.03–9.26)	0.04
Gender (male)	1.33 (0.812–2.19)			
Stage \geq III	2.19 (1.18–4.06)			
B symptoms present	2.75 (1.62–4.67)			
PNI \leq 41.3	3.88 (2.24–6.74)		2.72 (1.08–6.83)	0.03

institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patients. The study was approved by the Ethics Committee of Yokohama Municipal Citizen's Hospital.

References

- Go SI, Park S, Kang MH, Kim HG, Kim HR, Lee GW (2019) Clinical impact of prognostic nutritional index in diffuse large B cell lymphoma. *Ann Hematol* 98(2):401–411
- (1997) A clinical evaluation of the International Lymphoma Study Group classification of non-Hodgkin's lymphoma. The non-Hodgkin's lymphoma classification project. *Blood* 89:3909–3918
- (1993) A predictive model for aggressive non-Hodgkin's lymphoma: the international non-Hodgkin's lymphoma prognostic factors project. *N Engl J Med* 329:987–994
- Nagai H (2018) Revision of JSH Guideline for Tumors of Hematopoietic and Lymphoid Tissues: lymphoma. *Rinsho Ketsueki* 59(10):2146–2152

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.