The assessment of overall survival in bone sarcoma using Prognostic Nutritional Index

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INTRODUCTION:
Sarcomas are rare and heterogeneous group of tumors arising from putative mesenchymal tissue, accounting for about 1.0 % of all adult cancers. Sarcoma is one of rare cancer. Sarcomas are broadly classified into either neoplasm derived from soft tissue or bone. Bone tumors vary widely in their biological behavior. Bone sarcoma can at any age and in any anatomic sites. Due to the rarity and diversity of the disease, high-grade sarcomas still have a poor prognosis. Therefore, more accurate predictive prognostic factors are required to allow for development of personalized treatment plans. Several nutritional or inflammatory biomarkers, including Prognostic Nutritional Index (PNI) have been reported to predict the prognosis of osteosarcoma patients. The aim of this study is to evaluate PNI for the survival rate of bone sarcoma patients.

METHODS:
Between January 2008 and December 2022, we retrospectively reviewed medical records of 61 patients with primary bone sarcoma, who were treated at our institution. The inclusion criteria were as follows: patients who were pathologically diagnosed bone sarcoma arising from extremities and trunk. The exclusion criteria were shown Figure 1. We obtained retrospectively medical records of patients' characteristics. We calculated nutritional or inflammatory parameters from the laboratory data before the initial treatment. The definition of the parameters was shown as follows: Prognostic Nutritional Index (PNI) =10 × serum albumin(g/dl) + 0.005 × total lymphocyte counts (10^9/L); Geriatric Nutritional Index (GNRI) =1.489 ×serum albumin(g/l) + 41.7 × body weight/ideal body weight. The ideal mass was defined as a body mass index of 22. Body weight or ideal body weight were set to 1 when the patient's body weight exceeded the ideal body weight; Neutrophil (N) -Lymphocyte (L) Ratio (NLR) = N/L; Platelet (P)-Lymphocyte Ratio (PLR) =P/L; Lymphocyte Monocyte (M) Ratio (LMR) =L/M; Systemic Immune-Inflammation index (SII) =P×N/L; Systemic Inflammation Response Index (SIRI) =N×M/L; C-reactive protein-Albumin Ratio (CAR) =CRP/Alb. The duration of overall survival was defined as the interval between the date of initial treatment for the primary tumor and the date of death. Patients alive at the time of analysis were censored at date of last follow-up. Survival rates were estimated using the Kaplan-Meier method, and the difference between the groups were compared using the log-rank test. The univariate and multivariate analysis was performed using cox proportional hazards regression model.

RESULTS SECTION:
The characteristics of patients are shown in Table 1. The mean follow-up period was 50 months (range: 1 - 151 months). The mean overall survival was 106 months. The patients were divided into two groups according to the median of PNI: low PNI vs. high PNI. Overall survival of patients with low PNI was worse than that of patients with high PNI (Figure 2) (p=0.092). In the univariate analysis, tumor size, stage, margin and PNI have significant associations with overall survival. In the multivariate analysis, margin remains an independent prognostic factor for overall survival. Furthermore, the following two groups also show trend of difference; GNRI (p=0.1429), NLR (p=0.3670), LMR (p=0.0745), and SIRI (p=0.1421) using the log rank test. In the univariate analysis, PNI, GNRI and PLR have significant associations with overall survival. Especially, the HR of PNI is highest of all calculated parameters (HR: 2.659 [95% CI 0.8514-8.303]).

DISCUSSION:
PNI was developed by Onodera et al. Initially developed to predict perioperative complications, the PNI has now been reported to be useful as a prognostic factor in many types of cancer. The PNI can be easily calculated from serum albumin and total lymphocyte counts. Since albumin is a marker of nutritional status and inflammation, and lymphocytes are markers of nutritional and immune status, PNI reflects nutritional, immune, and inflammatory status. Markers such as GNRI, NLR, PLR, LMR, SII, SIRI, and CAR, which indicate nutritional and inflammatory status, have been reported as prognostic factors for cancer, including sarcoma. In the present study, PNI, like those markers, was a useful prognostic predictor of overall survival in bone sarcomas. We have some limitations in this study: there was no reference value for PNI, the study was conducted at a single center, and some patients had a short observation period.

SIGNIFICANS:
PNI can be easily calculated from serum albumin and total lymphocyte counts. PNI is a useful prognostic predictor of overall survival in bone sarcomas.

IMAGES AND TABLES:

Figure 1. Inclusion and exclusion criteria.

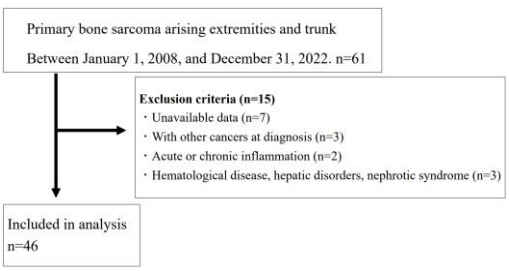
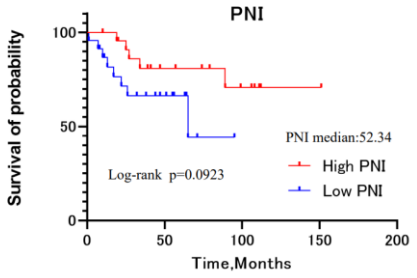


Table 1. Baseline characteristics of all patients.

Characteristics	Cases	Percentage(%)	Characteristics	Cases	Percentage(%)	Characteristics	Cases	Percentage(%)
Gender			**AJCC Stage**			**Surgery/Margin**		
Male	28	61	IA	5	11	R0	28	61
Female	18	39	IB	3	7	R1	4	9
Age			IIA	14	30	R2	2	4
50≧	23	50	IIB	16	35	Unresectable	12?	26
50<	23	50	III	1	2	**Chemotherapy**		
Body weight(kg)			IVA	4	9	No	19	41
59≧	22	48	IVB	3	7	Yes	27	59
59<	24	52	**Tumor size**			**Radiotherapy**		
BMI(kg/m²)			T1	19	41	No	28	61
22≧	23	50	T2	23	50	Yes	18	39
22<	23	50	T3	4	9	**Status at last follow-up**		
Tumor location			**Grade**					
Upper extremities	6	+1?	1	8	17	Alive	27	59
Lower extremities	25	+1?	2	8	17	Dead	13	28
Trunk	14	30	3	30	65	Unknown	6	13

BMI: Body mass index, FNCLCC: French Federation of Cancer Centers Sarcoma Group grading system, AJCC: American Joint Committee on Cancer classification.

Figure 2. Kaplan Meier curve for overall survival according to PNI; low PNI vs. high PNI.



The median of PNI is 51.63 (range, 28.56 to 61.35). The patients were divided into two groups according to the median of PNI: low PNI vs. high PNI. Overall survival of patients with low PNI was worse than that of patients with high PNI using log-rank test (p=0.0923).