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Full Length Article

Significance of the prognostic nutritional index in patients with glioblastoma: A retrospective study

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ABSTRACT

Objective: Accumulating evidence demonstrates that prognostic nutritional index(PNI) is linked to the clinical outcome of patients with malignant tumors, but few studies had investigated the clinical significance of PNI in glioblastoma multiforme(GBM). This study aimed to clarify the association between PNI and the clinical outcome of patients with GBM.

Methods: The clinical data of 84 patients with GBM were retrospectively analyzed. PNI was calculated from the following formula: 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3). X-tile software was used to determine the cut-off of PNI and other hematological parameters. GBM patients were dichotomized as two groups based on the PNI cut-off.

Results: The optimal PNI cut-off level was 44.4. There were 14 patients with a PNI < 44.4 and 70 patients with a PNI ≥ 44.4. The results showed that PNI score was associated with gender, serum albumin, and hemoglobin level. Univariate analysis suggested that age, extent of resection, adjuvant treatment, platelet count and PNI score were predictors of overall survival in patients with GBM. The 1- and 2-survival rates of patients with a PNI < 44.4 were 28.60 and 0%, respectively, while the corresponding values for patients with a PNI ≥ 44.4 were 52.90 and 5.70%, respectively. Based on multivariate analysis, a PNI ≥ 44.4 (HR:0.479, 95% CI:0.235–0.975,p = 0.042) remained an independent prognostic indicator for a favorable outcome of patients with GBM. Furthermore, patients with a PNI ≥ 44.4 may have a better efficacy of adjuvant treatment than patients with a PNI < 44.4 (HR:0.259, 95% CI:0.096–0.700, p = 0.008).

Conclusion: A PNI > 44.4 was an independent prognostic parameter of overall survival in patients with GBM and the efficacy of adjuvant treatment. Interventions aimed at correcting the nutritional and immune status of patients with GBM may, therefore, promote the effectiveness of adjuvant treatment and improve the survival outcomes.

1. Introduction

Glioblastoma multiforme (GBM) is the most common malignant glioma. Moreover, the tumors are highly invasive and likely to recur [1]. The clinical outcomes are various even if patients receive combined radiotherapy and temozolomide(TMZ) treatment following tumor resection [2], which indicates that potential prognostic factors may influence the overall survival(OS). Thus, identifying the variables associated with prognosis of patients with GBM can guide individual treatment.

Several recent studies suggest that the preoperative nutritional condition is associated with the OS in patients with cancer [3,4]. The prognostic nutritional index(PNI), which was calculated from the following formula: 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count(per mm^3) reflected the nutritional and immune status of patients with cancer, and was linked to the clinical outcome of patients with malignant tumors [5–11]. Though some studies indicate that albumin impacts the prognosis of GBM patients [12,13], few have investigated the clinical significance of PNI in GBM. Also, the optimal PNI cut-off to predict survival has been controversial and various methods have been used to determine the cut-off [5–11]. Therefore, this study aimed to clarify the association between PNI and OS in patients with GBM. X-tile software was used to identify the PNI cut-off level to predict OS.

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2. Patients and materials

2.1. Clinical data collection

We retrospectively analyzed the clinical data of patients with GBM, who had undergone tumor resection between January 2013 and December 2014 in the Department of Neurosurgery, West China Hospital, Chengdu,China. A total of 331 patients with glioma were identified, while only 84 patients with GBM were included in this study. Two clinical pathologists evaluated the pathological diagnosis of the patients included in this study according to the 2007 World Health Organization(WHO) brain tumor classification. Any discrepancy was discussed with a third experienced pathologist to obtain a definitive diagnosis. Patients' information, including demographic and tumor data, postoperative therapy, and serum variables(albumin, hemoglobin, lymphocyte, monocyte, neutrophil, and platelet counts) were collected to assess the association between these factors and the OS in patients with GBM. In this study, PNI was calculated from the following formula:$10 \times$ serum albumin (g/dL) + $0.005 \times$ total lymphocyte count(per mm^3). Patients with chronic or infectious disease or steroid treatment that influenced the status of albumin and lymphocyte counts or OS were excluded. OS was defined as the date of tumor resection to the date of death or the last follow-up. The last follow-up was performed in July 2016. In this study, all hematological variables were detected preoperatively. The patients' blood samples were collected on the second morning after their hospitalization, and the samples were tested by a technician at the Department of Clinical Laboratory. Informed consent was obtained from all patients, and the ethic committee of the hospital approved this study.

2.2. Treatment characteristics

All patients included in this study received surgical treatment, and pre- and post-operative MRI scan determined the extent of resection. Adjuvant treatment after tumor resection, included radiotherapy and chemotherapy [1], while not all patients completed the full adjuvant treatment. Therefore, for the convenience of statistical analysis, patients who completed the adjuvant treatment protocol were defined as the completely treated group(CTG) and those who did not receive radiotherapy or chemotherapy were classified as the not treated group(NTG). Those patients who did not receive all of the adjuvant treatment protocol were included in the partially treated group(PTG). Antiepileptic drugs (AEDs) were administered based on preference and experience of the doctor.

2.3. Statistical analysis

The Statistical Package for the Social Sciences version 17.0 was used to analyze the data statistically. X-tile software (Version 3.6.1, Yale University) was used to find the cut-offs for albumin, hemoglobin,lymphocyte,monocyte,neutrophil, and platelet counts, and the platelet-lymphocyte(PLR), lymphocyte-monocyte(LMR), and neutrophil-lymphocyte(NLR) ratios, as well as the PNI for predicting survival in patients with GBM. If the X-tile software was unable to identify the cut-offs of these parameters, either their respective median was used, or the cut-off was adopted from previous studies performed on glioma patients. For the dichotomous data, the chi-square test was used to examine possible associations between PNI and other prognostic factors. Survival function curves were calculated using the Kaplan–Meier method for all patients and stratified according to the parameters mentioned above. Multivariate analysis by Cox proportional hazard model was performed to analyze the variables with statistical significance in the univariate analysis. Statistical significance was set at $p \leq 0.05$ with two sides.

Table 1
Baseline characteristic of 84 patients with GBM and the relationship between PNI and other variables.

Variables	Cases,n	PNI < 44.4,n	PNI ≥ 44.4,n	P-value
Age,years				
<60	53	7	46	0.266
≥60	31	7	24	
Sex				
Male	50	5	45	0.047
Female	34	9	25	
Tumor side				0.416
Left	37	10	27	
Right	42	1	41	
Bilateral	5	3	2	
Tumor location				
Frontal lobe	33	4	29	0.369
Temporal lobe	45	5	40	0.142
Other lobe	38	7	31	0.695
Involvement of mutilobar	43	6	37	0.494
Preoperative seizure	8	1	7	0.74
Extent of resection				0.24
Gross total	59	8	51	
Subtotal	25	6	19	
Adjuvant treatment				0.775
CTG	35	6	29	
PTG	30	4	26	
NTG	19	4	15	
AEDs treatment	23	4	19	0.913
Monocyte				0.079
<0.31	42	10	32	
≥0.31	42	4	38	
Lymphocyte				0.092
<1.5	49	11	38	
≥1.5	35	3	32	
White cell				0.283
<6.9	41	5	36	
≥6.9	43	9	34	
Neutrophil				0.359
<7.5	62	12	50	
≥7.5	20	2	18	
Platelet				0.922
<151	37	6	31	
≥151	47	8	39	
Albumin				<0.001
<38.9	20	12	8	
≥38.9	64	4	60	
Hemoglobin				0.001
<120	15	7	8	
≥120	69	7	62	
NLR				0.142
<4	39	4	35	
≥4	45	10	35	
PLR				0.079
<113.76	42	4	38	
≥113.76	42	10	32	
LMR				0.558
<4.37	42	6	36	
≥4.37	42	8	34	

PNI, prognostic nutritional index; CAG, completely treated group; PTG, partially treated group; NTG, not treated group; AED, antiepileptic drug; PLR, platelet-lymphocyte ratio; LMR, lymphocyte-monocyte ratio; NLR, neutrophil-lymphocyte ratio.

3. Results

Eighty-four patients with GBM were included in this study. The clinical characteristics of the patients are listed in Table 1. Among these patients, there were 34(40.5%) women and 50(59.5%) men. The median age and its range were 53 and 43–62 years, respectively. The lesions involved in the bilateral cerebral hemisphere were identified in 5(6%) cases, with 37(44%) on the left side and 42(50%) on the right. Overall, 45(53.6%) lesions were located