Prognostic Nutritional Index Predicts Life Expectancy of Patients with End-Stage Oral Cancer: A Retrospective Study

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Abstract

Background: Generally, clinicians do not accurately estimate life expectancy in terminally ill patients with cancer. Aim: To evaluate the value of the Prognostic Nutritional Index (PNI) for accurately estimating the life expectancy of patients with end-stage oral cancer. Design: A longitudinal section study. Setting/participants: Fifteen patients (12 men; mean age: 71.7 years) who died of oral cancer between 2005 and 2014 (the terminal group) were included. The mean PNI values at the initial visit and at 3, 2, and 1 months before the deaths were comparatively analyzed. Results: The mean follow-up period was 133 days. At the initial examination, the PNI values were 49.1 ± 4.5 (p = 0.6723). The PNI value of the terminal group was 35.6 ± 5.1 at 2 months before death and 28.6 ± 3.0 at 1 month before death. The PNI values at 3, 2, and 1 months before death in the terminal group significantly differed from each other and from that at the initial visit and steadily decreased until death. Conclusions: Our findings suggest the utility of PNI as a prognostic index in patients with end-stage oral cancer patients. Furthermore, the PNI should be routinely considered in the nutritional management of patients with oral cancer nearing death.

Keywords

Life Expectancy, Nutrition Assessment, Oral Cancer, Prognosis, Retrospective Studies

1. Introduction

Accurate estimation of life expectancy in terminally ill patients with cancer is important from both the clinician's and the patient's perspectives. However,

studies have revealed that clinicians do not accurately estimate the time to death [1] [2] [3] [4] [5], making it difficult for the patients and their families to prepare themselves. Although several indices and scores exist for evaluating the life expectancy [6] [7], most of these include subjective components in the calculation, such as the presence of edema, anorexia, or delirium, which makes the objective assessment prone to inaccuracy. An objective scoring method to accurately predict the patient survival has therefore been sought. For this purpose, the Prognostic Nutritional Index (PNI) established by Onodera and Buzby [8] [9] can be used to objectively evaluate the prognosis in a range of patients with cancer. The PNI is calculated using a simple formula that is based on 2 routine serum measurements. Initially, the PNI was used to quantitatively estimate the postoperative complications in general surgical patients, with a PNI > 45 indicating cancer surgery; 45 - 40 suggesting the need for caution during surgery; and <40 contraindicating surgery [8]. Regarding dental surgery, a few reports have been considered to enable prognostic prediction in the nutritional field [10] [11]. Recently, the practicality of PNI has been confirmed in an array of terminally ill patients [12] with cancer of the cervix [13], esophagus [14], stomach [15] [16], colorectum [17], and pleura [18]. Nevertheless, it remains unknown whether the index can serve as a predicative tool in patients with end-stage oral cancer, as mastication and deglutition functions are lost and the dietary intake is decreased. These changes negatively affect the nutritional and immunological status, thereby rapidly worsening the overall health and eventually leading to the patient's death. Subjective global assessment (SGA) for the nutritional screening of patients with cancer is available [19] [20]. However, this index is regarded as a qualitative indicator because of the subjective judgment involved with it. Because a patient's life expectancy and the quality of life can be improved if a health professional performs proper nutritional management, it is necessary to optimize the nutritional assessment and the prediction of survival time. The present study explores the use of the PNI in predicting the life expectancy of patients with end-stage oral cancer.

2. Methods

2.1. Study Design

This longitudinal section study was performed after obtaining ethical approval and in-formed consent. The study was approved by the Ethics Committee of the Nagoya Ekisai Hospital (Approval No. 2017-011). The present study was conducted in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects. Verbal informed consent was obtained from all participants and/or their families. The cases were retrospectively analyzed based on the available medical records. This study was conducted on 148 oral cancer patients who were provided radical treatment in the Department of Oral and Maxillofacial Surgery, Nagoya Ekisaikai Hospital between January 2005 and April 2014. Among the patients who re-

ceived radical treatment, we excluded the following: 1) 98 patients without the recurrence metastatic after radical treatment. 2) 35 patients who remitted after performing salvage operation or CRT. 15 patients with oral cancer who eventually died at the Nagoya Ekisaikai Hospital between April 2005 and March 2014 after receiving resection and reconstruction surgery were selected. A patient diagnosed as having oral squamous cell carcinoma and receiving radiotherapy and chemotherapy before the surgery was excluded from group.

2.2. Data Collection

The following data were collected from the patient medical records: sex, age, site of primary tumor, C-reactive protein (CRP) levels, serum albumin levels, and peripheral lymphocyte count measured at the initial visit and at various time points during the follow-up period.

2.3. Tumor Staging

Tumor staging was performed according to the TNM classification method of the International Union against Cancer [21] during the initial visit.

Serum parameter measurement and data analysis.

The serum levels of CRP and albumin and peripheral lymphocyte count were estimated using the standard laboratory procedures. In terminally ill patients, the measurements were performed at the initial visit and routinely thereafter at every week, including at approximately 3, 2, and 1 months before their deaths. PNI value was calculated using the following formula:

$$PNI = \left[10 \times \text{serum albumin level} \left(\text{g/dL} \right) \right]$$
$$+ \left[0.005 \times \text{total peripheral lymphocyte count} \left(\text{per} \cdot \text{mm}^3 \right) \right]$$

2.4. Statistical Analysis

The weekly PNI data were analyzed using Shapiro-Wilk test to ascertain whether they were normal distribution we performed iteration measurement with 1-way layout analysis of variance and examined the factor effect based on the week number. After proving the significant factor effect by the number in a week, we compared the effect between the standards by multiple comparisons using the Bonferroni method. The statistical significance standard was set at 5%.

3. Results

The participants comprised 12 men and 3 women aged 55 - 89 years (mean age: 71.7 ± 8.5 years). The patients presented with a primary tumor on the tongue (n = 8), lower jaw (n = 4), upper jaw (n = 1), oral floor (n = 1), or buccal mucosa (n = 1), and their disease was diagnosed at stage I (n = 2), stage II (n = 4), stage III (n = 6), or stage IV (n = 3).

The detailed characteristics of the terminal participants are provided in Table 1.

Table 1. Patient characteristics.

Factor	Group	Overall
n		15
Age (years)		71.7 ± 8.5
Sex (n)	Male	12
	Female	3
site of primary	Tongue	9
	Upper iaw	1
	Lower jaw	4
	Buccal mucosa	1
T classification	T1	3
	T2	7
	T3	5
	T4	0
N classification	N0	7
	N1	5
	N2	2
	N3	1
Stage (n)	I	2
	II	4
	III	6
	IV	3
Observation period		583.5 ± 336.1

In the Shapiro-Wilk test, the PNI data of each month was regularly distributed.

The mean PNI value at the initial visit was 50.1 ± 7.9. However, the values gradually decreased over a period of time, with the mean values at 3, 2, and 1 months before the death being 41.4 ± 6.2, 35.6 ± 5.1, and 28.5 ± 3.0 (Figure 1). Furthermore, in the terminal group, the mean PNI values at 3 versus 2 months ($p = 0.000021$) and 2 versus 1 month ($p = 0.000028$) before death were significantly different from each other. The mean value at 3 months before death was significantly lower than that obtained during the initial visit ($p = 0.001173$) (Figure 1). PNI value at decreased before 1 month ($p < 0.05$), 2 months as compared with the initial diagnosis in 3 months of death ($p < 0.01$). Using iteration measurement with 1-way layout analysis of variance, we showed the significant factor effect by the number in month passed ($p < 0.05$). Multiple comparisons by the Bonferroni method demonstrated significant differences in all combinations between the initial diagnosis and at a month before death.

4. Discussion

4.1. Main Findings

In this study, we established that the PNI is a suitable tool for accurately predicting the life expectancy of patients with end-stage oral cancer. The disease has
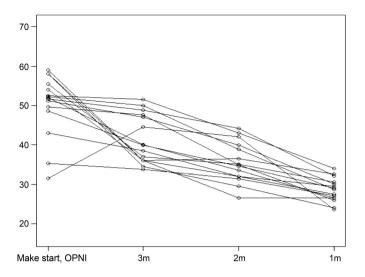
Figure 1. Prognostic Nutritional Index (PNI) values of oral cancer patients who eventually died from the disease. The PNI values were 50.1, 41.4, 35.6, and 28.5 at the time of the first examination and at 3 months, 2 months, 1 month, and 1 week before death, showing a gradual decrease over a period of time. In this study, the mean PNI values of the 15 study patients were 28.5 and 35.6 at 1 and 2 months before death, respectively.

a high mortality rate, with 5-year survival rate being approximately 50% [22]. In light of this low survival rate, it is imperative to accurately predict the life expectancy of the patients. If an early prognosis can be established by a trained health professional, the patients can spend their remaining time with an appropriate focus and make timely preparations for their death together with their loved ones. To date, the nutritional and overall statuses of patients with head and neck cancer have been evaluated using anthropometric indices, laboratory parameters, dietary intake assessments, and clinical scores [23] [24]. Various prognostic tools such as the Karnofsky performance status, Eastern Cooperative Oncology Group performance status, Palliative Performance Scale, Palliative Prognostic Score, and Palliative Prognostic Index were used interchangeably [25]. However, all these tools included subjective components. The PNI [8] [9] originally developed for general surgical patients to predict postoperative complications has recently gained attention as a more objective measurement tool for the prognosis of a broad range of terminally ill patients with cancer [12]-[18]. The merit of PNI lies in the fact that it can be easily calculated from only 2 serum markers: serum albumin value and peripheral lymphocyte count. The index can therefore be computed as a part of the routine hematological investigation. Serum albumin is a protein with a half-life of 20 days, and it is compounded by the liver; hence, it reflects the long-term variations in the whole-body nutritional status. In healthy individuals, one-third to half of serum albumin exists in the intravascular compartment and the remaining is distributed in the musculature and viscus. General dyscrasia, dysnephria, liver dysfunction, and poor nutrition are

some of the reasons for decrease in serum albumin levels in patients with oral cancer. Another factor is that the oral cavity is an important organ in nutrition, signifying that any abnormalities affecting the masticating and swallowing functions exert a measurable influence on the serum albumin value. Metabolic changes in patients with cancer also occur because of tumors producing aberrant amounts and profiles of cytokines. For instance, interleukin-6, interleukin-1, and tumor necrosis factor alpha levels are typically increased, thereby lowering the skeletal muscle and body fat, which in turn is accompanied by a decrease in immunocompetence [26] [27] [28].

4.2. What This Study Adds

We discerned that the PNI value significantly and steadily decreased at 3, 2, and 1 months before death, thereby providing an accurate measure of a patient's survival time. It was previously documented that patients with gastrointestinal cancer present with a mean PNI of 40.4, 39.2, and 35.4 at 3, 2, and 1 months before death, respectively [12]. These values differ from the mean PNI values observed in our study: 41.4, 35.6, and 28.5 at 3, 2, and 1 months before death, respectively. This deviation indicates that the nutritional status of patients with oral cancer is somewhat more compromised at 2 and 1 months before death when compared with that of patients with gastrointestinal cancer. In fact, a PNI value of 28.5 at 1 month before death, as estimated in the present study, corresponds to a value of 29.8 at 3 days before death in patients with gastrointestinal cancer, as reported previously [12]. This comparison reveals that patients with oral cancer do survive, albeit under severe nutritional deprivation, for as long as patients with gastrointestinal cancer have a slightly higher PNI. To generate a more accurate estimate of patient survival time, the PNI values for patients with oral cancer nearing their death should be verified using a larger number of participants and more frequent measurements at time points closer to death. In addition, to enhance the remaining quality of life, future research should focus on deciphering how the PNI can be applied to improve the nutritional management in the final stages of the patient's survival.

4.3. Study Limitations

Although participants were carefully selected to avoid bias, the study had a small sample size, thereby limiting its generalizability.

5. Conclusion and Limitations

Clinicians should consider using the PNI value when estimating life expectancy in patients with end-stage oral cancer. Considering the particular importance of appropriate nutritional management in these patients at the end stage of the disease, more research is necessary to investigate how the PNI value can be used in these patients to improve the quality of life near death.

Acknowledgements

Conflicts of Interest

The authors declare that there is no conflict of interest.

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