

Nutritional Risk Screening in Malignant Tumors: A Study of 375 Cancer Inpatients

Min Zhang

Xinxiang Medical University First Affiliated Hospital

Yuying Guo

Xinxiang Medical University First Affiliated Hospital

Xiaodi Zhang

Xinxiang Medical University First Affiliated Hospital

Yu Zhang

Shangqiu Third People's Hospital

Yuanyuan Fan

Yanshi City Peoples' Hospital

Yanting Liu

Xinxiang Medical University First Affiliated Hospital

Kelei Zhao

Xinxiang Medical University First Affiliated Hospital

Ruijuan Fan

Xinxiang Medical University First Affiliated Hospital

Ping Lu (✉ lupingdoctor@126.com)

Xinxiang Medical University First Affiliated Hospital

Research Article

Keywords: Neoplasms, Malnutrition, Nutrition risk screening, inflammatory factors

Posted Date: June 4th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-449297/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Different degrees of malnutrition are one of the most common complications in patients with malignant tumors, which often accelerate the progression of the disease and affect the therapeutic effect and prognosis of the disease. Therefore, in the early census of patients with malignant tumor, screening the possible nutritional risks and correcting the possible causes of various malnutrition are important measures to improve the quality of life of patients. Our study randomly included 375 patients diagnosed with malignant tumor in Henan province, and analyzed the relationship between nutritional risk and indicators include age, BMI, serum albumin, serum prealbumin, serum hemoglobin, tumor stage, tumor type, and inflammatory factors. we found that age, BMI, hemoglobin, and whether suffering from gastrointestinal tumors were the independent risk factors for nutritional risk in patients. We also found an significant correlation between inflammatory factors (IL-6 and IL-8) and nutritional risk status of cancer patients, so as to provide new prediction indexes for clinical management of nutritional risk and dynamic changes of nutritional status.

Introduction

Cancer is a catabolic inflammatory disease that often causes patients to experience malnutrition, or even cachexia in severe cases¹. Due to reduced food consumption, abnormal nutrient metabolism, and the adverse effects of radiotherapy and chemotherapy, nutritional problems are often encountered during the treatment of cancer. In 2017, a multi-center PreMiO study in Italy² found that 51% of patients with malignant tumors were malnourished; 9% are evidently malnourished, and 43% were at risk of malnutrition. The European society for clinical nutrition and metabolism (ESPEN) guidelines pointed out that malnutrition during cancer treatment reduces the quality of life, increases the side effects of treatment, and reduces the response to treatment, thereby affecting the survival of patients³. Worse still, the malnutrition may even cause patient death. In the early 1930s, research reports found that about 20%-50% of the deaths of malignant tumor patients were not directly caused by the malignancy itself, but from malnutrition or cachexia⁴. Therefore, nutritional screening and early intervention is important to prolong the survival period and improve the quality of life for cancer patients.

Nutrition Risk Screening 2002(NRS 2002) (Table 1) is a common chart to define the nutritional risk of patients. However, the importance of nutritional risk screening and evaluation and supplementary nutritional treatment has not attracted enough attention in the current clinical cancer treatment strategies. In the hospitals, many patients with malignant tumors are repeatedly treated with radiotherapy, chemotherapy, or surgery under the condition of malnutrition due to the lack of specialized nutritionists. This arise the likelihood of serious complications such as infection and organ failure increases, affecting the patient's prognosis during the treatment period⁵. Hence, nutritional supplements with comprehensive anti-tumor treatments following screening the nutritional status of cancer patients should be a requirement in the clinics.

Association of nutritional risk with some common clinical variables would be of great convenience to alert the oncologist on the need for a further nutritional assessment or nutritional support. In this study, we analyzed 375 cases with malignant tumors from the north of Henan province, China. The NRS 2002 was used to define the patients' nutritional risk, and various clinical factors were measured to find their association to high nutrition risk.

In this study, we collected 375 patients with Malignant tumor in Henan Province, the nutrition risk was screened according to European Nutrition Risk Screening (NRS 2002). Patients' Clinical indicators were collected to analyze the factors associated with a high nutrition risk score. In the perspective these data may help physician identify nutritional risk in advance and hence to plan a nutritional intervention.

Patients And Methods

Patients

Patient recruitment was carried out among malignant tumor patients admitted consecutively at the People's Hospital of Yanshi City and The First Affiliated Hospital of Xinxiang Medical University, Henan province, China. Inclusion criteria including: (1) patients with a clear diagnosis and an expected hospital stay of more than 3 days, (2) age above 18 years, (3) informed consent to participate in the study, (3) not undergone radiotherapy and chemotherapy at the time of data collection. Exclusion criteria included (1) end-stage patients, (2) patients with severe infection, (3) patients with severe liver or kidney failure, (4) Diabetes have not been effectively controlled.

Collection of clinical data

Personal information (name, age, gender, height, weight, ethnicity, department, date of admission, primary diagnosis, co-existing comorbidities) were collected following their willingness to participate in this investigation. The clinical data collected were included the patient's serum albumin, serum pre-albumin, tumor stage, and whether suffering from gastrointestinal tumors.

Nutrition risk screening

Using the European Nutrition Risk Screening (NRS 2002), the screening items included nutritional status score (0 to 3 points), disease severity score (0 to 3 points), and age score (age > 70 years old added 1 point), the total score (0-7 points) was the sum of the three. Those with a total NRS score of ≥ 3 are judged as having malnutrition risk, and those with an NRS of less than 3 have no nutritional risk. (The patients were reviewed every week if the total score less than 3, and if the rechecked result is ≥ 3 points, then the patient will be considered as at nutritional risk and suggested for nutritional support.)

Serum specimen collection

48 of the 74 patients were randomly selected in the study from the First Affiliated Hospital of Xinxiang Medical University. Among them, 25 cases of patients without nutritional risk and 23 cases of patients

with nutritional risk were divided into group A and group B respectively, 5ml of peripheral venous blood were collected using a coagulation tube, serum from the whole blood was collected by centrifuge at 3000 rpm for 10 minutes at room temperature. The expression of immune-related inflammatory factors IL-6 and IL-8 were detected by Enzyme-linked immunosorbent assay (ELISA).

ELISA

Human IL-6 ELISA Kit (abs510003) and Human IL-8 ELISA Kit (abs510004) were purchased from Abison Biotechnology (Shanghai, China), ELISA was performed according to the manufacturer's instructions. In brief, purified standards and experimental samples were diluted for coating microtiter plates for 2 hours at room temperature. The samples were then washed and 100 µL detection antibody was added into the wells for further incubation at room temperature for 2 hours. HRP-conjugated streptavidin (SA-HRP) was used at room temperature for 20 minutes in dark to bind the detection antibody. The catalytic reaction was stopped by the addition of 50 µl stop solution to each microwell. Within 30 minutes after adding the stop solution, the absorbance was measured at 450 nm, and with 540 nm or 570 nm as the calibration wavelength by using a microplate reader (Bio-Rad, [Hercules, CA](#)).

Statistical analysis

The experimental data was statistically analyzed by using SPSS 26.0 software. Measurement data were expressed as mean ± standard deviation. The independent samples t-test compares the difference of means between the two groups. The χ^2 -test compares the difference of composition ratios between the groups. Multiple regression analysis compared the differences in basic parameters between the two groups of patients. Spearman correlation analysis was used to analyze the correlation between two variables. $P<0.05$ was considered statistically significant.

Results

1 Characteristics of patients

A total of 375 patients diagnosed with nausea tumor in Henan Province from April 2016 to November 2019 were collected into our study. All patients are above 18 years old, including 170 males (45.3%) and 205 females (54.7%). There were 164 patients (47.30%) with nutritional risk and 211 patients (52.7%) without nutritional risk. There were 56 patients (4.96%) in stage I and II; 319 patients (95.04%) were in stage III and IV. 184 patients (66.67%) with gastrointestinal tumors; There were 191 cases (33.33%) with non-digestive tract tumor. Table 1.

Table 1 Summary of clinical data

	n	%
Overall	375	
Gender		
Female	205	54.7
Male	170	45.3
Age (years)	65	18-94
median		
Site of primary tumor		
Digestive tract tumor	184	49.1
Non-gastrointestinal tumor	191	50.9
Tumor staging		
I+II	56	14.9
III+IV	319	85.1
Nutritional risk		
With	164	47.3
Without	211	52.7

2 Relationship between common indicators and nutritional risk

In order to explore the nutritional risk factors, we divided the patients into two groups according to the nutritional risk and analyzed their age, BMI and serological (Table 2). The results of Mann-Whitney U test of measurement data showed that there were obvious differences in age, BMI and serological test indexes between the nutritional risk group and the non-nutritional risk group ($P < 0.001$) (Table 2).

Logistics regression analysis was performed on age, BMI and related serological indicators, and it was found that age ($P = 0.01$) was negatively correlated with nutritional risk. BMI ($P = 0.01$), albumin ($P = 0.01$), and hemoglobin ($P = 0.05$) were positively correlated with nutritional risk, while there was no obvious correlation between prealbumin and nutritional risk ($P = 0.05$) (Table 3).

To further investigate whether there was a correlation between gender, tumor stage, tumor type and the occurrence of nutritional risk factors, We use Univariate analysis of the data, the result of χ^2 -test showed that tumor stage and whether gastrointestinal tumor or not had an obvious correlation with the occurrence of malnutrition risk ($P < 0.001$), while gender had no correlation with the occurrence risk of malnutrition ($P > 0.05$). (Table 4)

Table 2

Nutritional risk	Without $n=211$ m	With $n=164$ m	Z	P
Age	61(53,67)	70(63.5,76.5)	-7.791	0.000
BMI	23.5(21.5,25.7)	20.8(18.4,23.55)	-6.906	0.000
serum albumin	43.5(40.6,46.5)	39.8(34.35,42.5)	-7.737	0.000
Serum prealbumin	209(168,260)	146(101.5,177)	-8.935	0.000
Haemoglobin	122(113,132)	109(94,122.5)	-6.111	0.000

Table 3

Item	b	SE	z	Wald χ^2	p	OR	95% CI
Age	-0.052	0.012	-4.474	20.015	0.000	0.949	0.927 ~ 0.971
BMI	0.170	0.038	4.420	19.539	0.000	1.185	1.099 ~ 1.277
serum albumin	0.089	0.024	3.782	14.305	0.000	1.093	1.044 ~ 1.145
Serum prealbumin	0.001	0.001	0.607	0.369	0.544	1.001	0.999 ~ 1.002
Haemoglobin	0.016	0.007	2.319	5.379	0.020	1.016	1.002 ~ 1.029

Table 4

variable	category	Without nutritional risk $n=211$		Nutritional risk $n=164$		χ^2	P
		n	%	n	%		
Gender	Female	116	54.98	89	54.27	0.019	0.891
	Male	95	45.02	75	45.73		
Tumor staging	I-II	49	23.22	7	4.27	26.098	0.000
	III-IV	162	76.78	157	95.73		
Whether digestive tract tumor	No	137	64.93	54	32.93	37.815	0.000
	Yes	74	35.07	110	67.07		

3Relationship between inflammatory factors and nutritional risk

Patient’s nutritional status is associated with metabolic changes and immune status impairment⁶ , more and more evidence proved that the systemic inflammation is associated with the increased weight loss⁷. The pro-inflammatory factors may influence nutritional status through inhibition of appetite, alteration of gastrointestinal function, alteration of the carbohydrate metabolism and insulin resistance⁸.

To explore the relationship between inflammatory factors and nutritional risk, we selected 48 cases from 375 patients randomly to express immune-related verification factors and divided the 48 patients into group A and B: 25 cases in Group A, who were tumor patients without nutritional risk; Group B included 23 tumor patients with nutritional risk. The level of immune-related inflammatory factors IL-6 and IL-8 in the two groups were detected respectively, and the relationship between IL-6 and IL-8 and the nutritional status of tumor patients was explored. The results showed that the level of IL-6 and IL-8 in the serum of patients with nutritional risk were obvious higher than patients without nutritional risk (Figure 1), and the difference is statistically significant $P<0.05$ (Table 5).

Table 5 Expression of cytokine in two groups

Cytokine	Group A	Group B	
pg/ml	Without nutritional risk	With nutritional risk	<i>P</i>
IL-6	2.10±3.03	22.76±38.81	0.013
IL-8	65.37±74.46	249.75±373.92	0.022

The baseline characteristics and peripheral blood indicators with statistical difference between patients with nutritional risk and patients without nutritional risk were selected, and the correlation between IL-6 and IL-8, these baseline characteristics and peripheral blood indicators was analyzed by Spearman correlation analysis. The results showed that IL-6 had a negative correlation with serum albumin and serum prealbumin, and IL-8 had a positive correlation with serum albumin in patients without nutritional risk ($P<0.05$). IL-6 was negatively correlated with serum prealbumin in patients at nutritional risk ($P<0.05$). IL-8 was not associated with BMI, serum albumin, serum prealbumin, or gastrointestinal tumor in patients at nutritional risk. The Spearman correlation coefficient between IL-8 and serum prealbumin of patients at nutritional risk was: -0.341, but it was not statistically significant, and it was considered related to the sample size. (Table 6)

Table 6 Correlation analysis of IL-6 and IL-8 with baseline characteristics and peripheral blood

	BMI/Kg/m ²		serum albumin		Serum prealbumin		Digestive tract tumor	
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
IL-6	-0.242	0.008	-0.457*	-0.118	-0.399*	-0.524*	0.311	-0.157
IL-8	0.192	-0.070	0.412*	-0.371	0.018	-0.341	0.290	-0.207

Discussion

Malnutrition is a risk factor for increased morbidity and decreased quality of life in cancer patients^{2,9}. The occurrence of nutritional risk in patients with malignant tumors is related to many clinicopathological characteristics. Some studies demonstrated that age is related to the occurrence of nutritional risks, elderly patients are more likely to have nutritional risks^{6,10}. Moreover, multiple studies have reported that BMI is associated with malnutrition in patients with malignant tumors³. BMI below 20 kg/m² has been found to have high sensitivity in the diagnosis of severe mal-nutrition in the older patients with cancer¹¹. Gastrointestinal tumor patients have a higher risk of malnutrition, this probably due to loss of appetite and the nutrient digestion and absorption dysfunction. Studies showed that patients with gastric cancer or upper gastrointestinal tumors (including esophageal cancer, gastric cancer, and duodenal cancer) had extremely high malnutrition risk rate of up to 94.6%¹².

Inflammatory factors also found associated with nutritional risk in cancer patients. Increasing evidence from basic biological studies indicated that there may be a correlation between malnutrition and inflammatory factors¹³. Previously reported studies suggest that malnutrition risk is related to the levels of serum albumin and hemoglobin, if the patient's serum total protein and serum albumin continue to decrease, it may indicate malnutrition¹⁴. At present, there are few studies on the relationship between interleukin family and nutritional risk.

In order to find an easy index to predict the cancer patient's nutritional risk, we adopted the indicators of patient clinical characteristics including the impact of age, gender, BMI, tumor stage, and digestive tract tumor on the nutritional risk of patients with malignant tumors. No correlation was found between the genders, prealbumin and nutritional risk, while the age has a negative correlation with nutritional risk, the BMI, albumin, and hemoglobin have a positive correlation with nutritional risk. What's more, we found that the expression of IL-6 and IL-8 in the serum of patients with nutritional risk was significantly increased (Fig. 1).

In conclusion, our study found that malnutrition generally exists in cancer patients. At the same time, we demonstrated that IL-6 and IL-8 inflammatory factors are related to the nutritional risk which may provide new indicators for nutritional screening and dynamic changes of nutritional status of patients with malignant tumors.

Declarations

Acknowledgements: We would like to thank all patients for participating in this study ; We thank the life and science research center of the Xinxiang Medical University first Affiliated Hospital for providing experimental venues for our study.

Funding: No funding was received to assist with the preparation of this manuscript.

Conflicting of Interests: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Availability of data and material: All authors certify that the data in this study are true and reliable.

Author contributions: All authors contributed to the study conception and design. The study was mainly designed by Ping Lu and Min Zhang. Material preparation, data collection were performed by Yuying Guo,Yu Zhang, Yuanyuan Fan, data analysis were performed by Min Zhang, Kelei Zhao, Ruijuan Fan. The first draft of the manuscript was written by Yanting Liu and Xiaodi Zhang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethical approval: Approval was obtained from the ethics committee of the First Affiliated Hospital of Xinxiang Medical University and the Ethics Committee of Shangqiu Third People's Hospital. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to participate: For all research involving human subjects, freely-given, informed consent to participate in the study must be obtained from participants.

Consent for publication Authors are responsible for correctness of the statements provided in the manuscript.

References

1. Kim DH. Nutritional issues in patients with cancer. *Intest Res* 2019;17(4):455-462.
2. Volkert D, Beck AM, Cederholm T, Cereda E, Cruz-Jentoft A, Goisser S, de Groot L, Grosshauser F, Kiesswetter E, Norman K and others. Management of Malnutrition in Older Patients-Current Approaches, Evidence and Open Questions. *J Clin Med* 2019;8(7).
3. Silva FR, de Oliveira MG, Souza AS, Figueroa JN, Santos CS. Factors associated with malnutrition in hospitalized cancer patients: a cross-sectional study. *Nutr J* 2015;14:123.
4. Williams AC. Nutritional Risk in Cancer Patients 65 and Older Undergoing Systemic Phase I Treatment. *J Adv Pract Oncol* 2020;11(5):465-474.
5. Cao J, Xu H, Li W, Guo Z, Lin Y, Shi Y, Hu W, Ba Y, Li S, Li Z and others. Nutritional assessment and risk factors associated to malnutrition in patients with esophageal cancer. *Curr Probl Cancer*

6. Antoun S, Rey A, Beal J, Montange F, Pressoir M, Vasson MP, Dupoirion D, Gourdiat-Borye A, Guillaume A, Maget B and others. Nutritional risk factors in planned oncologic surgery: what clinical and biological parameters should be routinely used? *World J Surg* 2009;33(8):1633-40.
7. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med* 1999;340(6):448-54.
8. Sieske L, Janssen G, Babel N, Westhoff TH, Wirth R, Pourhassan M. Inflammation, Appetite and Food Intake in Older Hospitalized Patients. *Nutrients* 2019;11(9).
9. Shakersain B, Santoni G, Faxen-Irving G, Rizzuto D, Fratiglioni L, Xu W. Nutritional status and survival among old adults: an 11-year population-based longitudinal study. *Eur J Clin Nutr* 2016;70(3):320-5.
10. Hickson M. Malnutrition and ageing. *Postgrad Med J* 2006;82(963):2-8.
11. Campillo B, Paillaud E, Uzan I, Merlier I, Abdellaoui M, Perennec J, Louarn F, Bories PN, Comite de Liaison A-N. Value of body mass index in the detection of severe malnutrition: influence of the pathology and changes in anthropometric parameters. *Clin Nutr* 2004;23(4):551-9.
12. Souza Cunha M, Wiegert EVM, Calixto-Lima L, Oliveira LC. Relationship of nutritional status and inflammation with survival in patients with advanced cancer in palliative care. *Nutrition* 2018;51-52:98-103.
13. Tan CS, Read JA, Phan VH, Beale PJ, Peat JK, Clarke SJ. The relationship between nutritional status, inflammatory markers and survival in patients with advanced cancer: a prospective cohort study. *Support Care Cancer* 2015;23(2):385-91.
14. Keller U. Nutritional Laboratory Markers in Malnutrition. *J Clin Med* 2019;8(6).

Figures

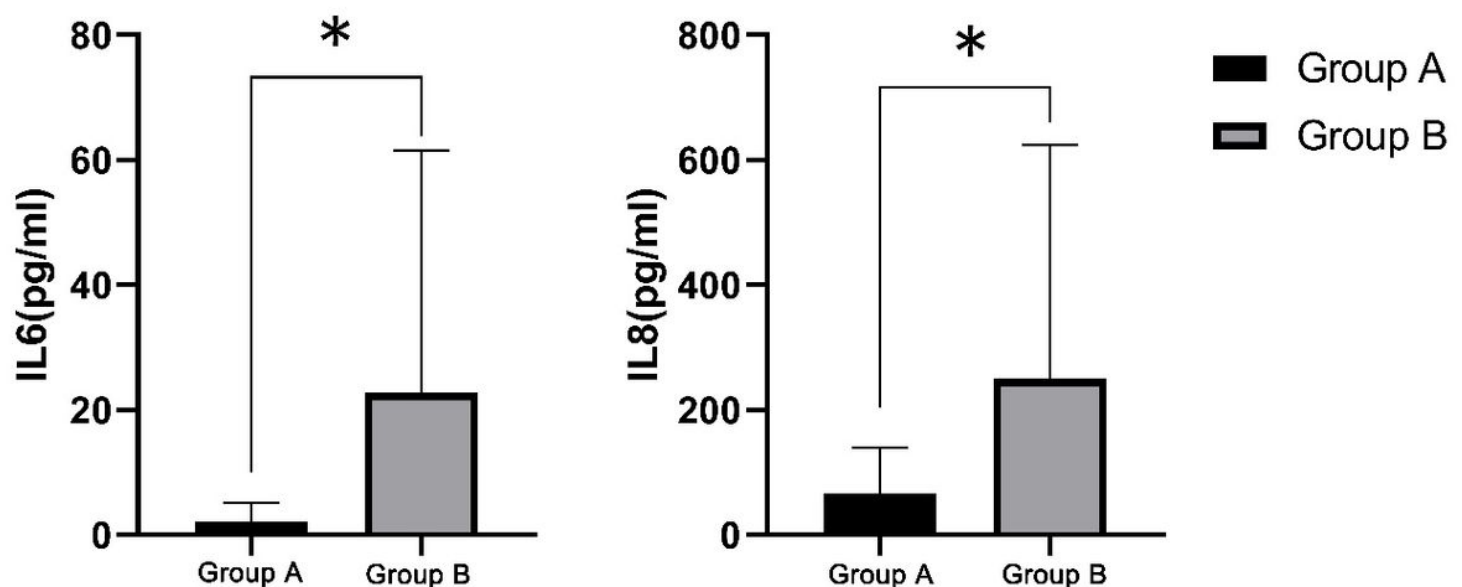


Figure 1

Expression of IL-6 and IL-8 between the two group

