Research Article

Journal of Clinical Cases

Low Prognostic Nutritional Index Is Closely Related To Disease Progression And Poor Prognosis In Patients With COVID-19 In Chengdu, China".

Qiqing Cui[2*],Fengjiao Gao[1*], Xiaoyan Yuan[1*], Rui Li[1], YongWang[1], Yanfeng Zhu[2#] and Dafeng Liu[1#]

[1]TheFirst Ward of Internal Medicine, Public Health Clinic Centre of Chengdu, Chengdu, China.
[2]School of Public Health, Chengdu Medical College, Chengdu, China*
These authors have contributed equally to this work.

[#]Corresponding authors:
DafengLiu, Yanfeng Zhu,
No.377 Jingming Road, Jinjiang District, Chengdu City, Sichuan ProvinceChengdu610066, China
No.783, Xindu Avenue, Xindu District, Chengdu City, Sichuan Province Chengdu 610500, China
Phone: +8613094494836: +8613648098858
E-mail address: ldf312@126.com ; cmc_zhuyanfeng@163.com

Received Date: 07 March 2024
Accepted Date: 21 March 2024
Published Date: 27 March 2024

Citation:
DafengLiu, Yanfeng Zhu. Low Prognostic Nutritional Index Is Closely Related To Disease Progression And Poor Prognosis In Patients With COVID-19 In Chengdu. Journal of Clinical Cases 2024.

1. Abstract

1.1. Background:
COVID-19 patients with lower immunonutritional status have a lower prognosticnutritional index (PNI) and are more likely to have severe disease and a poorprognosis.

1.2. Objectives:
This study aims to evaluate the relationship between PNI level and diseaseprogression and prognosis in COVID-19 patients.

1.3. Methods:
This retrospective analysis examined the PNI level of 1228 patientsdiagnosed with COVID-19. Patients were categorized into four groups: PNI1 group (PNI<50.65), PNI2 group (PNI 50.65-53.75), PNI3 group (PNI 53.76-57.20), and PNI4 group (PNI>57.20), based on the quartile value of PNI at admission.Comparisons were made between the four groups regarding clinical and outcomedata, and assessments were conducted to determine the association between PNI and disease progression and prognosis in patients with COVID-19.

1.4. Results:
As PNI levels decreased from the upper to thelower quartile group, HGB, ALB, TP, and TLC levels also decreased. Additionally, patient age increased, and there were longer coronavirus negativeconversion times and hospitalization durations. According to the multipleregression analysis, the severity of illness was associated with PNI levels, nutritional risk, and NRS2002 score upon admission. Furthermore, the Prognostic Nutritional Index (PNI), nutritional risk, and NRS2002 score during admission areall significant prognostic factors. The PNI demonstrates a high degree ofaccuracy in predicting severe illness and mortality among COVID-19 patients.

1.5. Conclusions:
A low PNI is significantly correlated with disease progression anda poor prognosis in COVID-19 patients. Early intervention for malnutrition isnecessary to lower the incidence of critical illness in individuals with a PNIlower than 49.12. Patients with a PNI lower than 40.45 necessitate continuousnutritional support to decrease mortality and enhance the likelihood ofrecovery.

2. Keywords:
2019 coronavirus disease (COVID-19), dietary risk, prognostic nutritional index(PNI), disease progression, prognosisClinical Trial

Registry:
ChineseClinical Trial Register Chi CTR 20000345631.

3. Introduction

The COVID-19 pandemic, caused by SARS-CoV-2, presents significant threats and challenges to global health and social development [1]. Following the World Health Organization's declaration of the pandemic on 15th March 2020, the number of confirmed cases has risen to over762 million and resulted in 6.8 million deaths by April 2023 [2]. COVID-19 is a disease that progresses from asymptomatic or mild upper respiratory tract infection to severe pneumonia [3,4]. Most patients infected with SARS-CoV-2 are mild and have a high recoveryrate. However, severe patients can rapidly progress to respiratory failure, multiple organ dysfunction, and even death, with most deaths involving elderlyand sickly patients who often have poor nutritional status [5,6]. A previous studyprovided evidence that malnutrition is one of the main predictors of death fromviral

infection [7]. Diarrhea is a common symptom in COVID-19 patients and canlead to nutrient malabsorption [8]. Decreased appetite leads to reducednutrient intake, and the psychological pressure of the disease increases therisk of anxiety and depression in patients, further affecting food intake [9].In addition, critically ill patients, often with severe inflammation andanorexia resulting in sharply reduced food intake, are more likely to developsevere illness. Therefore, systematic and urgent management of nutritionalassessment and further scheduling of COVID-19-infected patients isessential [10,11]. Expert statements endorsed by the European Society forClinical Nutrition and Metabolism Council and the practice guidelines forCOVID-19 nutrition management both advocate and highlight the importance ofnutritional status assessment [12]. However, for patients with the most severe manifestations of infection, assessing nutritional status with common tools canbe quite difficult due to physical limitations and difficulties in gathering anthropometric and dietary information. Therefore, we should consider usingrapid screening instruments to assess nutritional status, such as the prognosticnutritional index (PNI) and Nutrition Risk Screening 2002 (NRS2002). The European Society for Clinical Nutritionand Metabolism (ESPEN) recommends Nutrition Risk Screening 2002 (NRS2002) as anutritional screening tool for general inpatients [13]. For hospitalized COVID-19 patients, the literature has validated the feasibility of NRS2002 fornutritional risk screening [14,15].

Our previous study found that in COVID-19patients, nutritional risk and a high NRS 2002 score are not only closelyrelated to disease progression but also poor prognosis. Earlymalnutrition intervention is needed to delay disease progression for patientswith an NRS2002 score > 0.5, and continuous nutritional support therapy isneeded to reduce mortality and improve prognosis for patients with an NRS2002score > 5.5[16]. PNI is calculated by peripheral blood lymphocyte count andserum albumin (Alb) concentration, which can reflect the immune nutritionalstatus of patients and was originally used for nutritional assessment of non emergencygeneral surgery patients [17]. There is growing evidence that PNI can predictclinical outcomes in patients with certain types of cancer, including lung, gastrointestinal,breast, and gynecological tumors [18-19]. However, the current literature on therole of PNI in assessing and predicting the clinical outcomes of COVID-19 isstill limited. For hospitalized patients, some previous studies have verifiedthat PNI has a good predictive value for both severity and prognosis andanalyzed the optimal cutoff values for severity, death, and ICU admission [20-24],but the results of these articles are slightly different, and the sample sizeis not large. The distribution characteristics and differences in PNI amonglarge samples of COVID-19 patients with different sexes, ages, clinical types,infection sources, infection histories and vaccination histories, disease severitiesand prognoses are still unclear. It is unclear whether the optimal cutoff pointof PNI for predicting disease severity and death in a large COVID-19 populationis consistent with those reported in the literature. Therefore, this studyaimed to assess the association of immunonutritional status and PNI scores withdisease progression and prognosis in patients with COVID-19. [16]

4. Methods

4.1. Subjects

Across-sectional and short-term follow-up cohort study was conducted, retrospectively recruiting all 1228 patients with COVID-19 who presented to the Public Health Clinical Centre of Chengdu and were hospitalized in the isolationward between January 16, 2020, and January 30, 2022. The study receivedapproval from the Ethics Committee of the Public and Health Clinical Centre ofChengdu (ethics approval number: PJ-K 2020-26-01). Written informed consent waswaived by the Ethics Commission of the designated hospital because this studyconcerns emerging infectious diseases.

4.2. Inclusionand exclusion criteria

The study's inclusion criteria comprised the following: no sex limit; age ≥18 years; COVID-19; and inpatient isolation and treatment time >1 day.Theexclusion criteria consisted of the following:age<18years,inpatientisolation and treatment time <1 day.

4.3 Disease diagnosis, clinical typingand cure criteria [16,25]

Thedisease diagnosis, clinical typing, and cure criteria for COVID-19 patientswere established according to the seventh Trial Version of the Novel coronavirus pneumonia diagnosis and treatment guidance [25]. The diagnostic criteria specified that cases must meet at least one of thefollowing etiological markers: detection of positive nucleic acid of the novelcoronavirus by real-time fluorescence RT–PCR or sequencing of viral genes [16,25]. Clinical type sincluded asymptomatic infection, light, common, severe and critical illness. The criteria for classification were as follows: (1) Asymptomatic infectioncriteria can be met when there are no clinical symptoms and no pneumoniamanifestations visible on imaging; (2) The light type criteria indicate mildclinical symptoms and no pneumonia manifestations on imaging; (3) The commontype criteria include clinical symptoms such as fever and respiratory tractproblems, and pneumonia is visible on imaging; (4) The criteria for the severetype were met by one of the following: Respiratory distress, RR≥30 times/min; In theresting state, the oxygen saturation ≤93%; Arterial bloodoxygen partial pressure (PaO2) /oxygen concentration (FiO2) ≤300 mmHg (1 mmHg =0.133 kPa), In areas with high altitude (over 1000 meters above sea level), PaO2/FiO2 should be corrected according to the following formula:PaO2/FiO2* [atmospheric pressure (mmHg) /760]; Pulmonary imaging showed that lesions progressing over 50% in 24-48 hours were classified as severe; (5) The critically illness type criteria included one of the following conditions: respiratoryfailure requiring mechanical ventilation, shock, or multiple organ failure warranting ICU monitoring [16,25]. The criteria for discharge upon recovery were met when the patient's body temperature had returned to normal for a minimum duration of three days. The rewas significant improvement in respiratory symptoms and lung imaging reflecting reduced exudative lesions. Additionally, the presence of negative nucleic acidresults for two consecutive sputum samples, nasopharyngeal swabs or other respiratory specimens was ensured. These samples were taken at least 24 hours apart from each other. [16,25].

4.4. Grouping standards

Among the 1228 COVID-19 cases, 304, 306, 310, and 308 were classified into four groups based on PNI quartile values at admission. These groups were PNI <50.65 (PNI 1), 50.65~53.75 (PNI 2), 53.76~57.20 (PNI 3), and >57.20(PNI 4). PNI was calculated as 10× serum albumin (g/dl) +0.005× total lymphocyte count (per mm3). [26]. Amongthe 1228 COVID-19 cases, 1184 noncritical patients (patients with asymptomatic in fection, with light and with common clinical type) were divided into the non critical group, and 44 critical patients (patients with severe and with critically illness clinical type) were divided into the critical group.Among the 1228 COVID-19 cases, 1223 surviving patients were assigned to the cured group, and 5 dead patients were divided into the death group.

4.5. Definition of the nutritional risk, viral negative conversion time, disease severity and prognosis [16, 25]

Nutritional risk was evaluated using the NRS 2002 within 48 hours of admission. The assessment comprised three categories: evaluation of nutrition al status (based on weight loss, BMI, and food intake), measurement of disease severity (induced stress metabolism due to the extent of the disease), and age (whether or not it was 70 years or older). Abbreviations will be explicitly explained at first use. Scores ranged from 0 to 7. Patients with a score of 3 or more were classified as “at nutritional risk”, whereas a scorebelow 3 indicated “not at nutritional risk”. The disease severity including critical illness (COVID-19 patients with severe or criticallyill clinical type) and noncritical illness (COVID-19 patients with asymptomatic infection, light or common clinical type).Prognosisin cluded death and survival within 4 weeks of admission. The coronavirus-negative conversion time was defined as the time from disease onset to the time when thefirst negative nucleic acid test met the discharge criteria.

4.6. Data collection

Allclinical, laboratory, and demographic data, as well as the NRS2002 score and PNI, of 1228 cases were gathered to construct a database. The accuracy, completeness and authenticity of all data were meticulously monitored by the researchers.

4.7. Statistical analyses

Statistical analyses were conducted using SPSS 26.0(SPSS, Chicago, IL, USA) and Graph Pad Prism 8 (GraphPad, CA, USA). Normally distributed measurements are presented as the mean and standard deviation, while non normally distributed data are presented as the median and inter quartile range (IQR). Categorical data are presented as percentages orproportions. To compare data with a normal distribution and homogeneity of variance between multiple groups, we used one-way or two-way ANOVA.Sub sequently, we carried out LSD t tests to compare data between groups with different PNI levels. For data with a normal distribution and homogeneity of variance between groups with different PNI levels, we used independent samplest tests. The percentages or proportions were used to express the enumerated data, while chi-square tests were employed to compare the data between two ormore groups. Spearman correlation analysis was used for two-factor correlation analysis, and binary logistic regression analysis was utilized to examine the factors that influence disease severity and prognosis. Subject operating characteristic (ROC) analysis was conducted to evaluate lymphocytes and subpopulations’ ability to distinguish between patients with non severe and severe neocoronary pneumonia and between patients who survived and those who did not. $p<0.05$ was considered statistically significant.

4.8. Patient and Public Involvement

The research questions and study design were developed with out in volvement from patients or the general public. Patients were not involved in the recruitment of subjects or the conduct of the study. In addition, in vestigatorsassessed the burden of the intervention. The eligibility of the participants was evaluated followed by data collection. General results, devoid of personally identifiable information, can be dis seminated upon request. The Ethics Committee of the Public Health Clinical Centre of Chengdu approved this study (ethics approval number: PJ-K2020-26-01). Written informed consent was waivedby the Ethics Commission of the designated hospital because this study isrelated to emerging infectious diseases.

5. Results

5.1 Characteristics of the Study Population[16]

Atotal of 1228 patients with COVID-19 were recruited for this investigation. The demographic and clinical characteristics of the participants are detailed in Table 1. The patients’ median age was 37 years, male-dominated (78.83%), and only a small number of patients were critical illness cases (3.58%) or diedcases 5 (0.41%). The median duration of hospitalization was 15.0 days, and the coronavirus negative conversion time was 11.5 days (Table 1) [16]. Inaddition, there were 342 (27.85%) cases with one comorbidity, 228 (18.56%) cases with two comorbidities, 318 (25.90%) cases with three or more comorbidities, and 340 (27.69%) cases without comorbidities. (Table 1) [16]. Mostof them (87.21%) were imported cases, and only 12.79% of patients were domestically transmitted cases. Regarding infection history, 1180 (96.1) patients had primary in fections, and only 48 (3.9) patients had reinfections. According tovaccination history, only 107(8.7) patients were fully vaccinated, and 1121 (91.3)patients were not vaccinated (Table 1). Moreover, according to clinical type, 31.92% of patients had as ymptomatic in fection, 11.16% had light, 53.34% had common, 2.03% had severe, and 1.55% had critical illness. Of them, 12.79% of patients were native, and 87.21% were foreign [16]. Further more, the median TP level was 71.7 g/L, the ALB level was 43.9 g/L, the HGB level was 151.0 g/L [16], the total lymphocyte level was 1.9 ^109/L, and the PNI levelwas 53.75 g/L2 (Table 1).

Table 1: Baselinecharacteristics of COVID-19 patients.[16]

Variables	Total(n=1228)	Range
Male, n(%)	968 (78.83)	
Age(year), [M (IQR)]	37.0 (30.0–38.0)	18 ~ 87
Disease severity		

Journal of Clinical Cases

Noncriticalillness, n (%)	1,184 (96.42)	
Criticalillness, n (%)	44 (3.58)	
Number of comorbidities		
0, n (%)	340 (27.69)	
1,n (%)	342 (27.85)	
2,n (%)	228 (18.56)	
3 ormore, n (%)	318 (25.90)	
ClinicaltypeofCOVID- 19		
Asymptomatic, n (%)	392 (31.92)	
Light, n (%)	137 (11. 16)	
Common,n (%)	655 (53.34)	
Severe, n (%)	25 (2.03)	
Critical,n (%)	19 (1.55)	
Sourceofcases		
Domestically transmittedcases, n (%)	157 (12.79)	
Importedcases, n (%)	1071 (87.21)	
Prognosis		
Survive,n (%)	1223 (99.59)	
Death, n (%)	5 (0.41)	
The coronavirus negative conversion time(day), [M (IQR)]	11.5 (8.0–20.0)	2 ~ 89
Durationofhospitalization (day), [M (IQR)]	15.0 (12.0–20.0)	3 ~ 91
Body mass index (kg/m2) , [M (IQR)]	24.03+-3.59	15.21~38.26
ALBatadmission (g/L), [M (IQR)]	43.9 (41.5 –46.0)	27.3 ~ 55.3
TPatadmission (g/L), [M (IQR)]	71.7 (67.9 –75.6)	38.2 ~ 92.2
HGBatadmission (g/L), [M (IQR)]	151.0 (138. 0–159.0)	54 ~ 191
TLC atadmission (g/L), [M (IQR)]	1.9(1.45-2.46)	0.26-5.63
PNI atadmission (g/L), [M (IQR)]	53.75(50.65-57.2)	32-72

prognostic nutrition index (PNI) segments		
PNI 1 ,n%	304(24.8)	32.00-50.65
PNI 2	306(24.9)	50.65-53.75
PNI 3	310(25.2)	53.75-57.20
PNI 4	308(25.1)	57.20-72.00
Infectionhistory		
reinfection	48(3.9)	
Primary infection	1180(96.1)	
Vaccination history		
fully vaccinated	107(8.7)	
not vaccinated	1121(91.3	

Abbreviations: PNI, prognostic nutritionindex; ALB, albumin; TP, total protein; HGB, hemoglobin; TLC, total lymphocytes.

5.2. Comparisons among four different PNI level groups

Compared with those in the upper quartile PNI group and the other two PNI groups, al though the positivity rates of SARS-CoV-2 nucleic acid, infection history and vaccination history among the four groups were similar, in the lower quartile PNI group, the proportion of patients with three or more comorbidities and the proportion of domestically transmitted cases were larger, the criticalillness rate was higher, patients with severe and critical illness clinicaltypes were higher, and all patients who died were in this group; significant differences were all found (all P<0.05) (Table 2). Inthe lower quartile PNI group, patient age was oldest (Figure 1A), the coronavirus negative conversion time and the duration of hospitalization were longest (Figure 1B, 1C), and the HGB level, ALB level, TP level and total lymphocyte level were the lowest (Figure 2A, 2B, 2C, 2D). From the lower quartile PNI group to the upper quartile PNI group, with the decrease in PNI level, HGB level, ALB level, TP level and total lymphocyte level gradually decreased, patient agegradually increased, and the coronavirus negative conversion time and the duration of hospitalization gradually increased (Figure 2A, 2B, 2C, 2D, 1A, 1B, 1C).

Variables	**PNI group (n=1,228)**	**X2**	**P value**			
	<50.65(n=304)	50.65~53.75 (n=306)	53.76~57.20 (n=310)	>57.20 (n=308)		
Male, n(%)	199 (65.5))	235(76.8)	264(85.2)	270(87.7)	55.16	<0.001
Number of comorbidities					36.65	<0.001
0, n (%)	65 (21.4)	91(29.7)	99(31.9)	85 (27.6)		
1,n (%)	64 (21.1)	96(31.4)	96(31.0)	86 (27.9)		
2,n (%)	63 (20.7)	54(17.6)	48(15.5)	63 (20.5)		
3 ormore, n (%)	112 (36.8)	65(21.2)	67(21.6)	74 (24.0)		
Prognosis					15.25	0.002
Survive,n (%)	299 (98.4)	306(100.0)	310(100.0)	308 (100.0)		
Death, n (%)	5(1.6)	0(0.0)	0(0.0)	0 (0.0)		
Disease severity					86.70	<0.001
Criticalillness, n (%)	37 (12.2)	4(1.3)	2(0.6)	1(0.3)		
Noncriticalillness, n (%)	267(87.8)	302(98.7)	308(99.4)	307(99.7)		

Journal of Clinical Cases

Sourceofcases					108.74	<0.001
Domestically transmitted-cases, n (%)	90 (29.6)	34(11.1)	18(5.8)	15(4.9)		
Importedcases, n (%)	214(70.4)	272(88.9)	292(94.2)	293 (95.1)		
ClinicaltypeofCOVID- 19					153.7	<0.001
Asymptomatic, n (%)	55(18.1)	87(28.4)	123(39.7)	127(41.2)		
Light, n (%)	18(5.9)	32(10.5)	50(16.1)	37(12.0)		
Common,n (%)	194 (63.8)	183(59.8)	135(43.5)	143(46.4)		
Severe, n (%)	18 (5.9)	4(1.3)	2(0.6)	1(0.3)		
Critical,n (%)	19 (6.3)	0(0.0)	0(0.0)	0 (0.0)		
Infectionhistory					6.52	0.89
reinfection	5(1.6)	12(3.9)	17(5.5)	14(4.5)		
Firstinfection	299(98.4)	294(96.1)	293(94.5)	293(95.5)		
Repositivity of SARS-CoV-2 nucleic acid					3.36	0.339
with	59(19.4)	49(16.0)	51(16.5)	43(14.0)		
without	245(80.6)	257(84.0)	259(83.5)	265(86.0)		
Vaccination history					6.05	0.109
fully vaccinated	24(7.9)	25(8.2)	21(6.8)	37(12.0)		
not vaccinated	280(92.1)	281(91.8)	289(93.2)	271(88.0)		

Table 2: Comparison of baseline conditions between the four groups(n=1228)

Abbreviations: NRS2002, Nutritional Risk Screening 2002.

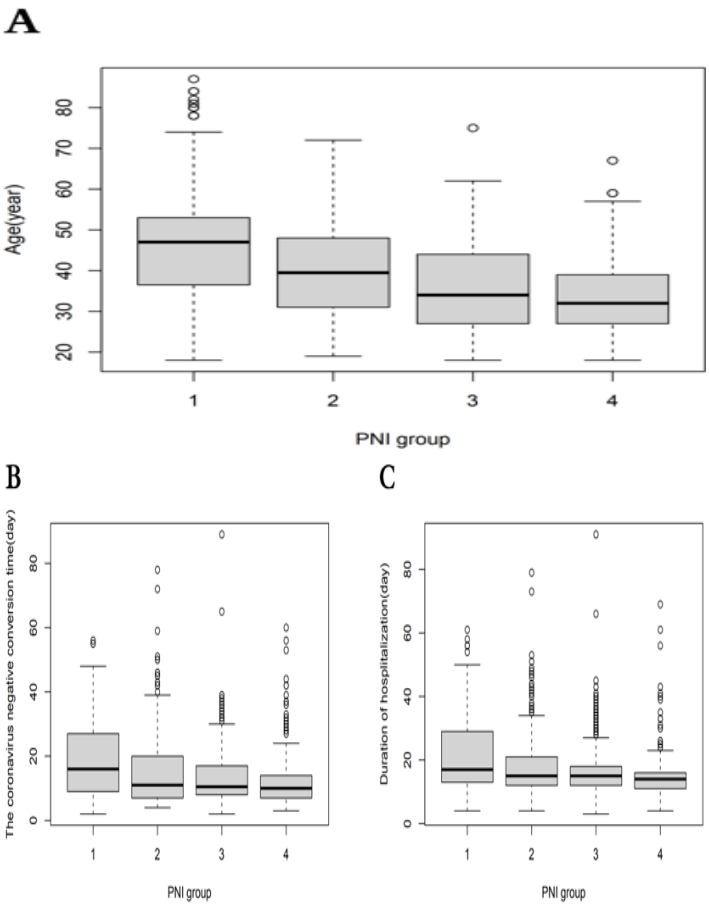

Figure 1: Comparison of age, the coronavirus negative conversion time and duration of hospitalization between four different PNI level groups. (n=1228; PNI<50.65, 50.65~53.75, 53.76~57.20 and >57.20 groups, n=304, 306, 310 and 308, respectively). (A)age. (B).the coronavirus negative conversion time. (C). duration of hospitalization. Wilcoxon rank-sumtests were used for inter group comparison.

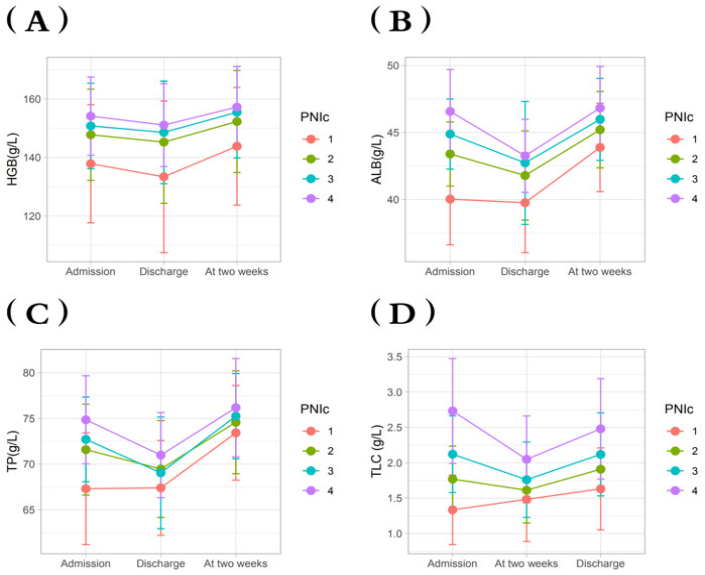

Figure 2: Comparison of HGB,ALB, TP and TLC between four different PNI level groups. (n=1228; PNI<50.65,50.65~53.75, 53.76~57.20and >57.20 groups, n=304, 306, 310 and 308, respectively). Abbreviations: HGB, hemoglobin; ALB, albumin; TP, total protein;TLC,total lymphocyte.

(A)HGB. (B)ALB. (C)TP .(D)TLC. All variables were presented as mean. Unpaired one-way ANOVA was used for intergroup comparisons. Unpaired t-tests were used for comparisons with the PNI >57.20group.

5.3. The relation ship of nutritional risk, NRS 2002 score, PNI, disease severity andprognosis in patients with COVID-19

Spearman correlation analysis showed that age, sex, clinical typeof COVID-19, number of comorbidities, time to negative coronary virus conversion,length of hospitalization, risk of malnutrition and NRS2002scorewere positivelyrelated to disease severity[16],whereas source,ALB level, TP level,HGB level,total lymphocyte level and PNI level were negatively associated with diseaseseverity (Table 3)[16].

Table 3: Spearman correlation analysis between nutritional parameters, NRS 2002, PNI and disease severity and prognosis (n=1228). [16]

Variables	Diseaseseverity		Prognosis	
	(1=critical,0=noncritical)		(1=cured,2=death)	
	r	P	r	P
Age (year)	0.207	<0.001	0.108	<0.001
Sex	0.061	0.033	0.061	0.033
Clinical type of COVID-19	0.357	<0.001	0.121	<0.001
Number of comorbidities	0.209	<0.001	0.085	0.003
Source	-0.399	<0.001	-0.167	<0.001
The coronavirus negative conversion time(day)	0.163	<0.001	-	-
Duration of hospitalization (day)	0.068	0.017	-	-
Nutritional risk	0.496	<0.001	0.218	<0.001
NRS2002score	0.513	<0.001	0.183	<0.001
ALB(g/L)	-0.199	<0.001	-0.107	<0.001
TP(g/L)	-0.181	<0.001	-0.101	<0.001
HGB(g/L)	-0.157	<0.001	-0.1	<0.001
TLC	-0.195	0	-0.091	0.001
PNI	-0.271	0	-0.141	<0.001

Abbreviations: NRS2002, nutritional risk screening 2002; ALB, albumin; TP, total protein; HGB, hemoglobin; PNI, prognostic nutritionindex;TLC, total lymphocyte count.

When controlling for age and number of comorbidities,partial correlation analysis showed that sex, clinical type of COVID-19, coronavirusnegative conversion time, duration of hospitalization, with-nutritional risk andNRS2002scorewere still positively related to disease severity, whilesource, ALB level, TP level,HGBlevel, total lymphocyte level and PNI level were still negatively related to diseaseseverity (Table 4).

Table 4: Partial correlation analysis between nutritional parameters, NRS 2002, PNI and disease severity and prognosis after controlling for age and number of comorbidities (n=1228)

Control variables	Variables	Diseaseseverity		Prognosis	
		(1=critical, 0=noncritical)		(1=cured, 2=death)	
		r	P	r	P
Age (year)	Sex	0.07	0.014	0.058	0.044
Number of comor bidities	Clinical type of	0.331	<0.001	0.112	<0.001
	COVID- 19				
	Sour ceofcases	−0.327	<0.001	−0.112	<0.001
	The coronavirus negative conversion time (day)	0.135	<0.001	–	–
	Durationof hospitalization (day)	0.089	0.002	–	–
	Nutritionalrisk	0.493	<0.001	0.204	<0.001
	NRS2002 score	0.635	<0.001	0.349	<0.001
	ALBatadmission (g/L)	−0.187	<0.001	−0.109	<0.001
	TPatadmission (g/L)	−0.181	<0.001	−0.110	<0.001
	HGBatadmission (g/L)	−0.196	<0.001	−0.171	<0.001
	TLC atadmission (g/L)	-0.161	0	-0.066	0.021
	PNI atadmission(g/L)	-0.208	0	-0.095	0.142

Abbreviations: NRS2002, nutritional risk screening 2002; ALB, albumin; TP, total protein; HGB, hemoglobin; PNI, prognostic nutritionindex;TLC, total lymphocytes.

The risk factorsfor disease severity by multiple linear regression analysis were PNIlevel, body mass index (BMI) level, with-nutritional risk, NRS 2002 score, source, clinical type of COVID-19 and sex (Table 5). Moreover, Spearman correlation analysis showed that factors positively related to prognosis were age, sex, clinical type of COVID-19, number of comorbidities, with-nutritional risk and NRS 2002 score, while source, ALB level, TP level, HGB level, total lymphocyte level and PNI level were negatively related to prognosis (Table 3). When controllingfor age and number of comorbidities, partial correlation analysis showed that sex, clinical type of COVID-19, with-nutritional risk and NRS 2002 score were still positively related to prognosis, while source, ALB level, TP

level, HGB level and total lymphocyte level were still negatively related to prognosis (Table 4). The risk factors for prognosis by multiple linear regression analysis wereHGB level, nutritionalrisk, NRS2002score, sex, coronavirus negative conversion time and PNI level (Table 5).

Table 5: Multiple stepwise regression analysis of influencing factors of disease severity and prognosis (n=1228)

Independent variables	B		Std. Error	Beta t	P
Disease severity	PNIatadmission (g/L)	-0.006	0.002	-3.834	<0.001
	BMI	0.005	0.001	4.36	<0.001
	Nutritionalrisk	−0.267	0.038	−7.027	<0.001
	NRS2002 score	0.151	0.011	13.768	<0.001
	Sourceofcases	−0.047	0.012	−3.907	<0.001
	Clinical type of COVID- 19	0.024	0.004	6.066	<0.001
	sex	−0.024	0.009	−2.651	0.008
Prognosis	HGB	-0.0004	0.0001	-4.339	<0.001
	Nutritionalrisk	−0.102	0.012	−8.808	<0.001
	NRS 2002 score	0.035	0.004	10.105	<0.001
	sex	−0.009	0.004	−2.157	0.012
	The coronavirus negative conversion time (day)	-0.0003	0.0001	-2.466	0.014
	PNI atadmission (g/L)	0.006	0.002	2.432	0.015

Abbreviations: NRS 2002, Nutritional Risk Screening 2002; PNI, prognostic nutrition index; BMI, body mass index, ALB, albumin; TP, total protein.

5.4. Prediction of the PNI level at admission on disease severity and prognosis inpatients with COVID-19

According to the ROC analysis, the PNI level at admission showed good utility for predicting critical COVID-19 patients (Table 6) and dead COVID-19 patients (Table 7). The areas under the curve were 0.8684 (Table 6, Figure 3) and 0.9923 (Table 7, Figure 4). The thres holds were 49.125 and 40.45, respectively (Tables 6 and 7). The sensitivities were 79.31% and 100.00%, respectively (Tables 6 and 7). The specificities were 85.15% and 99.86%, respectively (Table 6,7).

Table6: The performance of various methods for distinguishing between severe cases and nonsevere cases (n=1228)

Variable	Cutoff point	AUC (95% CI)	Sensit-ivity	Specif-icity	False positive	False negative
PNI	49.125	0.8684	79.31%	85.15%	20.69%	14.85%

Abbreviations: PNI, prognostic nutrition index; AUC, area under the curve; CI, confidence interval

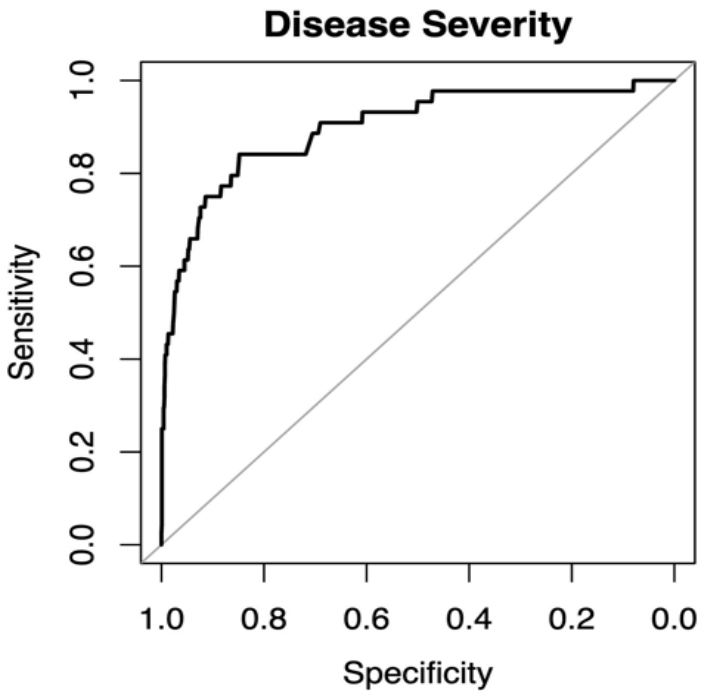

Figure 3: Using characteristics of PNI for discriminating the critical cases from the non-critical patients(n=1228; critical and non- critical groups, n=44 and 1184, respectively). ROC analysis showing the performance of PNI in distinguishing critical cases from non-critical patients. Abbreviations: ROC, receiver operating characteristic curve; AUC, area under the curve.

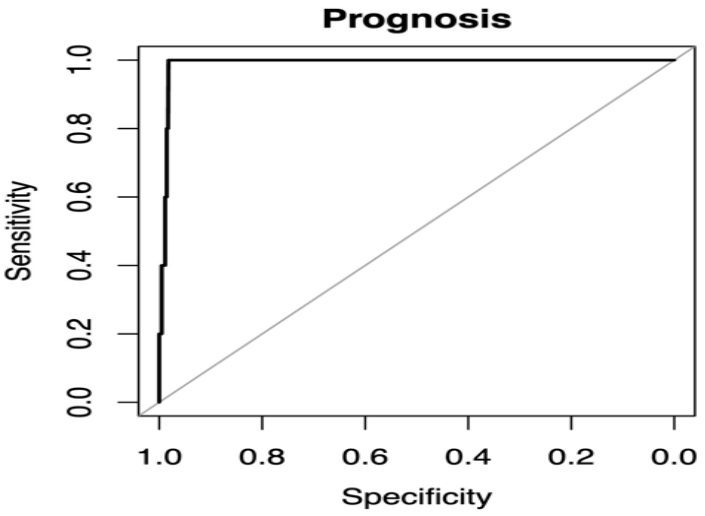

Figure 4: Using characteristics of PNI on admission for discriminating the surviving cases from the dead patients (n=1228; surviving and dead groups, n=1223 and 5, respectively). ROC analysis showing the performance of PNI in distinguishing the dead cases from the surviving

patients. Abbreviations: ROC, receiver operating characteristic curve; AUC, area under the curve.

Table 7: The performance of various methods for distinguishing between cured and dead patients (n=1228)

Variable	Cutoff point	AUC(95% CI)	Sensitivity	Specificity	False positive	False negative
PNI	40.45	0.9923	100.00%	99.86%	0.00%	0.14%

Abbreviations: PNI, prognostic nutrition index; AUC, area under the curve; CI, confidence interval.

6. Discussion

The prognostic nutritional index (PNI), calculated using peripheral blood lymphocyte counts and serum albumin (Alb) concentrations, was initially used in the nutritional assessment of nonemergency general surgical patients and is able to reflect the immunonutritional status of patients[26]. Recently, there has been growing evidence that PNI can be a useful prognostic indicator for predicting the prognosis of patients with certain types of cancer, including lung, gastrointestinal, breast, and gynecological tumors [18,19] and diseases other than cancer, such as acute heart failure, autoimmune disorders, hematologic malignancies, and chronic kidney disease in children [27-31]. In this study, PNI was applied for the first time in a large sample of COVID-19 patients in China to investigate its predictive value for disease progression and prognosis in COVID-19 patients. In this study, we found that patients in the lower PNI group were older and had longer hospitalization times and coronavirus negative conversion times, which may be related to low immunity and reduced nutritional intake and absorption in elderly individuals. This is consistent with previous studies. Nutrition plays a key role in improving immunity. In the case of viral infectious diseases, nutritional status affects the mutation of the viral genome from benign or low pathogenicity viruses to highly pathogenic viruses and their transmission within the host [32]. If nutritional risk is present, it directly affects immune defense. In addition, this study found that ALB levels, HGB levels, TP levels, and TLC levels increased with increasing PNI quartiles, whether at admission, discharge, or two weeks. ALB level, TP level, and HGB level are commonly used as indicators of malnutrition in clinical practice, with ALB levels being a significant factor in disease severity at admission, a reliable indicator of nutritional status, and a COVID-19 severity of prognosis. Therefore, we hypothesized that PNI could be used as a marker of disease progression and prognosis in COVID-19 patients.

A previous study of 140 COVID-19 patients (70 each of mild and severe cases) found that PNI was significantly lower in the severe group than in the mild group, that PNI was significantly lower in the severe death group than in the severe survival group, that PNI had a better predictive value for both the criticization and the prognosis, that those with a PNI lower than 39.08 were prone to develop a severe disease, and that those with a PNI lower than 33.05 [20] and 33.405 [21] had a higher risk of death. Overseas studies have found that the PNI of COVID-19 patients admitted to the ICU is lower than that of non-ICU patients [22,23], and those with PNI lower than 36.7[22] and 39.95[23]are prone to develop severe disease, and those admitted to the ICU have a 4.4-fold higher probability of death[22]. The PNI of patients who died in the ICU was significantly lower than that of patients who survived in the ICU[20,23], and the PNI predicted that the optimal cutoff points for ICU patient death were ≤38.75 [11] [38]and ≤42 [23]. However, these studies are only small-sample studies and are not generalizable. In this study, we took a large sample of COVID-19 patients in China and found that patients with a PNI lower than 49.12 were prone to develop serious illness, and those with a PNI lower than 40.45 had a high risk of death. After ROC analysis, the PNI score showed good utility in predicting critically ill COVID-19 patients and dead COVID-19 patients. However, this study still has some limitations. It was a single-center retrospective study, and limitations inherent to retrospective studies are unavoidable and do not allow for causal inferences. In addition, we did not consider the relationship between dietary habits, psychiatric conditions, and social support and the nutritional status of patients, and we did not systematically collect data on patient-specific dietary intake, diagnosis of malnutrition, and nutritional support, information that might be useful in the management of patients with COVID-19 from a clinical point of view. Finally, the small number of severe cases, especially deaths, combined with the large number of missing data collection processes, has resulted in unclear relationships between PNI and indicators such as history of infection, vaccination history, and source of infection. As the number of prepositive positives increases, further validation of the predictive value of PNI in predicting disease progression and prognosis in patients with COVID-19 is needed.

7. Conclusions

The results of the present study indicated that not only the with-nutritional risk and NRS2002 score [16] but also the PNI level at admission are important influencing factors of COVID-19 disease severity and prognosis.COVID-19 disease severity and prognosis were positively correlated with nutritional risk and NRS2002 score[16] but negatively correlated with ALB level, TP level, HGB level[16], total lymphocyte level and PNI level. In addition, the PNI level at admission has good predictive value for disease progression and poor prognosis. For patients with PNI levels>49.125, early intervention should be given to malnutrition to reduce the occurrence of critical diseases. For patients with PNI levels >40.45, nutritional support treatment should be actively given to reduce mortality and improve prognosis.

8. Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Public and Health Clinic Centre of Chengdu (ethics approval number:PJ-K2020-26-01), and the Ethics Committee waived written informed consent because of emerging infectious diseases.

9. Consent for publication

All of the participants understand that the information will be published without their child or ward's/their relative's (circle as appropriate) name attached but that full anonymity cannot be guaranteed. All of the participants understand that the text and any pictures or videos published in the article will be freely available on the internet and may be seen by the general public. The pictures, videos and text may also appear on other websites or in print and may be translated into other languages or used for commercial purposes. All of the participants were offered the opportunity to read the manuscript.

10. Funding

This research was supported by the Chinese Nutrition Society nutritionist empowerment project (CNS-DNEP2022-34), the Chengdu Municipal Health Commission (2019079; 2022276) and the Chengdu Science and Technology Bureau (2021-YF05-00536-SN).

11. Acknowledgments

We sincerely acknowledge all participants who participated in this study for their cooperation. Thanks to all members of this study group for their valuable contributions.

Authors' contributions

Concept and design: Qiqing Cui, Dafeng Liu; Data acquisition: Qiqing Cui, Fengjiao Gao, Xiaoyan Yuan, Rui Li, Yong Wang, Yanfeng Zhu, Dafeng Liu; data analysis and interpretation: Qiqing Cui, Fengjiao Gao, Xiaoyan Yuan, Rui Li, Yong Wang, Yanfeng Zhu, Dafeng Liu; Drafting the manuscript: Qiqing Cui, Fengjiao Gao, Xiaoyan Yuan, Rui Li, Yong Wang, Yanfeng Zhu, Dafeng Liu; administrative, technical, or material support: Qiqing Cui, Fengjiao Gao, Xiaoyan Yuan, Rui Li, Yong Wang, Yanfeng Zhu, Dafeng Liu; study supervision: Dafeng Liu, Yanfeng Zhu.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382 (8): 727–733.
2. World Health O: COVID-19 weekly epidemiological update, edition 138, 13 April 2023. In. Geneva: World Health Organization; 2023.
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720.
4. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395 (10223): 497-506.
5. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395 (10229):1054-1062.
6. Agarwal E, Miller M, Yaxley A, Isenring E. Malnutrition in elderly individuals: a narrative review. Maturitas. 2013; 76 (4): 296-302.
7. Reyes L, Arvelo W, Estevez A, Gray J, Moir JC, Gordillo B, et al. Population-based surveillance for 2009 pandemic influenza A (H1N1) virus in Guatemala, 2009. Influenza Other Respir Viruses. 2010;4(3):129-40.
8. Zhou Z, Zhao N, Shu Y, Han S, Chen B, Shu X. Effect of Gastrointestinal Symptoms in Patients With COVID-19. Gastroenterology. 2020; 158(8): 2294-2297.
9. Nguyen HC, Nguyen MH, Do BN, Tran CQ, Nguyen TTP, Pham KM,et al. People with Suspected COVID-19 Symptoms Were More Likely Depressed and Had Lower Health-Related Quality of Life: The Potential Benefit of Health Literacy. J Clin Med. 2020; 9(4): 965.
10. Caccialanza R, Laviano A, Lobascio F, Montagna E, Bruno R, Ludovisi S, et al. Early nutritional supplementation in noncritically ill patients hospitalized for the 2019 novel coronavirus disease (COVID-19): Rationale and feasibility of a shared pragmatic protocol. Nutrition. 2020; 74:110835.
11. Azzolino D, Saporiti E, Proietti M, Cesari M. Nutritional Considerations in Frail Older Patients with COVID-19. J Nutr Health Aging. 2020; 24(7):696-698.
12. Barazzoni R, Bischoff SC, Breda J, Wickramasinghe K, Krznaric Z, Nitzan D, et al; endorsed by the ESPEN Council. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. Clin Nutr. 2020; 39(6):1631-1638.
13. Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr. 2003; 22(4):415-21.
14. Silva DFO, Lima SCVC, Sena-Evangelista KCM, Marchioni DM, Cobucci RN, Andrade FB. Nutritional Risk Screening Tools for Older Adults with COVID-19: A Systematic Review. Nutrients. 2020;12(10):2956.
15. Sun Y, He J, Li W, Li S, Lin Y, Cen Y, et al. Preliminary Exploration of Setting the Disease Severity Score in the Nutritional Risk Screening of Patients with Severe Novel Coronavirus Pneumonia by Applying NRS2002. Int J Gen Med. 2021;14:1167-1172.
16. Zhou Y, Chen Y, Zhang X, Zhao B, Gao F, Yuan X, et al. Nutritional risk and a high NRS2002 score are closely related to disease progression and poor prognosis in patients with COVID-19. Front Nutr. 2023;10:1089972.
17. Alqahtani AM, AlMalki ZS, Alalweet RM, Al Mazrou SH, Alanazi AS, Alanazi MA, et al. Assessing the Severity of Illness in Patients With Coronavirus Disease in Saudi Arabia: A Retrospective Descriptive Cross-Sectional Study. Front Public Health. 2020;8:593256.
18. Wang Z, Wang Y, Zhang X, Zhang T. Pretreatment prognostic nutritional index as a prognostic factor in lung cancer: Review and meta-analysis. Clin Chim Acta. 2018;486:303-310.
19. Wang X, Wang Y. The prognostic nutritional index is the prognostic factor of gynecological cancer: A systematic review and meta-analysis. Int J Surg. 2019 Jul;67:79-86.

Journal of Clinical Cases

20. Wei W, Wu X, Jin C, Mu T, Gu G, Min M, et al. Predictive Significance of the Prognostic Nutritional Index (PNI) in Patients with Severe COVID-19. J Immunol Res. 2021;2021:9917302.
21. Nalbant A, Demirci T, Kaya T, Aydın A, Altındiş M, Güçlü E. Can prognostic nutritional index and systemic immune-inflammatory index predict disease severity in COVID-19? Int J Clin Pract. 2021;75(10):e14544.
22. Bayram M, Yildirim O, S Ozmen R, Soylu B, Dundar AS, Koksal AR, Ekinci I, Akarsu M, Tabak O. Prognostic Nutritional Index and CRP, age, platelet count, albumin level score in predicting mortality and intensive care unit admission for COVID-19. Biomark Med. 2021 Dec;15(18):1733-1740.
23. Kosovali BD, Kucuk B, Balkiz Soyal O, Mehmet Mutlu N. Can a prognostic nutritional index predict mortality in intensive care patients with COVID-19? Int J Clin Pract. 2021 Nov;75(11):e14800.
24. Hu X, Deng H, Wang Y, Chen L, Gu X, Wang X. Predictive value of the prognostic nutritional index for the severity of coronavirus disease 2019. Nutrition. 2021 Apr;84:111123.
25. National Health Commission of the People's Republic of China. The Seventh Trial Version of the Novel Coronavirus Pneumonia Diagnosis and Treatment Guidance. Available at: http://www.nhc.gov.cn /xcs/ zhengcwj /202003/ 46c9294a7 dfe4cef80dc7f5912eb1989. shtml [External Link]
26. Liao G, Zhao Z, Yang H, Chen M, Li X. Can Prognostic Nutritional Index be a Prediction Factor in Esophageal Cancer?: A Meta-Analysis. Nutr Cancer. 2020; 72(2):187-193.
27. Cheng YL, Sung SH, Cheng HM, Hsu PF, Guo CY, Yu WC, et al. Prognostic Nutritional Index and the Risk of Mortality in Patients With Acute Heart Failure. J Am Heart Assoc. 2017; 6(6):e004876.
28. Correa-Rodríguez M, Pocovi-Gerardino G, Callejas-Rubio JL, Fernández RR, Martín-Amada M, Cruz-Caparros MG, et al. The Prognostic Nutritional Index and Nutritional Risk Index Are Associated with Disease Activity in Patients with Systemic Lupus Erythematosus. Nutrients. 2019; 11(3):638.
29. Ahn SS, Jung SM, Song JJ, Park YB, Lee SW. Prognostic nutritional index is associated with disease severity and relapse in ANCA-associated vasculitis. Int J Rheum Dis. 2019 May; 22(5):797-804.
30. Lee SF, Ng TY, Wong FCS. The Value of Prognostic Nutritional Index in Follicular Lymphoma. Am J Clin Oncol. 2019; 42(2):202-207.
31. Zhang H, Tao Y, Wang Z, Lu J. Evaluation of nutritional status and prognostic impact assessed by the prognostic nutritional index in children with chronic kidney disease. Medicine (Baltimore). 2019; 98(34):e16713.
32. Guillin OM, Vindry C, Ohlmann T, Chavatte L. Selenium, Selenoproteins and Viral Infection. Nutrients. 2019 Sep 4; 11(9):2101.