Original Article

The Prognostic Value of the Preoperative Geriatric Nutritional Risk Index in Elderly Colon Cancer Patients Underwent Curative Resection

Küratif Rezeksiyon Yapılan Yaşlı Kolon Kanseri Hastalarında Preoperatif Geriatrik Beslenme Risk Indeksinin Prognostik Değeri

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ABSTRACT

Introduction: The aim of this retrospective study was to assess the prognostic significance of the geriatric nutritional risk index (GNRI) for elderly patients diagnosed with early-stage colon cancer.

Materials and Methods: Medical records of 114 elderly patients diagnosed with colon cancer who underwent curative surgery and received chemotherapy were analyzed. The calculation of the GNRI was derived from the measurement of serum albumin levels and the assessment of body weight. Patients were divided into two nutritional risk categories: low-GNRI (GNRI: <98), and high-GNRI (GNRI: ≥98) and compared.

Results: The 5-year overall survival (OS) rate of the low-GNRI group was significantly lower than that of the high-GNRI group (65.7% vs. 91.1%, p= 0.002). There was also a statistically significant difference in the 5-year recurrence-free survival (RFS) rate of the two groups (66.7% vs. 90.8%, p <0.001). The multivariate Cox regression analysis identified tumor sidedness (p= 0.038) and GNRI (p = 0.042) as independent prognostic factors for only OS.

Conclusion: The GNRI is an easily applicable and valuable prognostic factor for OS in elderly patients diagnosed with early-stage colon cancer. The current investigation indicates that a low-GNRI was correlated with poor OS.

Key words: Colon cancer, elderly, nutrition, prognosis

ÖZET

Giriş: Bu çalışmanın amacı, erken evre kolon kanseri tanısı almış yaşlı hastalarda geriatrik beslenme risk indeksinin (GNRI) prognostik önemini retrospektif olarak değerlendirmektir.

Gereç ve Yöntem: Küratif cerrahi uygulanan ve kemoterapi alan kolon kanseri tanılı 114 yaşlı hastanın tıbbi kayıtları incelendi. GNRI, serum albümin düzeyi ve vücut ağırlığı kullanılarak hesaplandı. Hastalar düşük GNRI (GNRI: <98) ve yüksek GNRI (GNRI: ≥98) kategorilerine ayrılarak kıyaslandı.

Bulgular: Düşük GNRI grubunun 5 yıllık genel sağkalım oranı, yüksek GNRI grubundan anlamlı derecede düşüktü (%65.7'ye karşılık %91.1, p= 0.002). İki grubun 5 yıllık nükssüz sağkalım oranlarında da istatistiksel olarak anlamlı bir fark vardı (%66,7'ye karşı %90,8, p <0,001). Yapılan çok değişkenli Cox regresyon analizi, yalnızca tümör tarafı (p= 0.038) ve GNRI'yi (p = 0.042) genel sağ kalım için bağımsız prognostik faktörler olarak tanımladı.

Sonuç: GNRI, erken evre kolon kanseri tanısı almış yaşlı hastalarda genel sağ kalım için kolay uygulanabilir ve değerli bir prognostik faktördür. Araştırmamız, düşük bir GNRI'nin azalmış genel sağ kalım ile ilişkili olduğunu göstermektedir.

Anahtar kelimeler: Beslenme, kolon kanseri, prognoz, yaşlı

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Introduction

Malnutrition occurs frequently among cancer patients, and according to several studies, nutritional status is significantly associated with colon cancer patient survival [1-3]. There are numerous nutrition-related tools, such as body weight, prognostic nutritional index (PNI), and controlling nutritional status (CONUT) score [4-7]. The geriatric nutritional risk index (GNRI), measured by the serum albumin level and the ideal body weight, is a simple screening tool to evaluate nutritional-related risk. It was first defined by Bouillanne et al. to estimate the risk of morbidity and mortality in elderly patients [8]. It has also been reported that a lower GNRI can predict longer hospitalization and long-term mortality in elderly patients diagnosed with chronic kidney disease, congestive heart failure and sepsis [9-13]. Regarding the clinical significance of GNRI in cancer patients, there are many studies that revealed the prognostic role of GNRI in various cancers, including gastric, head and neck, pancreatic and lung cancer [14-17]. A few studies have been conducted to investigate the correlation between the GNRI and the outcomes of survival and recurrence in patients diagnosed with colon cancer.

In our study, we aimed to determine whether GNRI is an accurate prognostic factor for recurrence free survival (RFS) and overall survival (OS) in elderly patients with early-stage colon cancer patients who underwent curative resection and received chemo-therapy.

Methods

Patients and data

The data of 480 patients diagnosed and followed with colon cancer at a tertiary cancer center between 2011 and 2019 were analyzed. A total of 204 patients were excluded from the study because they were younger than 65 years of age and stage IV, while 71 patients were excluded because of not receiving chemotherapy. Ninety-one patients with Stage I were excluded because they did not attend their follow-ups regularly and therefore the dates of recurrence and death could not be reached. Finally, the data from 114 patients were analyzed. We excluded patients who died within the first month of the operation due to post-operative complications and who had co-morbidities (i.e. chronic renal failure, liver failure, nephrotic syndrome) causing hypoalbuminemia.

Medical records revealed clinical and pathological information including age, gender, time of operation, preoperative body weight, height and albumin level, tumor sidedness, tumor invasion depth, lymph node metastasis, lymphovascular invasion (LVI), perineural invasion (PNI), differentiation type, and recurrence time. The American Joint Committee on Cancer Tumor Node Metastasis (TNM) classification system was utilized for staging [18].

Preoperative weight and height data of the patients were collected, and body mass index (BMI) was calculated by dividing the weight (in kilograms) by the square of the height (in meters). GNRI was calculated as: GNRI = 1.489 x serum albumin (g/l) + 41.7 x current body weight/ideal body weight. As previous studies reported, patients were divided into two nutritional risk categories: low-GNRI (GNRI: <98), and high-GNRI (GNRI: ≥98) [19, 20]. Patients with a high-GNRI were considered high risk for malnutrition, while patients in the low-GNRI category were considered low risk.

Statistical Analyses

The continuous variables were reported as means and standard deviations (SD). Using Student's t-test, the means were compared. The chi-square test or Fisher's exact test was used to compare groups whose categorical variables were calculated as numbers and

Table 1. Clinicopathological features of the patients according to GNRI groups

Features		GNRI≥ 98 (n= 79, %)	GNRI< 98 (n= 35, %)	p-value
Age		67 (65-76)	68 (65-84)	
Gender	Male	45 (57%)	19 (54.3%)	0.474
	Female	34 (43%)	16 (45.7%)	
Diabetes mellitus	No	64 (81%)	25 (71.4%)	0.642
	Yes	15 (19%)	10 (28.6%)	
BMI	<25	10 (11.5%)	7 (25.9%)	0.068
	≥25	77 (88.5%)	20 (74.1%)	
Tumor sidedness	Right	14 (51.9%)	24 (27.6%)	0.02
	Left	13 (48.1%)	63 (72.4%)	
TNM Stage	II	43(54.4%)	16 (45.7%)	0.256
	III	36(45.6%)	19 (54.3%)	
T stage	T1/T2	5 (6.3%)	1 (2.9%)	0.400
	T3/T4	74 (93.7%)	34 (97.1%)	
LN metastases	No	43 (54.4%)	16 (45.7%)	0.256
	Yes	36 (45.6%)	19 (54.3%)	
Differentiation	Well	17 (21.5%)	5 (14.3%)	0.472
	Moderate/poor	59 (74.9%)	29 (82.9%)	
PNI	No	58 (73.4%)	23 (65.7%)	0.703
	Yes	12 (15.2%)	7 (20%)	
LVI	No	49 (62%)	18 (51.4%)	0.244
	Yes	27 (34.2%)	13 (37.1%)	
Perforation/obstruction	No	64 (81%)	30 (85.7%)	0.374
	Yes	15 (19%)	5 (14.1%)	

Abbreviations: BMI: Body mass index; GNRI: Geriatric nutritional risk index; LVI:Lymphovascular invasion; LN:Lymph node; PNI: Perineural invasion

percentages. Overall survival (OS) was defined as the interval between operation and death. The definition of recurrence-free survival (RFS) was the duration between colon cancer surgery and recurrence of the disease. Survival curves were calculated using the Kaplan-Meier method. The log-rank test was applied to determine the differences between the curves. The hazard ratios (HRs) were derived using Cox regression analyses. All variables with a p value <0.05 in the univariate analysis were included in multivariate Cox regression analysis. P value< 0.05 was regarded as statistically significant, and 95% confidence interval (CI) was determined. SPSS software (version 27.0) was utilized for all statistical analyses.

Ethics Committee Approval

This study was performed in line with the principles of the Declaration of Helsinki. The study was approved by the institutional ethics committee (date: July 11, 2023, no: 952070b3-f214-466b-bea8-c8bb6ed6700a) and conducted in accordance with the related privacy statements and applicable regulatory requirements.

Results

Basic characteristics and pathological features

The median age of the 114 patients was 67 (range 65-84) years; 64 (56.1%) patients were male. The number of patients with T1/T2 was 6 (5.3%), while 108 (94.7%) of the patients

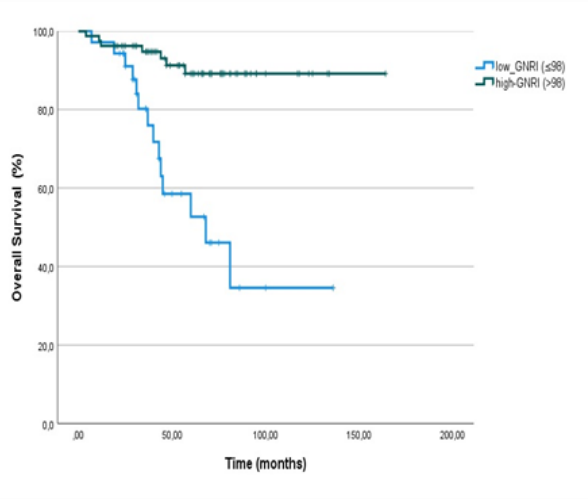

Figure 1. Kaplan Meier analyses of overall survival according to GNRI.

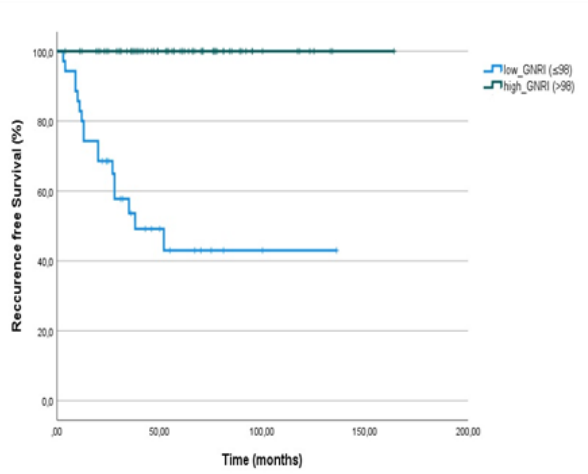

Figure 2. Kaplan Meier analyses of recurrence free survival according to GNRI.

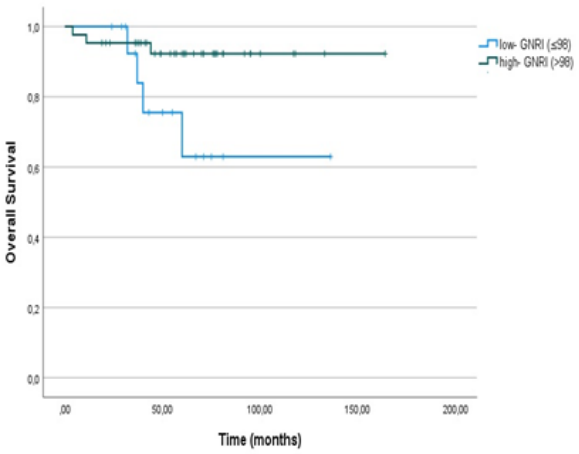

Figure 3. Estimates of overall survival by Kaplan-Meier according to the GNRI for stage 2 patients.

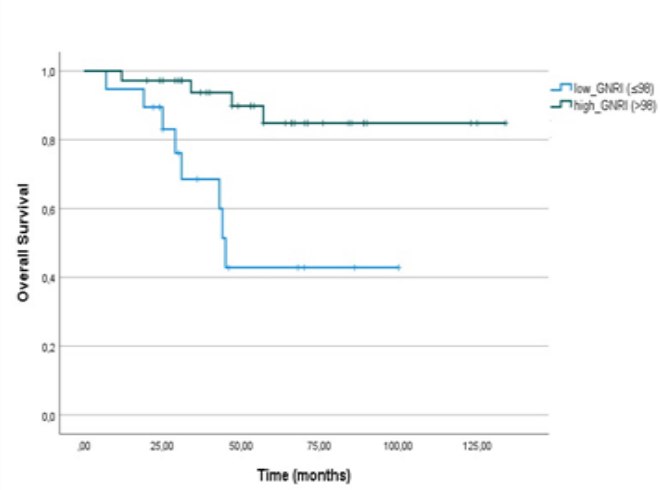

Figure 4. Estimates of overall survival by Kaplan-Meier according to the GNRI for stage 3 patients.

were staged as T3/T4. The number of patients with lymph node metastasis was 55 (48.2%). There were 59 (51.8%) patients with stage II, and 55 (48.2%) with stage III.

The mean GNRI was 103.5±11.9. Thirty-five (30.7%) of the patients had low-GNRI (GNRI≤ 98), and 79 (69.3%) had high-GNRI (GNRI> 98). Clinicopathological features of the patients according to GNRI groups were shown in Table 1. When the clinico-pathological features of the patients were compared according to the GNRI groups, only a significant correlation was found between tumor sidedness and GNRI. A total of 23.7% of left-sided tumors were categorized as low-GNRI, while 76.3% of them were in the high-GNRI group (p=0.02).

Survival analyses

The 5-year OS rate of the low-GNRI group was significantly lower than that of the high-GNRI group (65.7% vs. 91.1%, p=0.002; Figure 1). There was also a statistically significant difference in the 5-year RFS rate of the two groups (66.7% vs. 90.8%, p <0.001; Figure 2). Additionally, an assessment was conducted to determine the prognostic significance of the GNRI in relation to the

Table 2. Univariate and multivariate analyses of the factors associated with overall survival.

Variables		Univariate		Multivariate	
		95% CI	p-value	95% CI	p-value
Age	<75	1			
	≥75	1.235 (0.364-4.196)	0.735		
Gender	Female	1			
	Male	1.602 (0.662- 4.162)	0.296		
Tumor depth	T1-T2	1			
	T3-T4	2.003 (0.830 -4.835)	0.122		
Stage	2	1			
	3	2.022 (0.837-4.884)	0.118		
BMI	≥22	1			
	<22	1.765 (0.411-7.579)	0.445		
GNRI	High	1			
	Low	2.789 (1.172-6.637)	0.020	2.476 (1.031-5.942)	0.042
Tumor sidedness	Left	1			
	Right	2.797 (1.177-6.647)	0.020	2.528 (1.054-6.061)	0.038
Differentiation	Well/moderate	1			
	Poor	2.792 (0.645-12.083)	0.169		
LVI	No	1			
	Yes	1.084 (0.437-2.690)	0.862		
PNI	No	1			
	Yes	1.396 (0.468-4.162)	0.550		
Diabetes mellitus	No	1			
	Yes	1.951 (0.807-4.716)	0.138		
Obstruction/perforation	No	1			
	Yes	1.338 (0.450-3.980)	0.601		

Abbreviations: BMI: Body mass index; GNRI: Geriatric nutritional risk index; LVI:Lymphovascular invasion; PNI: Perineural invasion

stage of the tumor. In stage II, the 5-year OS rate was 86.7% in the group with a low-GNRI, while it was 88.6% in the group with a high-GNRI (p = 0.577; Figure 3). The 5-year OS rate in stage III patients was 58.3% in the group with low-GNRI, whereas it was 83.7% in the group with high-GNRI (p= 0.073; Figure 4).

Prognostic factors for OS

In the univariate analysis of factors related to OS, the HR for a low-GNRI was 2.789 (95% CI 1.172-6.637, p= 0.020). The other factor that was significantly correlated with OS was right tumor sidedness (p= 0.020). Gender, age, T stage, lymph node metastases, TNM stage, low-BMI, diabetes, presence of LVI, PNI and poor differentiation were not significantly associated with OS. The multivariate Cox regression analysis identified only tumor sidedness (p= 0.038) and GNRI (p= 0.042) as independent prognostic factors for OS (Table 2).

Prognostic factors for RFS

In the univariate analysis of prognostic factors related to RFS, GNRI was the only indicator that was correlated with RFS (HR: 4.265; %95 CI:1.641-11.087; p= 0.04). The other factors such as tumor sidedness, gender, age, T stage, lymph node metastases, TNM stage, low-BMI, diabetes, presence of LVI, PNI and poor differentiation were not significantly associated with RFS.

Discussion

Our study showed that the GNRI measured in the preoperative period in patients with early-stage colon cancer is prognostic in terms of OS and RFS. Although it has been previously shown that GNRI is prognostic for survival in several malignancies such as gastric, pancreatic, and lung cancer, there are few studies investigating the prognostic importance of GNRI in terms of survival in early-stage colon cancer patients. One of them was performed with 329 colorectal cancer

patients [20]. In this study, low-GNRI was reported to be associated with OS ($p< 0.001$) and was found to be an independent prognostic marker in multivariate analysis ($p=0.042$). The main difference between this study and ours is that there was no statistical relationship between low-GNRI and RFS in study performed by Doi et al. In our study, low-GNRI was both related to poor OS and poor RFS. The cut-off value of 98 for low-GNRI was similar as ours.

In addition, in our study high-GNRI group had a higher incidence of left colon cancer compared to the low-GNRI group and the association between GNRI and tumor sidedness was statistically significant. In recent studies about tumor sidedness demonstrated that right colon cancer was more aggressive than left colon cancer [21, 22]. Our study confirms these recent studies. Therefore, the association between high GNRI and left sidedness may depend on tumor biology. For this suggestion, more studies are needed at the molecular level.

The prognosis of colon cancer patients with low-GNRI is generally poorer, thus emphasizing the significance of improving nutritional status to improve survival. There are different markers such as prealbumin level and sarcopenia in the evaluation of nutritional status. But these markers are expensive and difficult to perform in elderly patients. Thus, GNRI can show nutritional status alone in elderly colon cancer patients as an easy and accessible marker that can be calculated by routine biochemistry. Several studies reported the impact of nutritional support on the prognosis of colon cancer patients and demonstrated the correlation between the use of oral nutritional supplements and reduced weight loss as well as a lower incidence of postoperative infection among colon cancer patients [23, 24]. Furthermore, it was observed that dietary factors play a significant role in the etiology of colon cancer [25, 26]. Nevertheless, the effects of these dietary treatments on the long-term prognosis of patients with colon cancer remain uncertain. Therefore, more research is needed to examine the potential of nutritional support in increasing the survival of individuals diagnosed with colon cancer. In this regard, GNRI can serve as a valuable tool for assessing patients who may benefit from nutritional support and for assessing the impact of such nutritional supports.

One of the limitations of our study is the lack of assessment regarding the association between GNRI and postoperative complications. This is because we were unable to access postoperative period information during the analysis of retrospective data. Secondly, there is no consensus regarding the GNRI cut-off value, which makes its practical use a challenge. Thirdly, we only included the stage II and III patients who were treated with CAPEOX or capecitabine monotherapy. Whether or not the patients could complete their chemotherapy regimens could not be reached because of retrospective data analysis. Therefore, survival analysis according to chemotherapy type and duration, and the relationship between survival and GNRI groups according to chemotherapy types could not be examined. Finally, we only assessed GNRI as a prognostic marker. Evaluating and comparing GNRI with other prognostic factors such as PNI, CONUT and sarcopenia could more effectively demonstrate the prognostic value of GNRI. Although several markers, such as CONUT, PNI have been evaluated in terms of their association with survival in colon cancer patients, it is still unclear which marker is the most effective. Prospective studies with a large number of patients are needed to compare these markers.

In conclusion, this study provides evidence that the GNRI serves as a basic and important prognostic indicator in elderly patients diagnosed with early-stage colon cancer. A low GNRI may be a prognostic indicator of poor OS and RFS.

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