Türkiye Klinikleri Tıp Bilimleri Dergisi
Turkiye Klinikleri Journal of Medical Sciences
Turkiye Klinikleri J Med Sci. 2023;43(1):83-9

ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/medsci.2022-91804

The Effect of Gastrointestinal Symptoms on Objective Criteria of Malnutrition in Dialysis Patients: Cross-Sectional Research

Diyaliz Hastalarında Gastrointestinal Semptomların Malnütrisyonun Objektif Kriterlerine Etkisi: Kesitsel Araştırma

Refika BÜBERCİ[a], Semahat KARAHİSAR ŞİRALİ[a], Murat DURANAY[a]

[a]Clinic of Nephrology, Ankara Training and Research Hospital, Ankara, Türkiye

ABSTRACT Objective: Gastrointestinal symptoms are common in chronic kidney disease (CKD) patients. This situation creates a tendency toward malnutrition. The aim of the current study was to determine the causes of gastrointestinal symptoms and to evaluate their effect on Prognostic Nutritional Index (PNI) and the Controlling Nutritional Status (CONUT) score which are the objective criteria to detect malnutrition. **Material and Methods:** A total of 66 hemodialysis and 51 peritoneal dialysis patients were included in this study. Patients were divided into two groups. Group I consisted of 26 patients who answered more than 50% of the 16 questions on a gastrointestinal symptoms Likert-type questionnaire as "frequently" or "very frequently". Laboratory and demographic features of patients were recorded. PNI score was calculated using the formula: [10×serum albumin value (g/dL)]+ (0.005×lymphocyte count/mm3). CONUT score was calculated by summing the scores given to certain ranges of total lymphocyte count, albumin, and total cholesterol value. A low PNI and high CONUT score indicates nutritional deficiencies. **Result:** There was no difference in demographic characteristics between groups. PNI score was lower and CONUT score was higher in Group I. Diabetes mellitus (DM) and CRP-albumin ratio (CAR) were found to be independent risk factors in the development of gastrointestinal symptoms. In multivariate regression analysis, it was observed that DM, non-steroidal anti-inflammatory drugs (NSAID) use, and CAR elevation rather than gastrointestinal symptoms affect the CONUT and PNI scores. **Conclusion:** DM and inflammation play roles in the development of gastrointestinal symptoms. Malnutrition is affected not only by gastrointestinal symptoms but also by underlying additional diseases, some drugs such as NSAID, and inflammation in dialysis patients.

Keywords: Controlling Nutritional Status score; dialysis; gastrointestinal symptoms; malnutrition; Prognostic Nutritional Index

ÖZET Amaç: Gastrointestinal semptomlar kronik böbrek hastalarında (KBH) yaygın görülür. Bu durum malnütrisyona eğilim yaratır. Mevcut çalışmanın amacı, gastrointestinal semptomların nedenlerini tespit etmek ve malnütrisyonu değerlendiren objektif kriterlerden olan Prognostik Beslenme İndeksi [Prognostic Nutritional Index (PNI)] ve Kontrollü Beslenme Durum [Controlling Nutritional Status (CONUT)] skoru üzerine etkisini değerlendirmektir. **Gereç ve Yöntemler:** Çalışmaya 66 hemodiyaliz, 51 periton diyaliz hastası alındı. Hastalar iki gruba ayrıldı. Gastrointestinal semptomları değerlendirmek için 16 sorudan oluşan Likert tipi anketteki soruların %50'den fazlasına "sık" veya "çok sık" cevaplarını veren 26 hasta Grup 1'i oluşturdu. Hastaların demografik ve laboratuvar verileri kaydedildi. PNI [10×serum albumin değeri (g/dL)]+ (0,005×lenfosit sayısı/mm3) formülüyle hesaplandı. CONUT skoru lenfosit sayısının, albumin değerinin ve total kolesterolün belirli aralıklarına puan verip, toplamı olarak hesaplandı. Düşük PNI ve yüksek CONUT skoru beslenme eksikliğini gösterir. **Bulgular:** İki grup arasında demografik özellikler açısından fark yoktu. Grup 1'de PNI düşük, CONUT skoru yüksek bulundu. Diabetes mellitus (DM) ve C-reaktif protein-albumin oranı (CAO) gastrointestinal semptomların gelişimi açısından bağımsız birer risk faktörü olduğu tespit edildi. Çok değişkenli regresyon analizinde gastrointestinal semptomlardan ziyade DM, CAO yüksekliği ve nonsteroid antiinflamatuar ilaç (NSAİİ) kullanımının PNI ve CONUT skorunu etkilediği tespit edildi. **Sonuç:** DM ve inflamasyon gastrointestinal semptomların gelişiminde rol oynamaktadır. Malnütrisyon diyaliz hastalarında sadece gastrointestinal semptomlardan değil aynı zamanda altta yatan ek hastalıklardan, NSAİİ gibi bazı ilaçlardan ve inflamasyondan etkilenmektedir.

Anahtar Kelimeler: Kontrollü beslenme durum skoru; diyaliz; gastrointestinal semptomlar; malnütrisyon; Prognostik Beslenme İndeksi

Correspondence: Refika BÜBERCİ
Clinic of Nephrology, Ankara Training and Research Hospital, Ankara, Türkiye
E-mail: refikakaraer@gmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Medical Sciences.

Received: 06 Jun 2022 ***Received in revised form:*** 03 Oct 2022 ***Accepted:*** 04 Oct 2022 ***Available online:*** 02 Nov 2022

Gastrointestinal symptoms are more common in dialysis patients than in the general population. Due to the differences in evaluation methods, identification, and inclusion and exclusion criteria, the prevalence in published studies ranges over a wide spectrum.[1] Gastrointestinal symptoms affect eating, digestion, and absorption events, causing malnutrition in patients.[2,3] In addition to subjective methods such as subjective global assessment and malnutrition inflammation score, objective methods such as anthropometric measurements and biochemical parameters are used to evaluate nutritional status. The Prognostic Nutritional Index (PNI) and Controlling Nutritional Status (CONUT) score, which were created initially to be applied in patients undergoing intensive care and post-surgery cancer patients, have been shown to be effective objective methods for determining the progression of many diseases and for evaluating malnutrition.[4-7] Over time, these indexes were applied in chronic kidney disease (CKD) and dialysis patients. It was found that these indexes could be predictors of malnutrition, CKD progression, and mortality.[8-10]

The aim of the current study was to determine the causes of gastrointestinal symptoms and to investigate the effect of gastrointestinal symptoms on PNI and CONUT scores.

MATERIAL AND METHODS

STUDY POPULATION AND LABORATORY MEASUREMENTS

A total of 66 hemodialysis and 51 peritoneal dialysis patients who were followed in the dialysis unit of our hospital between 2018 and 2020 were included in the study. The gastrointestinal symptoms questionnaire is a Likert-type questionnaire consisting of three subcategories. It is completed according to the frequency of symptoms as "never", "rarely", "occasionally", "frequently", and "very frequently" that may have caused disturbance in the previous three months (Table 1).[11] Patients were divided into two groups. Group I consisted of 26 patients who answered more than 50% of the 16 questions in questionnaire as "frequently" or "very frequently". Remaing patients form Group II. Demographic characteristics, comorbid diseases, medications used, and body mass indices (BMI) were recorded. Biochemical parameters, C-reactive protein (CRP), CRP-albumin ratio (CAR), and complete blood counts were measured. Patients diagnosed with hematological diseases, active infection, malignancy, New York Heart Association class III and IV heart failure, inflammatory bowel disease, patients on tube feeding or parenteral nutrition, patients who had peritonitis, had catheter infection, and were hospitalized for any reason in the last month before starting the study, patients who received dialysis for less than six month and patients with non-regular follow-up were excluded from the study. The ethical approval of the study was obtained from the Ankara Training and Research Hospital Ethics Committee of our hospital in accordance with Helsinki Declaration (date: December 1, 2022, no: E.-21/802/22.12.2021). Patient's written informed consent was taken.

CALCULATION OF CAR, PNI, CONUT SCORES

CAR was calculated using the formula: CRP value (mg/L)/albumin value (g/L)x1,000. A higher CAR indicates increased inflammation. The formula to calculate the PNI is [10xserum albumin value (g/dL)+0.005xperipheral lymphocyte count (/mm^3)]. A lower PNI indicates a high risk of malnutrition.[9,10] The CONUT score is calculated based on albumin, total cholesterol level, and total lymphocyte count.

TABLE 1: Gastrointestinal symptom questionnaire.

Oesophageal symptoms	**Heartburn and/or dysphagia**
Upper dysmotility symptoms	At least one of early satiety, postprandial fullness, bloating, nausea, or vomiting.
Bowel symptoms	At least one of self reported diarrhoea or constipation, loose or watery stools,
	>3 bowel movements each day, urgency, faecal incontinence,
	<3 bowel movements each week, hard or lumpy stools, or feelings of anal blockage.

Points are given to each laboratory interval and the sum of the points constitutes the CONUT score [(serum albumin: 3.5 g/dL: 0 points; 3.49-3.0: 2 points; 2.99-2.5: 4 points; and <2.5: 6 points; lymphocytes: 1,600/L: 0 points; 1,200-1,599: 1 point; 800-1,199: 2 points; and <800: 3 points; and total cholesterol: 180 mg/dL: 0 points; 140-179: 1 point; 100-139: 2 points; and <100: 3 points.)] High conut score indicates malnutrition.[8]

STATISTICAL ANALYSIS

SPSS 22 (SPSS inc. IBM 2010 USA) program was used for statistical analysis in the study. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to evaluate the normal distribution. Normally distributed parameters were expressed as mean and standard deviation, and non-normally distributed parameters were expressed as the median (interquartile range). Pearson's c^2 or Fisher's exact test was used for categorical data. Categorical variables were presented as frequency ratio (n) and percentage (%). Nonparametric variables were compared with the Mann-Whitney U test. Univariate and multivariate Cox regression analysis were performed to determine the relationship between gastrointestinal symptoms, PNI and CONUT scores, and all laboratory tests, comorbid diseases, drugs used, and demographic features. A difference was considered significant when $p<0.05$.

RESULTS

The mean age of the patients was 52.17±14.74 years, the mean dialysis period was 5.63±5.01 years, and 43.6% of the patients were women. 40 of the 66 hemodialysis patients received hemodialysis through the arteriovenous fistula, while the remaining 26 patients received hemodialysis through the central venous catheter. There were no significant differences in terms of gender, age, dialysis type, comorbid diseases, drugs, and BMI between groups. Dialysis time was significantly shorter in Group I compared to Group II. It was also found that calcium, albumin, hemoglobin, and PNI were lower, while uric acid, CRP, CAR, and CONUT were higher in Group I (Table 2). The most common symptoms were post-meal bloating (22%), constipation (20%), and heartburn (18%). In regression analysis, it was determined that diabetes mellitus (DM) [hazard ratio (HR): 4.912, p: 0.002], CAR (HR: 1.819, p: <0.001) were independent risk factors for the development of gastrointestinal symptoms (Table 3).

Two groups were created based on a CONUT score below or above three. After adjusting for age, gender, dialysis type, drugs, and comorbid diseases, DM (HR: 2.255, p: 0.007), CAR (HR: 1.120, p: 0.045), uric acid (HR: 1.324, p: 0.019), non-steroidal anti-inflammatory drugs (NSAID) use (HR: 2.876, p: 0.021) were observed to affect the CONUT score in regression analyses (Table 4). The effect of gastrointestinal symptoms on the CONUT score was observed only in univariate regression analysis.

Similarly, two groups were created based on a PNI score below or above 45. Regression analysis showed that after adjusting for confounding factors, DM, CAR, uric acid, and NSAID use affected the PNI score (HR: 2.880, p: 0.001; HR: 1.152, p: 0.012; HR: 1.31, p: 0.027; HR: 1.994, p: 0.04, respectively) (Table 5). It was also found that the gastrointestinal symptoms affected the PNI score only in univariate regression analysis.

DISCUSSION

In patients with CKD, gastrointestinal symptoms are observed more frequently than in the normal population according to both the results of the questionnaire and the endoscopic and colonoscopic findings. The direct effects of dialysis modalities, inflammation, comorbid diseases, and medications play roles in the development of gastrointestinal symptoms. Zuvela et al. reported that the prevalence of gastrointestinal symptoms ranged from 1.6 to 72.3% in hemodialysis patients and from 5 to 93.1% in peritoneal dialysis patients. They attributed this significant variation to the use of different methodologies. The most common symptoms were indigestion, abdominal pain, reflux, and constipation.[1] In the present study, post-meal bloating, heartburn, and constipation were the most common symptoms. There was no significant difference between the two groups in terms of DM. However DM was found to be independent risk factors in the development of gastrointestinal symptoms in regression analysis. DM is an important risk factor

TABLE 2: The comparison of demographic and laboratory data between groups.

Parameters	Group I (n=26)	Group II (n=91)	p value
Gender (female) (%)	37.5	44.6	0.212
Age (year)	56.12±11	51.54±15.13	0.174
Dialysis type (hemodialysis) (%)	50	57.4	0.256
DM (%)	31.3	22.8	0.121
CVD (%)	31.3	29.7	0.578
BMI (kg/m^2)	24.10 (4.24)	24.60 (5.78)	0.426
Dialysis time (year)	2.25 (3)	4 (7)	0.033
Urea (mg/dL)	122.56±40.04	119.79±30.68	0.532
Creatinine (mg/dL)	7.49±2.69	8.30±2.29	0.424
Calcium (mg/dL)	8.31±0.91	8.89±0.87	0.017
Phosphorus (mg/dL)	5.1 (2.13)	4.6 (1.9)	0.789
Parathormone (ng/L)	363.5 (412.75)	378 (379)	0.812
Albumin (g/dL)	3.5 (1.03)	3.8 (0.50)	0.038
Uric acid (mg/dL)	6.25 (1.9)	5.7 (1.3)	0.043
CRP (mg/L)	12.15 (16.56)	5.5 (7.45)	0.011
CAR	3.58 (4.94)	1.43 (2.04)	0.005
WBC (106/L)	6,151±2,070	6,813±1,741	0.532
Neutrophil (106/L)	4,975±1,783	433±1,282	0.207
Lymphocyte (106/L)	1,367±485	1,553±586	0.288
Monocytes (106/L)	603±303	545±153	0.631
Hemoglobin (g/dL)	9.6±1.36	11.10±1.45	0.001
Platelet (106/L)	221,000 (43,750)	210,000 (96,000)	0.356
Total cholesterol (mg/dL)	154.5 (77.5)	154 (59)	0.456
HDL (mg/dL)	39 (16.25)	40 (13)	0.158
LDL (mg/dL)	82 (62.75)	80 (48.5)	0.252
Triglycerides (mg/dL)	117 (115.75)	120 (100)	0.278
CONUT	3.5 (3.75)	2 (3)	0.028
PNI (%)	41.37±7.21	46.02±5.55	0.026
Cinacalcet (%)	20	80	0.543
PBD (%)	13.7	86.3	0.992
NSAID (%)	20	80	0.445
RAAS blocker (%)	18.2	81.8	0.648
Calcium channel blocker (%)	23.4	76.6	0.448
Anti-coagulant (%)	3.3	96.7	0.056

DM: Diabetes mellitus; CVD: Cardiovascular disease; BMI: Body mass index; CRP: C-reactive protein; CAR: CRP-albumin ratio; WBC: White blood cell; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; CONUT: Controlling Nutritional Status score; PNI: Prognostic Nutritional Index; PBD: Phosphorus binding drug; NSAID: Non-steroidal anti-inflammatory drugs; RAAS: Renin angiotensin aldosterone system.

TABLE 3: Univariate and multivariate Cox regression analysis of risk factors affecting the development of gastrointestinal symptoms.

	Univariate regression			Multivariate regression		
Parameters	HR	95% CI	p value	HR	95% CI	p value
DM	5.593	1.456-21.480	0.012	4.912	1.568-17.852	0.002
CAR	1.954	1.242-3.075	0.004	1.819	1.315-2.517	<0.001
CRP	1.332	1.153-1.538	<0.001			

HR: Hazard ratio; CI: Confidence interval; DM: Diabetes mellitus; CRP: C-reactive protein; CAR: CRP-albumin ratio.

TABLE 4: Univariate and multivariate Cox regression analysis of risk factors affecting CONUT scores.

	Univariate regression			Multivariate regression		
Parameters	**HR**	**95% CI**	**p value**	**HR**	**95% CI**	**p value**
DM	4.725	2.173-10.274	<0.001	2.255	1.245-4.086	0.007
Uric acid	1.6	1.204-2.126	0.001	1.324	1.048-1.674	0.019
CAR	3.399	1.780-6.487	<0.001	1.120	1.003-1.251	0.045
NSAID	4.596	1.610-13.120	0.004	2.876	1.170-6.638	0.021
Gastrointestinal symptoms	3.121	1.573-6.192	0.001			

CONUT: Controlling nutritional status score; HR: Hazard ratio; CI: Confidence interval; DM: Diabetes mellitus; CAR: C-reactive protein-albumin ratio; NSAID: Non-steroidal anti-inflammatory drugs.

TABLE 5: Univariate and multivariate Cox regression analysis of risk factors affecting PNI scores.

	Univariate regression			Multivariate regression		
Parameters	**HR**	**95% CI**	**p value**	**HR**	**95% CI**	**p value**
DM	3.964	1.703-9.228	0.001	2.880	1.563-5.308	0.001
Uric acid	1.492	1.138-1.958	0.004	1.310	1.031-1.664	0.027
CAR	3.475	1.636-7.378	0.001	1.152	1.031-1.286	0.012
Anti-coagulant	3.238	1.144-9.169	0.027			
NSAID	2.490	1.199-5.172	0.014	1.994	1.032-3.854	0.04
Gastrointestinal symptoms	2.856	1.389-5.875	0.004			

PNI: Prognostic Nutritional Index; HR: Hazard ratio; CI: Confidence interval; DM: Diabetes mellitus; CAR: C-reactive protein-albumin ratio; NSAID: Non-steroidal anti-inflammatory drugs.

for the development of CKD worldwide. Cerebrovascular and cardiovascular events, gastrointestinal disorders, and chronic inflammation as well as CKD accelerate mortality in diabetic patients. Up to 50% of patients with Type 1 and Type 2 DM have delayed gastric emptying, which can be documented with scintigraphy and 13C breath tests. Many patients with delayed gastric emptying have dyspepsia or gastroparesis.[12] Similar to DM, uremia has also been shown to cause delayed gastric emptying.[1]

In some studies, the effects of the number of drugs used, corticosteroid history, residual renal function, psychosomatic symptoms, dialysis modality, and gender rather than DM on gastrointestinal symptoms were determined.[1,13-15] In the present study, the effect of drug types on gastrointestinal symptoms was evaluated but no effect found in regression analysis. In addition, dialysis modality rates were similar between the two groups and an effect of dialysis modality on gastrointestinal symptoms was not found. In a study conducted by Kahvecioglu et al., it was reported that there was no effect of dialysis modality on gastrointestinal symptoms.[16]

Renal failure itself, changes in nutrition, and drugs cause changes in the gut microbiota.[17] Changes in the microbiota disrupt the intestinal barrier and cause translocation of bacterial components into the circulation. Therefore persistent systemic inflammation develops. Both the changes in the microbiota and systemic inflammation cause gastrointestinal symptoms. In the current study, inflammation parameters were found to be high in the group with gastrointestinal symptoms, and it was also determined in the regression analysis that inflammation affected the development of gastrointestinal symptoms.

Gastrointestinal symptoms cause malnutrition in chronic kidney patients over time and negatively affect quality of life. Today, both subjective and objective criteria are used to evaluate malnutrition. Although there is often a correlation between gastrointestinal symptoms and subjective criteria, occasionally, there is no association between objective criteria and gastrointestinal symptoms.[18] In the current study, PNI and CONUT scores, which are one of the objective criteria, were used to evaluate malnutrition. The lymphocyte count has an important

place in the formula of both of these scores. Malnutrition affects the structure of the lymphocytes of the thymus, causing disruption in T cell immunity. Also, essential vitamins and amino acids have a negative effect on both T and B cell numbers. However, the underlying mechanism is not fully understood.[19] In a study conducted in patients with anorexia nervosa, it was determined that total lymphocyte count decreased and CD4 and CD8 cell distribution was altered compared to the healthy group.[20] In another study conducted in hospitalized elderly patients, a relationship was found between total lymphocyte count and middle arm muscle circumference and triceps skin thickness.[21] After the realization that lymphocytes and albumin reflect nutritional status, various formulas including both of these variables were developed. PNI and CONUT scores were first applied in post-surgery cancer patients and in patients undergoing intensive care who receive total parenteral nutrition therapy. Consequently, PNI and CONUT scores were found to be important predictors in determining prognosis. Over time these indexes were applied in CKD and dialysis patients. In a study conducted on 252 peritoneal dialysis patients, it was reported that the CONUT score reflected nutrition, and mortality increased in patients with CONUT scores of three and above.[8] In another study evaluating PNI in 252 peritoneal dialysis patients, it was found that PNI is a risk factor for cardiovascular mortality.[9] In a study consisting of Stage 3, 4, 5 CKD patients, it was also reported that low PNI levels affect CKD progression.[10] In the current study, we found that PNI score was lower and CONUT score was higher, and we investigated possible risk factors that may affect the PNI and CONUT scores. In univariate regression analysis, gastrointestinal symptoms were found to affect CONUT and PNI score. However, in multivariate regression analysis, it was observed that the presence of DM, NSAID use, and elevation of uric acid and CAR affect the CONUT and PNI scores, but gastrointestinal symptoms had no relationship.

The limitations of current study are the difference between the number of patients in Group I and II, retrospective study design, and not evaluating patients' socio-economic status and psychosomatic symptoms.

CONCLUSION

Gastrointestinal symptoms are common in patients with CKD. DM and inflammation play roles in the development of gastrointestinal symptoms. In dialysis patients, malnutrition is affected not only by gastrointestinal symptoms but also by underlying additional diseases, medications, and inflammation.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Refika Büberci, Murat Duranay;* ***Design:*** *Refika Büberci, Murat Duranay;* ***Control/Supervision:*** *Murat Duranay, Refika Büberci;* ***Data Collection and/or Processing:*** *Semahat Karahisar Şirali, Refika Büberci;* ***Analysis and/or Interpretation:*** *Refika Büberci, Murat Duranay, Semahat Karahisar Şirali;* ***Literature Review:*** *Refika Büberci, Semahat Karahisar Şirali;* ***Writing the Article:*** *Refika Büberci;* ***Critical Review:*** *Murat Duranay.*

REFERENCES

1. Zuvela J, Trimingham C, Le Leu R, Faull R, Clayton P, Jesudason S, et al. Gastrointestinal symptoms in patients receiving dialysis: a systematic review. Nephrology (Carlton). 2018;23(8):718-27. [Crossref] [PubMed]
2. Aguilera A, Bajo MA, Espinoza M, Olveira A, Paiva AM, Codoceo R, et al. Gastrointestinal and pancreatic function in peritoneal dialysis patients: their relationship with malnutrition and peritoneal membrane abnormalities. Am J Kidney Dis. 2003;42(4):787-96. [Crossref] [PubMed]
3. Carrero JJ. Mechanisms of altered regulation of food intake in chronic kidney disease. J Ren Nutr. 2011;21(1):7-11. [Crossref] [PubMed]
4. Mori S, Usami N, Fukumoto K, Mizuno T, Kuroda H, Sakakura N, et al. The significance of the Prognostic Nutritional Index in patients with completely resected non-small cell lung cancer. PLoS One. 2015;10(9):e0136897. [Crossref] [PubMed] [PMC]
5. Peng D, Gong YQ, Hao H, He ZS, Li XS, Zhang CJ, et al. Preoperative Prognostic Nutritional Index is a significant predictor of survival with bladder cancer after radical cystectomy: a retrospective study. BMC Cancer. 2017;17(1):391. [Crossref] [PubMed] [PMC]
6. Nishikawa H, Yoh K, Enomoto H, Ishii N, Iwata Y, Takata R, et al. The Relationship between Controlling Nutritional (CONUT) score and clinical markers among adults with hepatitis C virus related liver cirrhosis. Nutrients. 2018;10(9):1185. [Crossref] [PubMed] [PMC]
7. Iseki Y, Shibutani M, Maeda K, Nagahara H, Ohtani H, Sugano K, et al. Impact of the Preoperative Controlling Nutritional Status (CONUT) score on the survival after curative surgery for colorectal cancer. PLoS One. 2015;10(7):e0132488. [Crossref] [PubMed] [PMC]
8. Zhou H, Chao W, Cui L, Li M, Zou Y, Yang M. Controlling Nutritional Status (CONUT) score as immune-nutritional predictor of outcomes in patients undergoing peritoneal dialysis. Clin Nutr. 2020;39(8):2564-70. [Crossref] [PubMed]
9. Peng F, Chen W, Zhou W, Li P, Niu H, Chen Y, et al. Low Prognostic Nutritional Index associated with cardiovascular disease mortality in incident peritoneal dialysis patients. Int Urol Nephrol. 2017;49(6):1095-101. [Crossref] [PubMed]
10. 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. [Crossref] [PubMed] [PMC]
11. Bytzer P, Howell S, Leemon M, Young LJ, Jones MP, Talley NJ. Low socioeconomic class is a risk factor for upper and lower gastrointestinal symptoms: a population based study in 15 000 Australian adults. Gut. 2001;49(1):66-72. [Crossref] [PubMed] [PMC]
12. Bharucha AE, Kudva YC, Prichard DO. Diabetic gastroparesis. Endocr Rev. 2019;40(5):1318-52. [Crossref] [PubMed] [PMC]
13. Chong VH, Tan J. Prevalence of gastrointestinal and psychosomatic symptoms among Asian patients undergoing regular hemodialysis. Nephrology (Carlton). 2013;18(2):97-103. [Crossref] [PubMed]
14. Dong R, Guo ZY. Gastrointestinal symptoms in patients undergoing peritoneal dialysis: multivariate analysis of correlated factors. World J Gastroenterol. 2010;16(22):2812-7. [Crossref] [PubMed] [PMC]
15. Silva LF, Lopes GB, Matos CM, Brito KQ, Amoedo MK, Azevedo MF, et al. Gastrointestinal symptoms and nutritional status in women and men on maintenance hemodialysis. J Ren Nutr. 2012;22(3):327-35. [Crossref] [PubMed]
16. Kahvecioglu S, Akdag I, Kiyici M, Gullulu M, Yavuz M, Ersoy A, et al. High prevalence of irritable bowel syndrome and upper gastrointestinal symptoms in patients with chronic renal failure. J Nephrol. 2005;18(1):61-6. [PubMed]
17. Meijers B, Evenepoel P, Anders HJ. Intestinal microbiome and fitness in kidney disease. Nat Rev Nephrol. 2019;15(9):531-45. [Crossref] [PubMed]
18. Li Y, Dong J, Zuo L. Is subjective global assessment a good index of nutrition in peritoneal dialysis patients with gastrointestinal symptoms? Perit Dial Int. 2009;29 Suppl 2:S78-82. [Crossref] [PubMed]
19. Shirakabe A, Hata N, Kobayashi N, Okazaki H, Matsushita M, Shibata Y, et al. The prognostic impact of malnutrition in patients with severely decompensated acute heart failure, as assessed using the Prognostic Nutritional Index (PNI) and Controlling Nutritional Status (CONUT) score. Heart Vessels. 2018;33(2):134-44. [Crossref] [PubMed]
20. Saito H, Nomura K, Hotta M, Takano K. Malnutrition induces dissociated changes in lymphocyte count and subset proportion in patients with anorexia nervosa. Int J Eat Disord. 2007;40(6):575-9. [Crossref] [PubMed]
21. Leandro-Merhi VA, Bráz VN, Aquino JL. Is total lymphocyte count related to nutritional markers in hospitalized older adults? Arq Gastroenterol. 2017;54(1):79-82. [Crossref] [PubMed]