Association of Nutritional Status with Depression and Sleep Disorders in Elderly End Stage Renal Disease Patients - Does Chronic Inflammation Cause it all?

Son Dönem Böbrek Yetmezlikli Yaşlı Hastalarda Beslenme Durumunun Depresyon ve Uyku Bozuklukları ile İlişkisi - Tümüne Kronik İnflamasyon Yol Açabilir mi?

ABSTRACT

OBJECTIVE: In our study we aimed to analyze the association between nutritional status and depression and sleep disturbance in elderly dialysis patients.

MATERIAL and METHODS: Seventy-three patients receiving dialysis treatment older than 65 years of age were enrolled in this study. Nutritional status was determined by Subjective Global Assessment (SGA). Patients were also evaluated with Beck Depression Inventory and Pittsburg Sleep Quality Index. Demographic and laboratory data were recorded.

RESULTS: According to SGA, 48 (65.8%) patients were well nourished and 25 (34.2%) patients had mild-moderate and severe malnutrition. When the well-nourished and malnourished patients were compared, the well-nourished group had higher albumin (p<.0001) and creatinine (p=.03) levels, higher body mass indices (p<.01), lower CRP levels (p<.0001), better quality of sleep (p<.0001) and lower depression scores (p<.0001) than the malnourished group. When we grouped patients as Group I (not depressive and good sleep quality), Group II (depressive but good sleep quality) and Group III (both depressive and poor sleep quality, we found that Group III had the lowest albumin (p < .0001) and highest CRP (p < .0001) values when compared to the other two groups.

CONCLUSION: Depression, sleep disorders, and the nutritional status are important factors which interact with each other and elderly dialysis patients with malnutrition should be well assessed for the presence of any inflammatory status and/or psychological-sleep disorders.

KEY WORDS: Elderly patients, Dialysis, Malnutrition, Depression, Sleep disorder

ÖZ

AMAÇ: Çalışmamızda yaşlı diyaliz hastalarında beslenme durumu ile depresyon ve uyku bozukluğu arasındaki ilişkiyi incelemeyi amaçladık.

GEREÇ ve YÖNTEMLER: Çalışmaya diyaliz tedavisi almakta olan 65 yaş üzerindeki 73 hasta alındı. Beslenme durumu "Subjektif Global Değerlendirme (SGD)" ile belirlendi. Hastalar ayrıca "Beck Depresyon Görüşmesi" ve "Pittsburg Uyku Kalitesi İndeksi" ile değerlendirildi. Hastaların demografik ve laboratuvar verileri kaydedildi.

BULGULAR: SGD sonuçlarına göre, 48 (%65.8) hastanın beslenme durumu iyi düzeyde iken 25 (%34.2) hasta hafif-orta ve ciddi derecede beslenme bozukluğuna sahipti. Beslenme durumu iyi olan hastalar ile malnutrisyonu olan hastalar karşılaştırıldığında, beslenmesi iyi olan grubun daha yüksek albümin (p<0,0001) ve kreatinin (p=0,03) düzeyleri ile vücut kitle indeksine (p<0,01), daha düşük CRP düzeylerine (p<.0001), daha iyi uyku kalitesine (p<0,0001) ve daha düşük depresyon skorlarına (p<0,0001) sahip olduğu görüldü. Hastaları, Grup I (depresyonu olmayan ve iyi uyku kalitesine sahip), Grup II (depresyonu olan ancak iyi uyku kalitesine sahip), Grup III (depresyonu olan ve kötü uyku kalitesine sahip) şeklinde gruplandığımızda Grup III'ün diğer gruplara kıyasla en düşük albümin (p<0,0001) ve en yüksek CRP (p<0,0001) düzeylerine sahip olduğu bulundu.

SONUÇ: Depresyon, uyku bozuklukları ve beslenme durumu birbirleriyle ilişkili önemli etkenlerdir ve malnutrisyonu olan yaşlı diyaliz hastaları inflamatuvar durum ve/veya psikolojik ve uyku bozuklukları varlığı açısından iyi değerlendirilmelidir.

ANAHTAR SÖZCÜKLER: Yaşlı hastalar, Diyaliz, Malnutrisyon, Depresyon, Uyku bozukluğu

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INTRODUCTION

The proportion of elderly people is rising throughout the world and this finds reflection in the increasing percentage of elderly patients in the end-stage renal disease (ESRD) population. This elderly group of patients shows a tendency to have an increased frequency of co-morbid conditions, infectious diseases, malignancies, cardiovascular diseases and malnutrition (1). Elderly or not, the majority of hemodialysis patients suffer from sleep disturbances and depression which are the most common psychological disorders among these patients (2, 3). It has been demonstrated that quality of sleep and depressive symptoms are important determinants of interdialytic weight gain, overall quality of life, oral intake and nutritional status in chronic dialysis patients and it has been suggested that antidepressant medication can improve depressive symptoms and nutritional status in ESRD patients with depression (4-8).

Protein-energy malnutrition is a common phenomenon in ESRD patients and a risk factor for poor quality of life and increased morbidity and mortality (9, 10). Presence of depression and sleep disturbances might have additional effects on nutritional status via their effects on quality of life or food intake. In this study we aimed to analyze the association between nutritional status and psychological factors such as depression and sleep disturbance in elderly dialysis patients.

PATIENTS and METHODS

Seventy-three dialysis patients older than 65 years of age were enrolled in this study. The study was conducted in accordance with the Declaration of Helsinki and informed consent was obtained from all patients before enrollment. During initiation of the study, all patients were on maintenance dialysis treatment for at least 12 months and had been free of acute infectious, inflammatory and any other illness that required hospitalization for the previous 3 months. All included patients with chronic inflammatory status [C-reactive protein (CRP) levels continuously elevated, or elevated for at least 3 of last 6 months on monthly routine follow-up] were evaluated for presence of any malignancy, chronic infection (tuberculosis etc) by clinical and laboratory examination and patients with any of the above mentioned pathologhical conditions were excluded. HD patients were receiving 4-h HD sessions three times weekly with bicarbonate-buffered dialysate and biocompatible polysulphone membranes. All PD patients were using a Baxter's Ultra Bag system (Baxter Health Care Co. Deerfield, Ill., USA). Patients with inadequete dialysis (for HD; Kt/V < 1.2, and for PD; weekly Kt/V < 2) were not included and any clinically hypervolemic patients were included after reaching their ideal dry weight according to radiological and physical examination. None of the patients were receiving any antidepressive treatment including tricyclic antidepressants.

Nutritional status was determined by Subjective Global assessment (SGA), which is a method, based on subjective and

objective aspects of the medical history and physical examination. SGA has been shown, in many studies, to be a simple, reliable and reproducible method for assessing the nutritional status in ESRD patients (11). We used a 7-point Likert-type scale of four criteria: weight loss, anorexia, subcutaneous fat and muscle mass. Each criterion was scored for producing a global assessment. Scores of 1–2 represented severe malnutrition (group C); 3–5, moderate to mild malnutrition (group B); and 6–7, normal nutrition (group A) (12). Then patients were regrouped according to SGA score, as well-nourished (SGA=A) or malnourished (SGA=B or C).

Beck Depression Inventory (BDI), which is a questionnaire that includes 21 questions, was used to measure the presence and degree of depression. These 21 questions were answered on a four-point Likert scale in which "0" represents the absence of a problem and "3" represents an extreme problem, with a total range of 0 to 63 points. The standard cut-offs are as follows: 0-9 indicates that a person is not depressed, 10-18 indicates mild-moderate depression, 19-29 indicates moderate-severe depression and 30-63 signifies severe depression. Higher total scores indicate more severe depressive symptoms (13).

Quality of sleep was measured using the Pittsburgh Sleep Quality Index (PSQI). This self-administered questionnaire assesses quality of sleep during the previous month and contains 19 self-rated questions yielding seven components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, and sleep disturbances, use of sleep medications and daytime dysfunction. Each component is scored from 0 to 3, yielding a global PSQI score between 0 and 21 points, with higher scores indicating lower quality of sleep. The PSQI is useful in identifying good and poor sleepers. Patients who have a PSQI score > 5 are considered to be a 'poor sleeper' (14).

Demographic data was collected during questionnaries and biochemical data was collected from patient records. Collected laboratory data included hemoglobin, blood urea nitrogen, creatinine, calcium, phosphorus, total cholesterol, triglycerides, uric acid, albumin, parathyroid hormone, and CRP values of the last 3 monthly routine follow-ups and the mean value of each parameter was recorded as the final data.

Statistical analyses were performed with the SPSS software (Statistical Package for the Social Sciences, version 11.0, SSPS Inc, Chicago, Ill, USA). All numerical variables are expressed as the mean \pm standard deviation (SD). Normality of data was analyzed by using the Kolmogorov-Smirnov test. All numerical variables with normal distribution were expressed as the mean \pm standard deviation (SD) while variables with skew distribution were expressed as median (Interquartile range). Differences between two groups were analyzed and compared by the Independent Samples *t* test or Mann-Whitney U test. We used the One Way-ANOVA test to analyze intergroup differences of more than 2 groups and also used a Tukey test for Post Hoc analyses. In case of skew distribution we used the Kruskal-Wallis test

for comparing the three groups. Categorical variables were compared with the chi-square test. A P value of less than .05 was considered statistically significant.

RESULTS

The baseline demographic, clinical, and laboratory features of the patients are summarized in Table I. According to PSQI and BDI scorings 15 patients (20.5%) had sleep disorder, 26 (32.9%) had mild to moderate depression and 9 (15.1%) had moderate to severe depression. BDI scores and PSQI scores were correlated (r:.583, p < .0001). According to SGA, 48 (65.8%) patients were

Table I: Demographic, clinical, and laboratory parameters of the study population.

	Mean±SD (Range) Median (IR) (n: 73)	
Age (yr)	72.5 ± 6.0 (65 – 87)	
Sex (F/M)	41/32	
Dialysis modality (HD/PD)	50/23	
Dialysis duration (mo)	59 (72)	
SGA (0-7)	6 (2)	
BDI (0-63)	9 (7)	
PSQI (0-21)	4 (2)	
Body mass index (kg/m ²)	25.63 ± 4.54 (16.71 – 34.29)	
Hemoglobin (g/dL)	11.3 (1.75)	
Ferritin (mg/dL)	427.26 ± 281.45 (24-1180)	
Blood urea nitrogen (mg/dL)	66.84 ± 21.28 (29 – 128)	
Creatinine (mg/dL)	8.93 ± 2.81 (2.1 – 13.4)	
Calcium (mg/dL)	9.3 (1.25)	
Phosporus (mg/dL)	5.08 ± 1.53 (2.1 – 8.1)	
Total cholesterol (mg/dL)	lesterol (mg/dL) $184.16 \pm 46.6 (99 - 314)$	
Triglycerides (mg/dL)	181.3 ± 80.97 (48 – 442)	
Uric acid (mg/dL)	6.63 ± 1.64 (3.6 – 11)	
Albumin (g/dL)	4.01 ± 0.47 (2.5 – 5)	
PTH (pg/mL)	368.06±292.55 (12.3-1180)	
C-reactive protein (mg/dL)	9.44 ± 6.47 (1.6 – 28)	

SGA: Subjective Global Assessment, BDI: Beck Depression Inventory, PSQI: Pittsburgh Sleep Quality Index, PTH: Parathyroid hormone

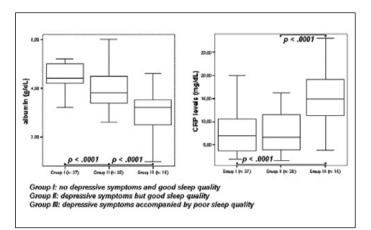


Figure 1: Patients with depressive symptoms accompanied by poor sleep quality had the lowest albumin and highest CRP values when compared to other 2 groups [(albumin; 3.4 ± 0.5 vs 4.0 ± 0.4 and 4.2 ± 0.2 g/dL) and (CRP; 15.6 ± 7.3 vs 8.3 ± 6.2 and 7.4 ± 4.3 mg/dL), p < .0001]

well nourished and 25 (34.2%) patients had mild-moderate and severe malnutrition. When the well-nourished and malnourished patients were compared, the well-nourished group had higher albumin and creatinine levels, higher body mass indices, lower CRP levels, better quality of sleep and lower depression scores than the malnourished group (Table II). When patients were grouped according to presence of poor sleep quality and compared with each other; poor sleepers had lower albumin, calcium and higher CRP levels, lower SGA and higher BDI scores (Table III). Similarly, when patients were grouped into 3 according to presence of mild or moderate-severe depressive symptoms and no depressive symptoms, patients with moderatesevere depressive scores had the lowest albumin, highest CRP levels, lowest SGA and highest PSQI scores. According to analyses, nondepressive patients had the highest body mass index values and moderate-severely depressive patients were also older compared to their not depressive counterparts. (Table IV). However this difference was not found when we grouped patients according to the presence of both symptoms; Group I (n: 37, not depressive and good sleep quality), Group II (n: 20, depressive but good sleep quality) and Group III (n: 15, both depressive and poor sleep quality). One patient had poor sleep quality but had no depressive symptoms, so that the patient was not evaluated in the statistical analysis of these groups. In this analysis we found that patients with depressive symptoms accompanied by poor sleep quality had the lowest albumin and highest CRP values when compared to other 2 groups [(albumin; 3.4 ± 0.5 vs 4.0 ± 0.4 and 4.2 ± 0.2 g/dL) and (CRP; 15.6 ± 7.3 vs 8.3 ± 6.2 and 7.4 ± 4.3 mg/dL), p < .0001, Figure 1].

	Well-nourished patients Mean±SD Median (IR) (n: 48)	Malnourished patients Mean±SD Median (IR) (n: 25)	p-values
Age (y)	69.5 (10.75)	67.0 (12.5)	.905
Gender (F/M)	26/22	15/10	.804
Dialysis modality (HD/PD)	(29/19)	(21/4)	.064
Dialysis duration (mo)	60.0 (69.75)	42.0 (83.0)	.506
BDI (0-63)	8.68 ± 2.75	16.28 ± 4.56	< .0001
PSQI (0-21)	3.50 ± 0.82	5.56 ± 1.73	< .0001
Body mass index (kg/m ²)	26.59 ± 4.37	23.71 ± 4.33	<.01
Hemoglobin (g/dL)	11.25 (1.78)	11.4 (1.7)	.949
Ferritin (mg/dL)	417.17 ± 248.67	446.16 ± 339.59	.687
Blood urea nitrogen (mg/dL)	67.72 ± 20.80	65.16 ± 22.50	.628
Creatinine (mg/dL)	9.43 ± 2.52	7.99 ± 3.14	.038
Calcium (mg/dL)	9.45 (1.18)	9.15 (1.65)	.201
Phosphorus (mg/dL)	5.22 ± 1.47	4.81 ± 1.63	.283
Ca x P product	48.32 ± 14.97	44.73 ± 19.11	.381
Total cholesterol (mg/dL)	183.83 ± 44.85	184.78 ± 50.67	.938
Triglycerides (mg/dL)	193.33 ± 83.50	159.34 ± 72.80	.106
Uric acid (mg/dL)	6.57 ± 1.70	6.70 ± 1.58	.786
Albumin (g/dL)	4.28 ± 0.25	3.50 ± 0.36	< .0001
PTH (pg/mL)	359.45 ± 304.43	384.09 ± 275.21	.753
C-reactive protein (mg/dL)	7.5 ± 4.2	13.0 ± 8.2	<.0001

Table II: Demographic, clinical, and laboratory data for well-nourished and malnourished patients.

BDI: Beck Depression Inventory, PSQI: Pittsburgh Sleep Quality Index

DISCUSSION

All elderly patients have an increased risk for both malnutrition and depression even if they do not have a chronic illness. For example German et al. reported a 28% frequency for depression and a higher rate of malnutrition presence in these depressed patients older than 65 years of age (15). Similarly Feldblum et al reported a malnutrition rate of 18.5% with mini nutritional assessment in a patient group of 259 patients older than 65 years of age (16, 17). These patients were also found to have the highest depressive scores. Otherwise healthy geriatric patients are also known to have poor sleep quality. Previous literature reported that 40- 50% of elder patients have poor sleep quality, which was also associated with depressive symptoms and lower oral feeding (18 - 20).

Depression and poor sleep quality are both common and important problems that affect quality of life in ESRD patients. Some previous studies reported that a 50-85% frequency for sleep disturbances and a 20-25% frequency for depression (18 - 20). In our study population presence of depressive symptoms was higher than these previous studies (total of 48%) while presence of sleep disturbances was lower (20.5%). It has been proposed that numerous factors including metabolic changes and treatment-related factors may contribute to the high prevalence of sleep problems in dialysis patients. Sabbattini et al reported that there is a relation between high PTH levels and sleep disorders in the ESRD population, which might be related to pruritus and bone pain, and those patients who are poor sleepers have lower hemoglobin levels compared with

	Good Sleep Quality (n: 58)	Poor Sleep Quality (n: 15)	p-values
Age (y)	69.0 (11.0)	69.5 (13.0)	.736
Gender (F/M)	31/27	10/5	.561
Dialysis modality (HD/PD)	(39/19)	(11/4)	.358
Dialysis duration (mo)	60.0 (72.0)	35.5 (78.0)	.439
BDI (0-63)	9 (5)	17.5 (9)	< .001
SGA (0-7)	6 (IR:0, range: 2-7)	3.5 (3)	< .0001
Body mass index (kg/m ²)	25.89 ± 4.45	24.56 ± 4.91	.330
Hemoglobin (g/dL)	11.25 (1.48)	11.91 (2.45)	.552
Ferritin (mg/dL)	441.33 ± 273.19	376.61 ± 314.14	.435
Blood urea nitrogen mg/dL)	69.22 ± 21.61	57.66 ± 17.72	.061
Creatinin (mg/dL)	9.21 ± 2.7	7.85 ± 3.04	.094
Calcium (mg/dL)	9.45 (1.31)	8.95 (1.21)	.084
Phosphorus (mg/dL)	5.21 ± 1.42	4.58 ± 1.85	.152
Ca x P product	48.68 ± 14.53	40.93 ± 21.97	.104
Total cholesterol (mg/dL)	182.01 ± 45.36	192.76 ± 52.30	.461
Triglycerides (mg/dL)	188.4 ± 79.3	152.92 ± 84.58	.159
Uric acid (mg/dL)	6.52 ± 1.64	6.97 ± 1.65	.416
Albumin (g/dL)	4.15 ± 0.35	3.47 ± 0.5	< .0001
PTH (pg/mL)	364.42 ± 298.27	383.5 ± 278.7	.841
C-reactive protein (mg/dL)	7.82 ± 5.19	15.6 ± 7.31	< .0001

Table III: Demographic, clinical, and laboratory data for PSQI poor and good sleep quality groups.

BDI: Beck Depression Inventory, PSQI: Pittsburgh Sleep Quality Index, SGA: Subjective Global Assessment Score

patients who are good sleepers (21, 22). We did not find such a relationship between sleep quality and hemoglobin, PTH, calcium, or phosphorus values.

Malnutrition, another common problem that is associated with poor life expectance and lower life quality in ESRD patients, was reported to be present in at least 30% of dialysis patients (23). Of these 30 percent patients nearly another 30% (6-8 % of total) usually have severe malnutrition (24). We also found a similar frequency for malnutrition in our study population. There were 5 patients (6.8 %) with severe and 20 patients (27.4%) with mildmoderate malnutrition, and a total malnutrition rate of 34.2% in the study population. These malnourished patients had lower albumin and higher CRP levels as expected. It is well known that malnutrition in dialysis patients is closely associated with chronic inflammation as a part of malnutrition-inflammationatherosclerosis syndrome (MIA) and at the end, is one of the most important causes of mortality in this patient group (25). An important finding in our study was that these malnourished patients also had higher depressive symptoms and lower sleep quality.

We found that both poor sleep quality and depressive symptoms were closely associated with malnutrition, low albumin and high CRP levels. Patients with moderate-severe depressive symptoms had the highest malnutrition rates and highest CRP but lowest albumin levels. Similarly patients with poor sleep quality had higher CRP levels and malnutrition rates. Depending on these findings we think that depression and poor sleep quality are closely associated with inflammatory conditions and malnutrition. In fact, in previous studies it was reported that higher malnutrition-inflammation scores were associated with the presence of moderate-to-severe depression and poor sleep and life quality in hemodialysis patients (26) **Table IV:** Demographic, clinical, and laboratory data for patient groups with mild, moderate-severe and no depressive symptom groups according to BDI.

	No Depressive Symptoms Mean±SD Median (IR) (n: 38)	Mild-Moderate Depressive Symptoms Mean±SD Median (IR) (n: 26)	Moderate-Severe Depressive Symptoms Mean±SD Median (IR) (n: 9)	p-values
Age (y)	69.13 ± 5.58	70.91 ± 7.56	74.36 ± 6.94	<.05*
Gender F/M	23/15	13/13	5/4	.565
Dialysis modality (HD/PD)	22/16	21/5	7/2	.081
Dialysis duration (mo)	69.39 ± 44.03	68.88 ± 59.86	48.55 ± 49.18	.524
PSQI (0-21)	3.63 ± 0.99	4.16 ± 1.34	6.27 ± 1.90	< .0001* < .0001**
SGA (0-7)	6.15 ± .71	4.88 ± 1.45	3.01 ± 1.65	<.0001* <.0001** <.0001 [†]
Body mass index (kg/m²)	28.09 ± 3.75	22.86 ± 3.78	22.96 ± 3.76	< .0001* < .005 [†]
Hemoglobin (g/dL)	11.09 ± 2.05	12.07 ± 1.22	10.96 ± 2.42	.091
Ferritin (mg/dL)	436.94 ± 245.32	412.34 ± 298.59	433.37 ± 396.77	.944
Blood urea nitrogen (mg/dL)	67.55 ± 20.64	67.84 ± 21.09	61.00 ± 25.90	.684
Creatinine (mg/dL)	9.71 ± 2.35	7.87 ± 3.00	8.74 ± 3.28	<.05†
Calcium (mg/dL)	9.30 (1.03)	9.15 (1.45)	9.40 (1.45)	.991
Phosphorus (mg/dL)	5.34 ± 1.56	4.73 ± 0.92	4.96 ± 2.31	.284
Ca x P product	49.16 ± 16.05	43.28 ± 13.28	49.35 ± 24.95	.343
Total cholesterol (mg/dL)	182.78 ± 48.15	191.96 ± 47.23	162.85 ± 32.88	.340
Triglycerides (mg/dL)	194.63 ± 72.63	179.80 ± 93.09	123.85 ± 48.05	.108
Uric acid (mg/dL)	6.61 ± 1.95	6.69 ± 1.38	6.51 ± 1.53	.970
Albumin (g/dL)	4.22 ± 0.25	3.96 ± 0.47	3.38 ± 0.48	<.0001* <.0001** <.05 [†]
PTH (pg/mL)	406.79 ± 330.87	328.38 ± 207.79	327.01 ± 370.12	.573
C-reactive protein (mg/dL)	7.94 ± 4.6	8.52 ± 7.1	16.51 ± 6.33	< .0001* < .001**

BDI: Beck Depression Inventory, PSQI: Pittsburgh Sleep Quality Index, SGA: Subjective Global Assessment Score

* p values for differences between patients with no depressive symptoms and patients with moderate-severe depressive symptoms

** p values for differences between patients with mild-moderate depressive symptoms and patients with moderate-severe depressive symptoms

† p values for differences between patients with no depressive symptoms and patients with mild-moderate depressive symptoms

and the malnutrition-inflammation score was independent risk factor for depression in peritoneal dialysis patients (27). Similarly Micozkadioglu et al reported an association between depressive findings and malnutrition-inflammation complex in hemodialysis patients (28). Supporting these findings, there is some evidence that major depression is accompanied by activation of the inflammatory response system, and that proinflammatory cytokines may play a role in the etiology of depression (29, 30), namely the relationship between depressive symptoms and inflammation may be bi-directional. Proinflammatory cytokines, which are commonly increased in ESRD patients, are responsible for increased protein catabolism, poor oral intake, and malnutrition in maintenance dialysis patients (31). Accordingly, proinflammatory cytokine-induced chronic inflammation could be a common cause of depression and malnutrition in chronic HD patients. It is plausible that depressive symptoms and inflammatory cytokines have direct or indirect effects on specific areas of the brain and interact in several central nervous system pathways to change appetite, food intake, and nutritional status (32, 33).

Depending on our findings we think that depression and sleep disorders are important factors influencing the nutritional status and could be independent risk factors for malnutrition in elderly ESRD patients. However it still seems that these psychological problems as well as malnutrition might be results of chronic inflammation in these patients. So we think that elderly ESRD patients with malnutrition should be well assessed for presence of any inflammatory status and/or psychological-sleep disorders that might accompany this clinical stiuation. Antidepressive treatment might improve nutritional status in this group of patients but chronic inflammation still seems to be the major problem.

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