

Nutritional approach outcomes in palliative care patients with malnutrition

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ABSTRACT

Aims: In this study, we aimed to investigate the effects of dietary patterns on activity and performance scores, symptom levels, laboratory parameters, anthropometric measurements and mortality in palliative care patients with high malnutrition risk score.

Methods: The effects of enteral and parenteral feeding methods, which are the predominant feeding methods, on admission-discharge laboratory parameters, performance scales, activity indices, anthropometric measurements, symptom scales, infection status, duration of antibiotic use and mortality were evaluated in 103 patients aged 18 years and older who were hospitalized in the palliative care service.

Results: When evaluated on the scales, it was seen that enteral fed patients had better initial scores than parenteral fed patients. There was no difference between the nutrition groups in the mean length of stay in the palliative care service and the frequency of infection, whereas the duration of antibiotic use was longer, transfer to the intensive care unit (74% vs. 12%, $p < 0.05$) and mortality rates (13% vs. 4%, $p < 0.05$) were significantly higher in the parenterally fed group.

Conclusion: The data from this study showed that in palliative care patients with malnutrition, patients with lower activity and performance scores required more parenteral nutrition and that the need for parenteral nutrition, edema and poor performance at baseline were independent predictors of mortality.

Keywords: Enteral nutrition, nutritional support, palliative care, parenteral nutrition

INTRODUCTION

'Palliative care' is a discipline that aims to improve the quality of life by providing physical, social, psychological, and spiritual support to patients, their relatives or caregivers at the end stage of diseases such as cancer with limited treatment options.¹ Scales showing the current status of palliative care and disease prognosis were used. Some of these include the Palliative Performance Score (PPS), Palliative Prognostic Score (PaP), Palliative Prognostic Index (PPI), Barthel Activity Index (BAI), and Karnofsky Performance Scale (KPS).

After nutritional status assessment in palliative care units, patients in need of nutritional support should be identified, appropriate nutritional treatment administered individually, and the results monitored.² In patients with a high malnutrition risk score or malnutrition, a decrease in the duration of hospitalization, a decrease in the complications of the current disease, and improvement in general well-being and activity scores are expected with appropriate nutritional therapy.

In this study, we aimed to investigate the effect of nutritional therapy on laboratory parameters, including inflammatory markers, anthropometric measurements, activity and performance status, and symptom levels determined using appropriate scales, as well as the effect of nutritional therapy on hospitalization duration and mortality in patients aged ≥ 18 years with high malnutrition risk scores who were followed up in a palliative care unit.

METHODS

This study was designed as a prospective, follow-up study. Ethical approval was obtained from the Non-interventional Clinical Researches Ethics Committee of Kırıkkale University (Date: 09.10.2019, Decision No: 2019.10.05). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study included 103 patients aged 18 years and older who were hospitalized for at least three days or more in the palliative care service of the department of internal medicine between

15.11.2019 and 15.03.2020 and who had a risk score of 3 or higher determined by Nutritional Risk Screening-2002 (NRS-2002) during hospitalization. The exclusion criteria were as follows: patients under 18 years of age, patients hospitalized for less than three days, patients with a risk score of less than 3 as determined by the NRS-2002 during hospitalization, and patients with limb amputation.

Background information, smoking history, diseases that caused hospitalization, comorbidities that were not the primary reason for hospitalization, diet, presence of infection, duration of antibiotic use, height, body weight, and BMI (body-mass index) were recorded for each patient. CBC (complete blood count) parameters including Hb (hemoglobin), Plt (platelet), LEU (leukocytes), NEU (neutrophils), LYM (lymphocytes), glucose, CRP (C-reactive protein), TC (total cholesterol), TGL (triglycerides), HDL (high density lipoprotein), LDL (low density protein), BUN (blood urea nitrogen), Cr (creatinine), Na (sodium), K (potassium), Alb (albumin), Ca (calcium) and P (phosphorus) were measured during hospitalization. CBC parameters, including Hb, Plt, LEU, NEU, LYM, glucose, BUN, Cr, Na, K, and Alb values, were recorded at discharge from the palliative care service. CRP/alb, Neu/Lym (NLR), and Plt/Lym (PLR) ratios were calculated at admission and discharge as markers of infection. At admission and before discharge from the palliative service, anthropometric measurements, including KPS, BAI, Edmonton Symptom Assessment Scale (ESAS), PPS, NRS-2002, Upper mid-arm circumference (UMAC), and calf circumference of all patients were determined and recorded. The ESAS, which evaluates the severity of the symptoms of pain, sadness, insomnia, fatigue, nausea, anorexia, anxiety, well-being, and shortness of breath with a score between 0 and 10 points, was administered by the researcher in accordance with the statements of patients and their relatives. The PPS, which included the patient's symptoms, ability to perform daily activities, dependency status, and medical care needs, and the PPS, which included the sub-headings of self-care, nutrition, mobility, activity/disease finding, and level of consciousness, were also completed and recorded by the researcher. The comorbidity status of patients was determined during hospitalization using the Charlson Comorbidity Score.³

Within the first three days of hospitalization, the nutritional regimen was determined by the Hospital Nutrition Team in accordance with the ESPEN (European Society for Clinical Nutrition and Metabolism guidelines). Enteral nutrition was the preferred method of nutrition in all patients, and a parenteral nutrition regimen was initiated in patients with chronic intestinal failure, failure in adequate enteral nutrition intake within 48 hours, and patients who did not accept or tolerate oral intake.⁴ A feeding route in which more than 60% of the patients' daily nutritional needs were met was considered the dominant feeding route. The manner in which patients left the palliative care service was recorded.

The effects of enteral and parenteral nutrition, which were the predominant feeding methods for all patients hospitalized in the palliative care service and included in the study, on laboratory parameters, performance scales, activity indices, anthropometric measurements, symptom scales, infection status, duration of antibiotic use, and mortality were evaluated.

Statistical Analysis

SPSS Statistics 21.0 (IBM SPSS Inc, Chicago) was used for statistical analysis. Descriptive statistics related to continuous data were expressed as mean±standard deviation. A value of p<0.05 was considered statistically significant. Whether the data were normally distributed was checked by Kolmogorov-Smirnov test and Shapiro-Wilk test. Bonferroni correction was applied for multiple comparisons.

RESULTS

A total of 103 patients were included in the study. During their hospitalization in the palliative care service, 73 patients received predominantly enteral nutrition (9 with nasogastric tube, 6 with percutaneous endoscopic gastrostomy (PEG), 58 with oral nutritional fluids) and 30 patients received predominantly parenteral nutrition (5 with central parenteral nutrition and 25 with peripheral parenteral nutrition). Demographic data and statistical results are given in **Table 1**. No significant difference was found between enteral and parenteral nutrition groups in admission UMAC and Calf circumference measurements.

Table 1. Demographic data of patients hospitalized in palliative care service with malnutrition according to dietary patterns

	Enterally feeding patients n=73	Parenterally feeding patients n=30	Total n=103	p
Age (years)	67.7±14.9	73.9±12.5	69.5±14.4	0.07
Gender (%)				
Female	32 (44)	10 (33)	42 (40)	0.44
Male	41 (56)	20 (67)	61 (60)	
Height (cm)	164.0±10.9	167.4±10.4	165.7±10.7	0.14
Body weight (kg)	59.0±11.7	60.5±12.5	62.2±12.1	0.89
Smoking (%)				
Yes	41 (56)	19 (63)	60 (58)	0.66
No	32 (44)	11 (37)	43 (41)	
BMI (kg/m ²)	22.0 ± 4.6	21.5±4.2	21.8±4.4	0.79
Reason for hospitalization (%)				
Malnutrition	17 (23)	5 (17)	22 (21)	0.32
Infection	35 (48)	19 (63)	54 (53)	0.34
Pain	16 (22)	3 (10)	19 (18)	0.08
General condition disorder	5 (7)	3 (10)	8 (8)	0.28

Data are presented as the mean±SD or number (percentage ratio). BMI: Body-mass index

The distribution of comorbid diseases of palliative care patients receiving enteral and parenteral nutrition is shown in **Table 2**. Hospitalization and discharge laboratory values of the patients are shown in **Table 3**.

better in enteral fed patients ($p < 0.01$) (**Table 4**). All symptoms of patients hospitalized in the palliative care service who received enteral nutrition therapy were significantly reduced at discharge (**Table 5**).

When the two feeding groups were compared, it was found that baseline PPS and KPS scores and BAI were significantly

No significant difference was found between the enteral and parenteral nutrition palliative care patient groups in terms of

Table 2. Distribution of comorbid diseases of palliative care patients receiving enteral and parenteral nutrition

Comorbid disease	Enterally feeding patients n=73	Parenterally feeding patients n=30	Total n=103	p
Diabetes mellitus (%)	24 (32)	9 (30)	33 (32)	0.95
Hypertension (%)	49 (67)	21 (70)	70 (67)	0.95
Anemia (%)	58 (79)	27 (90)	85 (83)	0.32
Cerebrovascular accident (%)	11 (15)	5 (17)	16 (16)	0.84
Dementia (%)	16 (21)	10 (33)	26 (25)	0.33
Malignancy (%)	39 (53)	16 (53)	55 (53)	0.99
Coronary artery disease (%)	22 (30)	11 (37)	33 (32)	0.68
Heart failure (%)	14 (19)	10 (3)	17 (17)	0.23
Acute kidney injury (%)	16 (21)	6 (20)	22 (21)	0.99
Chronic kidney disease (%)	18 (24)	5 (17)	23 (22)	0.53
Pulmonary thromboembolism (%)	6 (8)	2 (7)	8 (8)	0.78
COPD (%)	24 (32)	11 (37)	35 (34)	0.88
Pressure sore (%)	16 (21)	17 (57)	33 (32)	<0.01
Infection (%)	58 (79)	27 (90)	85 (83)	0.32
Edema (%)	26 (36)	20 (67)	46 (45)	<0.01
Charlson Comorbidity Score*	8.1±0.4	9.3±0.6	8.4±3.1	0.75
Duration of antibiotic use (days)*	13±1	19±3	15±12	0.02

Data are presented as numbers (percentage ratios) or mean±SD. COPD: Chronic obstructive pulmonary disease

Table 3. Comparison of hospitalization and discharge laboratory parameters in patients receiving enteral and parenteral nutrition therapy in palliative care service

Laboratory parameters	Enterally feeding patients n=73			Parenterally feeding patients n=30			P*
	Hospitalization	Discharge	p	Hospitalization	Discharge	p	
Hemoglobin g/dl	11.1±2.1	11.0±1.7	0.51	11.2±0.4	10.2±0.3	0.03	0.03
Leukocytes x10 ³ /mm ³	10.8±10.5	9.1±4.5	0.11	10.7±2.8	10.8±1.3	0.26	0.07
Neutrophils x10 ³ /mm ³	7.2±5.2	6.5±3.6	0.22	6.5±0.6	9.5±1.2	0.44	0.02
Lymphocytes x10 ³ /mm ³	1.3±0.8	1.6±0.8	<0.01	1.2±0.1	1.0±0.1	0.22	<0.01
Neutrophils/ lymphocytes	8.1±1.0	5.1±0.5	<0.01	8.1±1.6	17.1±4.7	<0.01	<0.01
Platelets x10 ³ /mm ³	284±147	282±134	0.42	258±16	191±21	0.50	0.02
Platelet/lymphocyte	498±241	197±12	<0.01	325±62	257±41	0.15	0.61
Creatinine mg/dl	1.2±0.4	1.2±0.5	0.21	1.3±0.7	1.2±0.6	0.29	0.15
Urea mg/dl	33±10	27±12	0.12	31±9	32±6	0.18	0.54
Glucose mg/dl	113±23	110±30	0.33	108±25	106±24	0.27	0.19
Sodium mmol/L	135±4	138±3	0.18	134±5	133±4	0.12	0.14
Potassium mmol/L	4.0±0.5	3.9±0.8	0.22	3.9±0.6	4.1±0.3	0.35	0.18
Phosphorus mmol/L	2.5±1.0	2.7±0.8	0.30	2.4±0.8	2.3±1.0	0.28	0.32
Calcium mmol/L	7.7±0.9	7.9±0.8	0.21	7.6±0.7	7.7±0.8	0.22	0.24
CRP mg/L	70.9±66.1	52.7±58.1	0.01	67.8±8.6	87.5±9.8	0.15	0.01
Albumin g/dl	3.1±0.6	3.0±0.6	0.01	3.1±0.6	2.5±0.6	<0.01	0.01
CRP/albumin	24.6±2.8	19.0±2.7	0.03	23.3±3.2	39.2±5.2	<0.01	<0.01
Total cholesterol mg/dl	178±9	-	-	158±10	-	-	0.19
Triglycerides mg/dl	144±8	-	-	116±10	-	-	0.38
HDL mg/dl	40±2	-	-	43±3	-	-	0.42
LDL mg/dl	105±8	-	-	90±8	-	-	0.29

Data are presented as mean±SD. *Statistical significance level of the comparison of the difference in hospitalization-discharge in parenterally fed patients and the difference in hospitalization-discharge in enteral fed patients. CRP: C-reactive protein, HDL: High density lipoprotein, LDL: Low density protein

Table 4. Comparison of hospitalization and discharge performance scores in palliative care patients receiving enteral and parenteral nutrition therapy

Performance scales	Enterally feeding patients n=73			Parenterally feeding patients n=30			p*
	Hospitalization	Discharge	p	Hospitalization	Discharge	p	
Barthel Activity Index	40±3	41±3	0.06	30±3	15±3	<0.01	<0.01
Palliative Performance Score	42±2	44±3	0.17	20±2	7±3	<0.01	<0.01
Karnofsky Performance Score	42±2	44±2	0.23	29±2	15±3	<0.01	<0.01

Data are presented as mean±SD. *Statistical significance level for the comparison of the difference between hospitalization and discharge in patients receiving parenteral nutrition and the difference between hospitalization and discharge in patients receiving enteral nutrition

Table 5. Comparison of hospitalization and discharge symptoms in enteral and parenteral fed palliative care patients with the Edmonton Symptom Assessment Scale

Symptom	Enterally feeding patients n=73			Parenterally feeding patients n=30			p*
	Hospitalization	Discharge	p	Hospitalization	Discharge	p	
Pain	5±2	2±1	<0.01	6±1	3±1	<0.01	0.88
Fatigue	6±1	4±2	<0.01	6±1	5±2	<0.01	<0.01
Nausea	5±2	2±1	<0.01	6±1	3±1	<0.01	0.46
Sadness	5±2	2±1	<0.01	7±1	6±1	0.07	<0.01
Concern	6±2	4±1	<0.01	7±1	7±2	0.16	<0.01
Insomnia	4±2	2±1	<0.01	5±2	4±2	0.02	<0.01
Feeling bad	6±2	4±2	<0.01	7±1	7±2	0.02	<0.01
Loss of appetite	5±2	3±2	<0.01	7±1	6±2	0.03	<0.01
Shortness of breath	4±1	2±1	<0.01	5±2	5±2	0.88	<0.01
Skin/nail changes	4±1	2±1	<0.01	4±1	4±1	0.10	<0.01
Mouth sores	4±1	2±1	<0.01	4±2	4±2	0.09	0.16
Numbness in the hands	3±1	2±1	<0.01	3±1	3±1	0.20	0.18

Data are presented as mean±SD. *Statistical significance level for the comparison of the difference between hospitalization and discharge in patients receiving parenteral nutrition and the difference between hospitalization and discharge in patients receiving enteral nutrition

mean length of stay in the ward. While most of the enterally fed patients were discharged (84%), the majority of patients requiring parenteral nutrition were admitted to the intensive care unit (73%). The mortality rate during hospitalisation was significantly higher in patients receiving parenteral nutrition (13% versus 4%, p<0.01).

When the two groups were compared in terms of baseline BAI, KPS, PPS scores, all baseline activity index and performance scores were significantly higher in the surviving group. While enteral nutrition was the predominant mode of nutrition in surviving patients, parenteral nutrition was the predominant mode of nutrition in deceased patients.

The effect of categorical variables such as type of nutrition, presence of pressure sores and presence of edema on mortality was tested by logistic regression analysis. It was found that the mortality rate was 22.8 times higher in parenteral fed patients compared to enteral fed patients and the need for parenteral nutrition had a significant effect on the increase in mortality (p<0.01). Mortality rate was 3.6 times higher in patients with edema compared to patients without edema and the presence of edema had a significant effect on mortality (p=0.02). On the other hand, although the presence of pressure sores was significantly higher in the deceased patient group, it did not lead to a statistically significant increase in mortality.

When the baseline activity index, performance scores and length of hospital stay were included in the regression analysis, in addition to the need for parenteral nutrition and edema, patients' baseline low KPS score emerged as

a variable affecting mortality. Although the presence of comorbidities and comorbidity scores did not differ between those who survived and those who died, edema continued to be an independent determinant of mortality when acute kidney injury, chronic kidney disease and congestive heart failure, which may be related to edema, were included in the regression analysis.

In the comparison between surviving (n=4) and deceased (n=26) parenteral fed patients, anemia and edema increased mortality (p=0.019 for anemia and p=0.001 for edema). In the enterally fed patient group, high leukocyte count (p=0.033), infection (p=0.013) and pulmonary embolism (p=0.044) were found to increase mortality in the comparison between survivors (n=61) and deaths (n=12). The most common causes of death were multi-organ failure and sepsis, followed by respiratory failure and myocardial infarction.

DISCUSSION

The study included 103 patients aged 18 years and older who were hospitalized for at least three days or more in the palliative care service of the department of internal medicine. 73 patients received predominantly enteral nutrition and 30 patients received predominantly parenteral nutrition. The patients included in the study were heterogeneous in terms of underlying diagnoses and disease severity. When comparing enteral and parenteral nutrition groups, no significant difference was observed in serum biomarkers and inflammatory parameters during hospitalisation; however, the initial performance scores of patients who could not

tolerate enteral nutrition and required parenteral nutrition were significantly worse. In this group of patients with impaired baseline performance scores who subsequently required parenteral nutrition, an increase in intensive care requirements and in-hospital mortality rates was observed. The need for parenteral nutrition was associated with higher mortality rates and intensive care requirements.

Palliative care aims to reduce symptoms and improve the quality of life of patients and their relatives.⁵ Early detection of malnutrition and implementation of effective nutritional treatments are important for hospitalized patients, especially in palliative care services. The current disease status is decisive in the choice of diet. Orrevall et al.⁶ showed that nausea, vomiting, and gastrointestinal obstruction are the most common reasons for parenteral nutrition in palliative care patients.

In a study of 384 patients, elevated CRP, NEU, NLR, and PLR decreased mean survival, but only neutrophil count was an independent predictor of mean survival in multivariate analyses.⁷ In our study, no significant effect of inflammatory markers, including baseline Leu, Neu, CRP, CRP/albumin, PLR, and NLR, on mortality was observed in malnourished patients hospitalized in palliative care.

One study showed that KPS scores were worse in the group requiring parenteral nutrition at discharge from the palliative care service than in enteral-fed patients.⁸ In our study, no significant improvement was observed in BAI, PSS or KPS scores in patients who were able to receive enteral nutrition upon discharge and who had better performance scores at baseline. In patients who could not tolerate enteral nutrition during hospitalisation, had lower performance scores and required parenteral nutrition, deterioration in performance scores and overall health status was observed.

In a study of 446 patients, it was found that the amount of edema decreased significantly in patients who responded to nutritional therapy and gained weight gain.⁹ In another study, 21% of participants received less than 50% of the calculated daily energy requirement, and the rate of edema development was six times higher in these patients, although the amount of weight lost at discharge was slightly higher than that in other patients.¹⁰ Although we found diet and edema to be independent determinants of mortality, we did not evaluate the relationship between malnutrition or daily caloric intake and edema.

In a study of 2099 patients, the prevalence of pressure sores was 12.9%.¹¹ The nutritional status of 27% of patients was inadequate, and a significant difference was found between the nutritional status of patients with and without pressure sores.¹¹ The fact that pressure sores were observed more frequently in patients receiving parenteral nutrition therapy in our study may be related to their poor nutritional status, activity, and performance scores. When all patients included in the study were evaluated, although the proportion of patients with pressure sores and edema was significantly higher in the deceased patient group than in the surviving patient group, the effect of pressure sores on mortality was not significant in contrast to the presence of edema.

Elke et al.¹² reported that enteral and parenteral nutrition had no effect on mortality in patients hospitalized in intensive care units. In a meta-analysis, mortality and complication rates, except for infection, were found to be similar in enteral-fed and parenteral-fed patients.¹³ In a study conducted in Japan with 3750 non-cancer patients, mortality rates were significantly lower in the enteral-fed patient group.¹⁴ In our study, in the multiple regression analysis evaluating the factors affecting mortality in palliative care patients receiving nutritional therapy due to malnutrition, it was found that the need for parenteral nutrition had an independent effect on the increase in mortality ($p < 0.01$) and that the mortality rates in the parenterally fed patient group were 22.8 times higher than in the enterally fed patients. The rates of transfer to the intensive care unit and in-hospital mortality were found to be higher in patients with low performance scores who could not tolerate enteral feeding during admission. Although the enteral and parenterally fed patient groups did not differ in terms of infection frequency, the duration of antibiotic use was significantly shorter, and discharge rates were higher in the enterally fed patient group. In addition, high leukocyte count and the presence of infection were found to be significant determinants of mortality in enterally fed patients.

Limitations

The heterogeneous nature of the patients included in the study in terms of underlying diagnoses and disease severity makes it difficult to attribute the data to a specific disease group. Although our study associates the need for parenteral nutrition with low performance scores, there is a limitation in that this situation may stem from the initial clinical severity of the patients rather than a cause-and-effect relationship.

CONCLUSION

The results of this study on palliative care patients with malnutrition support studies reporting that mortality is significantly lower in patients who can be fed enterally than in those who require parenteral nutrition. In conclusion, the data obtained from this study showed that patients with malnutrition and low activity and performance scores in palliative care require more parenteral nutrition. In our study, an increase in mortality rates was observed in patients with low performance scores who required parenteral nutrition. The need for parenteral nutrition was associated with higher mortality rates and intensive care requirements.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval was obtained from the Non-interventional Clinical Researches Ethics Committee of Kırıkkale University (Date: 09.10.2019, Decision No: 2019.10.05).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights—including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

Concept: H.K., İ.K.; Design: M.T., H.K.; Supervision: H.K.; Resources: M.T., H.K.; Materials: M.T., H.K.; Data Collection and/or Processing: M.T., İ.K.; Analysis and/or Interpretation: H.K., İ.K.; Literature Search: H.K., İ.K.; Writing: M.T.; Critical Review: H.K., İ.K.

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