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About the Journal

Clinical Science of Nutrition is an international, peer-reviewed, open access journal. It publishes research articles, reviews, case reports, and letters to the editor on all aspects of nutrition and dietetics.

Clinical Science of Nutrition is a triannual journal that is published in English in April, August, and December.

Abstracting and indexing

Clinical Science of Nutrition is covered in the following abstracting and indexing databases;

- TR-Index
- EBSCO
- Gale
- CNKI

Aims and Scope

The journal aims to contribute to the literature by publishing high impact content and become one of the leading publications of the field while functioning as an open discussion forum on significant issues of current interest. Clinical Science of Nutrition also aims to have significant input in emphasizing the increasing importance of clinical nutrition in Turkey and the region, identifying the effects of differences between societies on study results in a clearer way and converting clinical applications into scientific publications as well as forming a bridge between West and East.

The scope of Clinical Science of Nutrition includes original research articles, review articles, case reports, conference reports, and letters to the editor as well as editorials, abstracts from international and national congresses, panel meetings, conferences and symposia. As an online-only publication, in addition to traditional manuscript submissions, Clinical Science of Nutrition is also able to process video, audio and interactive software submissions. Authors are encouraged to submit their content in the most appropriate medium to best convey their findings to the audience of Clinical Science of Nutrition.

The journal covers all aspects of nutrition and dietetics including prevalence of malnutrition and its effects on clinical results; nutritional support and delivery methods and their advantages and disadvantages; nutritional support products and their side effects; immune system and nutritional support; ERAS protocol and nutritional support; home parenteral and enteral nutrition; nutrition support teams and their necessity, challenges and potential solutions of nutritional support.

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Complications of enteral tube-fed patients at home

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ABSTRACT

Objective: Home enteral tube feeding (HETF) is a life-sustaining and vital form of treatment for medically stable patients who have functional gastroinstestinal tracts and do not need hospitilazation but can't meet their nutritional requirements with oral intake. However, this intervention is not without its complications. This study aimed to assess the nutritional status of adult patients undergoing HETF and to investigate the prevalence of nutrition-related complications.

Methods: A prospective study was conducted, with each HETF patient monitored over a 28-day period. Data regarding patient descriptive characteristics, HETF characteristics, biochemical parameters, anthropometric measurements, and occurrences of nutrition-related complications were collected and analyzed.

Results: The study enrolled 22 patients, comprising 10 males (mean age: 68.8±11.7 years) and 12 females (mean age: 67.7±13.7 years). Malnutrition was observed in 31.8% of patients. Inadequate intake of dietary fiber, vitamin D, vitamin K, potassium, and magnesium was noted. Gastrointestinal complications were prevalent in 77.3% of patients, followed by metabolic complications in the same proportion, mechanical complications in 50% of cases, and pressure ulcers in 45.5% of cases. Factors such as gender, age, feeding position, feeding route, type of product consumed, and fiber content did not significantly influence the incidence of gastrointestinal complications.

Conclusions: Complications associated with HETF were common among the study population. The findings underscore the necessity of a specialized multidisciplinary team to ensure effective HETF management and to mitigate or prevent associated complications.

Keywords: home enteral tube feeding, malnutrition, complication, nutritional status

Introduction

Enteral tube feeding (ETF) is a life-sustaining nutritional therapy in which nutrients are delivered directly into the gastrointestinal tracts via tubes to stable patients with functional gastrointestinal tracts but unable to meet their nutritional requirements with oral intake.[1,2] Keeping the patient in the hospital only for nutritional therapy is inappropriate in terms of bio-psycho-social and economically costly for health institutions and society.[3] Therefore, Home Enteral Tube Feeding (HETF) treatment can be applied to the patients who are medically stable and do not need hospitalization.[2]

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HETF has been described as a safe and effective nutritional intervention since its introduction in the 1970s.[4] The annual prevalence of HEN in the US has increased from 463 per million population in 1995 to 1385 per million in the most recent report published in 2017.[5,6] According to the British Artificial Nutrition Research (BANS) 2018 report, there are 6270 HETF patients in the UK.[7]

Although HETF is a safe and effective nutritional intervention, there are problems encountered during treatment. It can lead to complaints that are not life-threatening , but negatively affect the quality of life due to long-term use, and sometimes patients have to apply to a health center or even to stay in hospitals.[8-10] These complaints can be grouped under three headings as metabolic, mechanical, and gastrointestinal complications.[11] Although prevalence levels vary[3,12-14], these problems appear to be similar globally.

This study was planned and conducted to determine the nutritional status of adult patients receiving HETF in the province of Mardin, Turkey and to evaluate their nutrition-related complications.

Material and Method

Ethical requirements

Ethics committee approval was obtained for the study from Mardin Artuklu University (dated 01/11/2021 and numbered 2021/2). In addition, necessary permissions were obtained from the Mardin Provincial Health Directorate to access patient information. Informed consents were obtained from the caregivers since the cognitive status of the patients were not suitable for communication.

Main Points

- Enteral tube feeding is a life-sustaining nutritional therapy.
- Patients fed with an enteral tube may have inadequate macro and micronutrient intakes.
- Patients fed with enteral tube at home have a high incidence of gastrointestinal complications.
- A multidisciplinary team (physician, dietitian, nurse) needed for an effective Home Enteral Tube-Fed patients.

Study design

The study is a prospective study[15] with 28 days of follow-up enteral tube-fed patients at home between November 2021 and June 2022.

Participants

Patients living in Mardin and fed with enteral tube at home for more than one month were included in the study. They were registered by Home Health Services (HHS) and over 18 years of age when tube feeding was started. Their informed consent were duly obtained before the collection of data. The sample size was not calculated in the study and all patients who could be reached between November 2021 and June 2022, who met the inclusion criteria and agreed to participate in the study (consent was obtained from the caregiver) were included in the study. Individuals for whom accurate data could not be obtained from the caregiver and for whom anthropometric measurements were not possible due to extremities deformity were excluded.

The number of registered adult patients receiving HETF in November 2021 is 40. 18 patients were excluded from the study, including four patients with extremities deformities, three refused to participate in the study, nine died, one hospitalized, and one due to lack of information. The study was completed with 22 patients.

Data collection

Patients were visited at their homes. The data were collected by the researcher through a questionnaire prepared based on the literature. Demographic, health status, and nutritional information (24-hour food consumption record, route of administration, etc.) were obtained from caregivers. Biochemical findings were obtained from the HHS patient file (the most recent laboratory results in the last three months).

The results of the biochemical tests were obtained from HHS patient files. Since the biochemical tests prescribed by the doctors were not the same for all the patients, it was not possible to use them for the metabolic complications and malnutrition evaluation by biochemical tests; the malnutrition status were evaluated using BMI values. Sarcopenia evaluated by calf circumference (CC). Anthropometric measurements (knee height (KH), mid upper arm circumference (MUAC), calf circumference) were measured by the researcher in accordance with the technique. Body weight and height were calculated with

the formula developed for bedridden patients using CC and MUAC measurements, and then BMI was calculated by formula.[16]

MUAC was evaluated using the table of reference values published by the National Center for Health Statistics (NCHS) for men and women aged 18-74. CC evaluated using a cut-off value of 31 cm.[17] BMI value was assessed using ESPEN BMI cut-off points.[18]

The Bristol Stool Scale and a literature-based complication form prepared by us were used to determine complications related to tube feeding. Caregivers were asked to record daily the patient's stool type according to the Bristol Stool Scale, stool frequency, and complications for 28 days.

Metabolic complications were defined as follows: dehydration, fluid intake less than 90.0% of the daily estimated requirement, hyperglycemia glycemia>200 mg/dL, and hypoglycemia glycemia<80 mg/dL.[19] Other biochemical findings were evaluated using reference intervals.

Gastrointestinal complications were defined as follows: constipation, no defecation for more than 72 hours, or stool type 1, type 2 according to the Bristol Stool Scale, or use of medication for constipation, diarrhea, more than three defecations per day, or stool type as type 6 or type 7 according to the Bristol Stool Scale.

Energy, macro and micro nutrient and fluid requirements

Daily energy requirements were estimated using the Harris Benedict formula and Long Activity Factors.[20] Daily protein requirements were estimated as 1.2-2.0 g/kg/day by adjusting the patient's biochemical findings, body weight, and skin integrity in line with ESPEN recommendations.[21] The daily energy and protein requirements were determined after the necessary adjustments were made in body weight, taking into account the BMI value of the person.[22,23] The daily fluid requirement was taken as 30 ml/kg/day.[24]

It was considered sufficient if the patients daily energy, protein, and fluid intakes are more than 90.0% of the estimated requirements. Daily micronutrient and fiber intakes were considered adequate if average intakes equal to or above the estimated requirement.[22] The Turkey Dietary Guidelines (TUBER) 2022 data were used as a reference for micronutrients and fiber.[25]

Statistical analysis

After the data collection process was completed, all data were analyzed using the SPSS Statistics for Windows, version 25.0. Kruskal Wallis test, Mann Whitney U test and chi-square test were used for the non-parametric hypothesis tests. In all analyses, $p<0.05$ was accepted as a statistically significant value.

Results

The study was completed with 22 patients. The mean age of the patients was 68.2 ± 12.6 years. The indications for HETF of all patients were chronic neurological diseases. The descriptive data of the patients and antropometric measurements are shown in Table 1 and Table 2. HETF-related complications of patients are shown in Table 3. In the table, *"number of affected patients"* refers to the number of patients who have complications, and *"number of events"* refers to the number of complications.

The energy and nutrients intakes of the patients and the rates of meeting their estimated requirements are given in Table 4. In the table, the individual consumption of the patients and the rate of meeting their estimated requirements are not shown. Instead, the group's average consumption (mean ± SD; median: lower–upper) and the average rate of meeting their estimated requirements are given. Almost all of the patients with HETF received more than 100% of TUBER reference values of vitamins A, E, C, B1, B2, B6, niacin, pantothenic acid, biotin, and phosphorus, iron, zinc, copper and molybdenum. Energy intake of 27.3% of the patients, protein intake of 45.5%, potassium and fiber intake of all (five patients were on a fiber-free diet), vitamin D, vitamin K, and magnesium intake of more than 65%, folic acid, sodium, manganese and selenium intake of more than 50%, vitamin B12, calcium, and iodine intake of more than 25% were found to be at an inadequate intake level. When the average intakes of the group were evaluated, it was determined that dietary fiber, vitamin D, potassium, and magnesium intakes were inadequate.

It was found that the variables did not affect the occurrence of gastrointestinal complications (Table 5).

Table 1. The descriptive data of the patients

Descriptive Data	Male	Female	Total
Number of patients			
Number (%)	10 (45,5)	12 (54,5)	22 (100)
Age (years)			
Mean±SD	68,8 ± 11,7	67,7 ± 13,7	68,2 ± 12,6
Median (min-max)	72,5 (49,0-87,0)	70,0 (44,0-88,0)	72,5 (44,0-88,0)
≥ 70 years (Number (%))	6 (60,0)	6 (50,0)	12 (54,5)
Medical diagnosis* (n, %)			
Neurological diseases	10 (45,5)	12 (54,5)	22 (100)
Oncological diseases	0 (0,0)	1 (8,3)	1 (4,5)
Diyabetes Mellitus	3 (30,0)	2 (16,7)	5 (22,7)
State of consciousness (n, %)			
Conscious	5 (50,0)	3 (25,0)	8 (36,4)
Unconscious	5 (50,0)	9 (75,0)	14 (63,6)
Mobility status (n, %)			
Bedridden	9 (90,0)	11 (91,7)	20 (90,9)
Not-bedridden	1 (10,0)	1 (8,3)	2 (9,1)
Enteral nutrition routes of administration			
PEG	8 (80,0)	9 (75,0)	17 (77,3)
NG	2 (20,0)	3 (25,0)	5 (22,7)
Methods of enteral nutrition administration			
Bolus	10 (100,0)	10 (83,3)	20 (91,0)
Intermittent	0 (0,0)	1 (8,3)	1 (4,5)
Continuous	0 (0,0)	1 (8,3)	1 (4,5)
Duration of HETF			
< 1 year	1 (10,0)	5 (41,7)	6 (27,3)
≥ 1 and < 5 years	6 (60,0)	6 (50,0)	12 (54,5)
≥ 5 and < 10 years	2 (20,0)	0 (0,0)	2 (9,1)
≥ 10 years	1 (10,0)	1 (8,3)	2 (9,1)
Mean±SD (years)	4,3±3,4	2,2±2,8	3,1±3,2
Median (min-max) (years)	3,5 (0,5-12,0)	1,8 (0,5-10,5)	2 (0,5-12)
Pump			
Yes	0 (0,0)	1 (8,3)	1 (4,5)
No	10 (100,0)	11 (91,7)	21 (95,5)

* More than one answer was received, and percentages were calculated based on the number n.
PEG: Percutaneous endoscopic gastrostomy, NG: Nasogastric

Table 1. Continued

Descriptive Data	Male	Female	Total
Probe washing (pre and post)			
Yes	10 (100,0)	12 (100,0)	22 (100,0)
No	0 (0,0)	0 (0,0)	0 (0,0)
Position during and after feeding			
Lying position (0°)	1 (10,0)	1 (8,3)	2 (9,1)
Semi-recumbent position (30-45°)	3 (30,0)	10 (83,4)	13 (59,1)
Sitting position (90°)	6 (60,0)	1 (8,3)	7 (31,8)
Type of nutritional product			
Isocaloric	3 (30,0)	3 (25,0)	6 (27,3)
High energy and protein	1 (10,0)	3 (25,0)	4 (18,2)
Immunonutrition	4 (40,0)	3 (25,0)	7 (31,8)
Diabetes/hyperglycemia specific	2 (20,0)	3 (25,0)	5 (22,7)
Fiber content			
Yes	7 (70,0)	10 (83,3)	17 (77,3)
No	3 (30,0)	2 (16,7)	5 (22,7)
Use of blenderized tube food			
Yes	4 (40,0)	2 (16,7)	6 (27,3)
No	6 (60,0)	10 (83,3)	16 (72,7)
Stool type			
Mean ± SD	3,1±1,5	3,0±1,2	3,1±1,3
Median (min-max)	Type4 (Type1-Type5)	Type3,5 (Type1-Type4)	Type4 (Type1-Type5)
Defecation frequency (day)			
Mean ± SD	2,5±2,1	2,1±1,4	2,3±1,7
Median (min-max)	1,2(1,1-7,0)	1,7(1,0-6,0)	1,5(1,0-7,0)

* More than one answer was received, and percentages were calculated based on the number n.
PEG: Percutaneous endoscopic gastrostomy, NG: Nasogastric

Discussion

Nutrition-related complications in addition to the nutritional status of patients receiving HETF were evaluated prospectively. ESPEN guidelines recommend that life expectancy should be longer than one month for initiation of HETF. In our study, the median HETF duration of the patients was 2 (0.5-12 years) years. The median HETF duration and distribution were found to be significantly longer than those reported by other publications. Paccagnella et al. reported in a prospective study, 261, 251 and 788 HETF days for adult patients with neurovascular, neurodegenerative and head trauma, respectively.[26] Folwarski et al.[27] reported 615 HETF days (IQR 1275 days) for adult patients with neurological disease. Cawsey et al.[28] reported 187 HETF days.

In our study, the most commonly used enteral access for feeding was PEG (77.3%) and bolus (91%) administration. This finding is consistent with ESPEN guidelines, which recommend PEG for long-term enteral nutrition or PEJ tube when PEG is contraindicated.[4] The British Artificial Nutrition Research (BANS) 2018 report reported that 80% of patients had gastrostomy in the feeding route.[7]

Table 2. Anthropometric evaluations of the patients

Anthropometric measurement	Assessment	Male	Female	Total
		Number (%)	Number (%)	Number (%)
BMI (kg/m^2)				
Mean ±SD		21,5±2,8	25,2±4,6	23,5±4,3
Age <70				
BMI < 20	Malnutrition	1 (10,0)	1 (8,3)	2 (9,1)
20 ≤ BMI ≤ 27	Normal	3 (30,0)	3 (25,0)	6 (27,3)
BMI < 27	Obese	0 (0,0)	2 (16,7)	2 (9,1)
Age ≥70				
BMI < 22	Malnutrition	4 (40,0)	1 (8,3)	5 (22,7)
22 ≤ BMI ≤ 27	Normal	2 (20,0)	1 (8,3)	3 (13,6)
BMI < 27	Obese	0 (0,0)	4 (33,3)	4 (18,2)
Calf circumference				
Mean ±SD		26,5±4,4	29,0±3,7	27,9±4,2
< 31		8 (80,0)	9 (75,0)	17 (77,3)
≥ 31		2 (20,0)	3 (25,0)	5 (22,7)
MUAC percentile values				
Mean ±SD		26,4±2,8	27,9±3,5	27,2±3,2
≤ 5		4 (40,0)	2 (16,7)	6 (27,3)
> 5 and ≤ 25		6 (60,0)	4 (33,3)	10 (45,5)
> 25 and < 75		0 (0,0)	5 (41,7)	5 (22,7)
≥ 75		0 (0,0)	1 (8,3)	1 (4,5)

BMI: Body mass index, MUAC: Mid-upper arm circumference

It is not recommended the use of blenderized tube food in patients receiving HETF by ESPEN; because the macro and micronutrient content is not standardized and increses the contamination risk.[4] In our study, the use of blenderized tube food in addition to the industrial nutrition product was found to be 27.3% but low than literature.[29,30]

The mean BMI of the patients was 23.5±4.3 kg/m^2. When evaluated according to BMI, it was found out that 31.8% of the patients were malnourished. Our results were similar with the other studies.[31,32] The decrease in muscle mass, muscle strength and physical performance is defined as sarcopenia.[33] When the CC measurement was evaluated, it was seen that 77.3% of the patients are sarcopenic.[34]As a result of the evaluation by using the NCHS 18-74 age group precentile table, it was observed that 72.7% of the patientes had MUAC measurements below the 25th percentile. Other studies also have found the similiar results.[35,36] Decrease in body muscle mass and protein stores are explained by the malnutrition, the absence or decrease in physical activity, and the advanced age. Furthermore, the nutritional products are nutritionally less bioavailability compared to natural foods.

The mean energy intake of the patients in our study was found as 25±6 kcal/kg/day. Mean energy intake of patients were found 24 kkcal/kg/day and 24.4±8 kcal/kg/day in the litarature.[26,27] According to ESPEN guidelines, daily energy requirement varies between 25-30 kcal/kg/day during the recovery period.[37] In line with the recommendation, when studies evaluating adult patients receiving HETF are examined, it is seen that the average daily energy intake is 25-30 kcal/kg/day, similar to the result of our study.[3,24,26-28,38] In our study, daily estimated energy and protein requirements of the patients were

Table 3. The HETF-related complications of patients

Complications	Male (n:10)		Female (n:12)		Total (n:22)	
	Number of affected patients	Number of events	Number of affected patients	Number of events	Number of affected patients (%)	Number of events
Metabolic Complications						
Hyperglycemia[a] (n:20)	1	1	2	1	3 (15,0)	1
Hyponatremia[a] (n:20)	5	1	1	1	6 (30,0)	1
Hypokalemia[a] (n:20)	0	0	1	1	1 (5,0)	1
Hypocalcemia[a] (n:20)	2	1	1	1	3 (15,0)	1
Dehydration[b]	1	-	1	-	2 (9,1)	-
Malnutrition[c]	5	-	2	-	7 (31,8)	-
Mecanic Complications						
Obstruction of feeding tube	2	1	1	1	3 (13,6)	1
Dislocation of the feeding tube	0	0	1	1	1 (4,5)	1
Peristomal leak (chronic)[d]	7		1		8 (36,4)	
Granulation tissue[d]	0		1		1 (4,5)	
Gastrointestinal Complications						
Nausea/Vomiting	1 1 2	3 5 30	1	3	2 (9,1) 1 (4,5) 2 (9,1)	3 5 30
Total number of patients (%)	4 (40,0)		1 (8,3)		5 (22,7)	
Abdominal distention[e]	1 1	2 4	1	13	1 (4,5) 1 (4,5) 1 (4,5)	2 4 13
Total number of patients (%)	2 (20,0)		1 (8,3)		3 (13,6)	
Constipation	2 2 1 2	1 5 8 9	1 2 1 3	1 3 6 9	3 (13,6) 2 (9,1) 2 (9,1) 1 (4,5) 1 (4,5) 5 (22,7)	1 3 5 6 8 9
Total number of patients (%)	7 (70,0)		7 (58,3)		14 (63,6)	
Diarrhea	2	1	2	1	4 (18,2)	1
Total number of patients (%)	2 (20,0)		2 (16,7)		4 (18,2)	
Complications associated with skin integrity						
Pressure ulcer[d]	6		4		10 (45,5)	
Total number of patients (%)	6 (60,0)		4 (33,3)		10 (45,5)	

a: Metabolic complications were evaluated using the most recent biochemical data from the last three months in the HHS patient file. Percentages are given based on the number of patients for whom the relevant parameter was evaluated.
b: Hydration was evaluated using the rate of meeting the estimated daily fluid requirement.
c: Malnutrition was assessed using BMI.
d: Persistent complications during the 28-day follow-up
e: Number of days with complications

Table 4. The energy and nutrients intakes of the patients and the rates of meeting their estimated requirements

Energy and nutrients	Total		
	Mean ±SD	Median (min-max)	%
Energy (kcal/kg/day)	25,0±6,0	24,4 (13,8-42,9)	96,9±17,9
Protein (g/kg/gün)	1,3±0,4	1,2 (0,7-2,3)	97,1±27,9
Fiber (g/day)	13,4±8,8	16 (0-24)	53,5±35,0
Fluid (mL/day)	2479,3±700,7	2445 (1620-4841,5)	142,8±36,0
Vitamin A (mcg/day)	1234,3±476,4	1278 (0-2000,0)	174,5±72,8
Vitamin D (mcg/day)	13,9±11,6	10,7 (6,3-61,6)	81,8±79,8
Vitamin E (mg/day)	33,9±15,2	30,8 (13,7-84,0)	279,3±128,4
Vitamin K (mcg/day)	92,1±26,7	84,6 (59,4-162,0)	90,2±35,3
Vitamin C (mg/day)	172,1±77,6	160,0 (79,2-425,6)	168,4±72,8
Folate (mcg/day)	332,4±110,5	313,8 (180,0-608,0)	100,0±33,9
Thiamine (mg/day)	2,0±0,4	2,0 (1,1-2,8)	175,0±38,0
Riboflavin (mg/day)	2,4±0,6	2,4 (1,3-3,5)	197,1±57,2
Vitamin B6 (mg/day)	2,4±0,6	2,4 (1,4-3,4)	153,7±45,8
Vitamin B12 (mcg/day)	5,1±2,0	4,9 (2,2-9,8)	117,9±43,9
Niacin (mg NE/day)	21,3±7,3	20,2 (8,0-33,0)	211,0±58,6
Pantothenic acid (mg/day)	9,4±3,4	9,7 (2,6-16,0)	186,3±69,2
Biotin (mcg/day)	71,5±23,7	64,5 (28,8-140,0)	176,4±61,0
Potassium (g/day)	1998,3±498,4	1977,3 (936,0-2916,0)	41,1±10,3
Sodium (g/day)	1279,1±375,1	1334,1 (550,0-2140,0)	98,2±29,1
Calcium (mg/day)	1167,3±377,4	1151,0 (640,0-2451,6)	119,0±40,0
Phosphor (mg/day)	958,8±232,8	986,0 (468,0-1440,0)	170,5±41,6
Magnesium (mg/day)	290,0±67,0	282,9 (151,2-460,0)	89,6±24,0
Iron (mg/day)	18,1±4,8	17,5 (9,4-25,6)	157,5±43,3
Zinc (mg/day)	18,1±4,2	18,0 (8,6-30,0)	170,5±44,1
Manganese (mg/day)	3,6±1,2	3,4 (1,8-5,3)	121,1±42,1
Copper (mcg/day)	2237,1±549,8	2267,5 (1008,0-3400,0)	156,6±47,4
Iodine (mcg/day)	178,9±47,6	186,9 (79,2-300,0)	119,2±31,7
Selenium (mcg/day)	75,9±23,6	67,7 (36,0-120,0)	108,3±33,9
Molybdenum (mcg/day)	163,9±54,5	155,0 (72,0-320,0)	252,2±83,8

met at an average rate of 96.9±17.9% and 97.1±27.9%, respectively, and were at an adequate intake level. On the other hand, 27.3% of the patients had insufficient energy intake and 45.5% protein intakes. Narasimhan et al.[32] it was reported that the estimated daily energy needs of the patients were met by an average of 93.1±19.7%, and the estimated daily protein requirements were met by an average of 98.5±21.7%. Baker et al.[22] found that the estimated daily energy requirement was met by 63±15% and protein by 61±15%. Potassium and fiber intake were insufficient for all patients. Vitamin D, vitamin K and magnesium intake were insufficient for more than 65% patients. Folic acid, sodium, manganese and selenium intake were insufficient for more than 50% patients.

Table 5. Gastrointestinal complications related to patient characteristics, type and management of HETF

Complication	Variable	*p-value*
Nausea/Vomiting	Gender	0,135*
	Age	0,367***
	Product type[a]	0,582**
	Fiber content[b]	0,820***
	Route of administration[c]	1,000***
	Feeding position[d]	0,629**
Abdominal distention	Gender	0,571*
	Age	0,774***
	Product type[a]	0,397**
	Fiber content[b]	0,880***
	Route of administration[c]	0,595***
	Feeding position[d]	0,320**
Constipation	Gender	0,675*
	Age	0,539***
	Product type[a]	0,119**
	Fiber content[b]	0,649***
	Route of administration[c]	0,352***
	Feeding position[d]	0,960**
Diarrhea	Gender	1,000*
	Age	0,045***
	Product type[a]	0,484**
	Fiber content[b]	0,940***
	Route of administration[c]	0,907***
	Feeding position[d]	0,225**

*: Chi-square test, **: Kruskal Wallis H test, ***: Mann Whitney U test
a: Isocaloric, High energy and protein, Immunonutrition, Diyabetes/hyperglycemia specific
b: Fiber content, Fiber free
c: PEG: Percutaneous endoscopic gastrostomy, NG: Nasogastric
d: Lying position, Semi-recumbent position, Sitting position

Vitamin B12, calcium and iodine intake were insufficient for more than 25% patients. Vitamin A, E, C, B1, B2, B6, niacin, pantothenic acid, biotin, phosphorus, iron, zinc, copper and molybdenum intake were found to exceed 100% of the TUBER reference values for all patients. Similarly, Folwarski et al.[39] found that the vitamin levels consumed in their study were above the RDA level. In addition, it was reported that approximately 50% of the patients had insufficient intake of vitamin D, vitamin B3, vitamin B5 and vitamin B9, more than 20% of the patients had vitamin K intake, and the majority of patients had insufficient intake of sodium, chlorine, calcium and fluoride. Iacone et al.[40] reported that more than 50% of the patients had insufficient intake of fiber, potassium, fluorine and vitamin K. Considering the results of our study and publications, it is thought that there is a need for further studies and regulation of nutritional content of nutritional products in patients with long-term HETF.

In the literature, the incidence of peristomal leakage in patients receiving HETF is 60%, the incidence of granulation tissue development is 67%, the incidence of tube occlusion is 30%, the need for tube replacement is 26%, and the incidence of constipation is 63%. It is observed that the incidence of vomiting increased to 40%, the incidence of diarrhea to 34%, and the incidence of abdominal distension to 50%.[12,13,24,35] In our study peristomal leakage, granulation tissue, tube

obstruction (opened by the caregiver), tube replacement, constipation, vomiting/regurgitation and diarreha are reported 36%, 4.5%, 13.6 %, 4.5%, 63.6%, 22.7% and, 18.2% respectively. It is thought that the high average ages of the patients, 91% of them being bedridden, constantly feeding a liquid diet, low fiber consumption (5 patients were fed with fiber-free products) are effective in the development of constipation. In the study, 45.5% of the patients developed pressure ulcers. Pressure ulcers were seen higher rates than other studies (20%,18.7%).[35,41] It is thought that this may be due to the high rate of bed dependency (91%); 72.7% of the patients were fed with enteral tube at home for more than 1 year.

In our study, hyperglycemia was found in 15% of the patients, dyslipidemia in 33.3%, hyponatremia in 30%, hypocalcemia in 15%, and hypoproteinemia in 23.1%. Lim et al.[42] hyperglycemia and hypoglycemia developed in 12.1% of the patients, electrolyte disturbances were reported in 5.1% of the patients, and vitamin and trace element deficiency was reported in 4%. In the study, it is seen that the biochemical tests observed outside the reference range are not clearly given. De Luis et al.[36] reported hypernatremia in 6 patients (1.3%) and hyperglycemia in 33 patients (4.8%) in a study where they prospectively evaluated the incidence and characteristics of all adult patients fed enterally at home (with oral enteral and enteral tube) for 12 years. However, complications in the study were not categorized separately for patients fed oral enteral and tube enteral feeding. The effects of gender, age, product type, fiber content, feeding route and feeding position on the incidence of gastrointestinal complications were evaluated in the study. It was found that the incidence of complications was not affected for all variables. Similarly, Barone et al.[8] found that age and gender did not affect complication rates. In contrast, Wanden-Berghe et al.[3] found that gender, feeding position, route of feeding, type of product, and fiber content significantly affected the incidence of gastrointestinal complications. Our findings show that complications were common in the study group, but did not exceed the rates stated in the literature. The prevalence of complications in the study can be attributed to the fact that the patients evaluated within the scope of the study were old and had multiple diseases, 72.7% were fed with enteral tube for more than 1 year, 91% were bedridden, and their follow-up and evaluation could not be performed by an HHS/ multidisciplinary team.[4,8,32,43,44]

The study has some limitations. The results of the biochemical tests were obtained from HHS patient files. Since the biochemical tests prescribed by the doctors were not the same for all the patients, it was not possible to use them for the malnutrition evaluation; the malnutrition status were evaluated using only BMI values and metabolic complications were not evaluated all the patients.

Counclusion

It was found out that complications were common. A multidisciplinary team (physician, dietitian, nurse) specialized in this field is needed in Home Health Services for an effective HETF and prevention/reduction of complications. It is considered important and necessary to include a dietitian in the team in order to detect the risk of malnutrition in the early period, to make necessary interventions in nutrition therapy, to prevent malnutrition, to increase the quality of life, and to reduce medical expenses.

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Ethical approval

This study has been approved by the Mardin Artuklu University Non-Interventional Clinical Research Ethics Committee (approval date 01.11.2021, number 2021/2). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: NNA, ZPÖ; data collection: NNA, KA; analysis and interpretation of results: NNA, KA; draft manuscript preparation: NNA. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Asiedu GB, Carroll K, Griffin JM, Hurt RT, Mundi M. Home enteral nutrition: Use of photo-elicitation to capture patient and caregiver experiences. *Health Sci Rep*. 2018;1:e56. [Crossref]
2. Martin K, Gardner G. Home Enteral Nutrition: Updates, Trends, and Challenges. *Nutr Clin Pract*. 2017;32:712-721. [Crossref]
3. Wanden-Berghe C, Patino-Alonso MC, Galindo-Villardón P, Sanz-Valero J. Complications Associated with Enteral Nutrition: CAFANE Study. *Nutrients*. 2019;11:2041. [Crossref]
4. Bischoff SC, Austin P, Boeykens K, et al. ESPEN practical guideline: Home enteral nutrition. *Clin Nutr*. 2022;41:468-488. [Crossref]
5. Howard L, Ament M, Fleming CR, Shike M, Steiger E. Current use and clinical outcome of home parenteral and enteral nutrition therapies in the United States. *Gastroenterology*. 1995;109:355-365. [Crossref]
6. Mundi MS, Pattinson A, McMahon MT, Davidson J, Hurt RT. Prevalence of Home Parenteral and Enteral Nutrition in the United States. *Nutr Clin Pract*. 2017;32:799-805. [Crossref]
7. Stratton R, Evill R, Smith T. BANS Report 2018: Home Enteral Tube Feeding (HETF) in Adults (2010-2015). 2018. Available at: https://www.bapen.org.uk/pdfs/reports/bans/bans-report-2018.pdf (Accessed on May 29, 2023).
8. Barone M, Viggiani MT, Amoruso A, et al. Influence of age and type of underlying disease on complications related to home enteral nutrition: a single Italian center experience. *JPEN J Parenter Enteral Nutr*. 2014;38:991-995. [Crossref]
9. Velapati SR, Schroeder SE, Schroeder DR, et al. Use of Home Enteral Nutrition in Malnourished Post-Bariatric Surgery Patients. *JPEN J Parenter Enteral Nutr*. 2021;45:1023-1031. [Crossref]
10. Crosby J, Duerksen DR. A prospective study of tube- and feeding-related complications in patients receiving long-term home enteral nutrition. *JPEN J Parenter Enteral Nutr*. 2007;31:274-277. [Crossref]
11. Strollo BP, McClave SA, Miller KR. Complications of Home Enteral Nutrition: Mechanical Complications and Access Issues in the Home Setting. *Nutr Clin Pract*. 2017;32:723-729. [Crossref]
12. McNamara EP, Flood P, Kennedy NP. Enteral tube feeding in the community: survey of adult patients discharged from a Dublin hospital. *Clin Nutr*. 2000;19:15-22. [Crossref]
13. Crosby J, Duerksen D. A retrospective survey of tube-related complications in patients receiving long-term home enteral nutrition. *Dig Dis Sci*. 2005;50:1712-1717. [Crossref]
14. Bozciğeroğlu RD, Karadağ A. Evde Enteral Tüple Beslenen Hastaların Yaşadıkları Sorunlar ve Bu Sorunlara Yönelik Yapılan Girişimlerin Belirlenmesi. *Hemşirelikte Araştırma Geliştirme Derg*. 2012;14:15-26.
15. Sönmez V, Alacapınar FG. Örneklendirilmiş Bilimsel Araştırma Yöntemleri. 8th ed. Ankara: ANI Yayıncılık; 2021: 49.
16. Pekcan G. Yetişkin bireylerde antropometrik yöntemlerle beslenme durumunun değerlendirilmesi. In: Mercanlıgil S, Dağ A, editors. Hastalıklarda Diyet Tedavisi. Ankara: Türkiye Diyetisyenler Derneği Yayını; 2013: 1-18.
17. Rolland Y, Lauwers-Cances V, Cournot M, et al. Sarcopenia, calf circumference, and physical function of elderly women: a cross-sectional study. *J Am Geriatr Soc*. 2003;51:1120-1124. [Crossref]
18. Cederholm T, Bosaeus I, Barazzoni R, et al. Diagnostic criteria for malnutrition - An ESPEN Consensus Statement. *Clin Nutr*. 2015;34:335-340. [Crossref]
19. Orlandoni P, Peladic NJ, Di Rosa M, et al. The outcomes of long term home enteral nutrition (HEN) in older patients with severe dementia. *Clin Nutr*. 2019;38:1871-1876. [Crossref]
20. Ruggeri E, Giannantonio M, Agostini F, Ostan R, Pironi L, Pannuti R. Home artificial nutrition in palliative care cancer patients: Impact on survival and performance status. *Clin Nutr*. 2020;39:3346-3353. [Crossref]
21. Gomes F, Schuetz P, Bounoure L, et al. ESPEN guidelines on nutritional support for polymorbid internal medicine patients. *Clin Nutr*. 2018;37:336-353. [Crossref]
22. Baker ML, Halliday V, Robinson P, Smith K, Bowrey DJ. Nutrient intake and contribution of home enteral nutrition to meeting nutritional requirements after oesophagectomy and total gastrectomy. *Eur J Clin Nutr*. 2017;71:1121-1128. [Crossref]
23. Thibault R, Abbasoglu O, Ioannou E, et al. ESPEN guideline on hospital nutrition. *Clin Nutr*. 2021;40:5684-5709. [Crossref]
24. Silver HJ, Wellman NS, Arnold DJ, Livingstone AS, Byers PM. Older adults receiving home enteral nutrition: enteral regimen, provider involvement, and health care outcomes. *JPEN J Parenter Enteral Nutr*. 2004;28:92-98. [Crossref]
25. T.C. Sağlık Bakanlığı Türkiye Halk Sağlığı Kurumu. Türkiye beslenme rehberi 2022 (TÜBER). Ankara: T.C. Sağlık Bakanlığı Yayını; 2022. Available at: https://hsgm.saglik.gov.tr/depo/birimler/saglikli-beslenme-ve-hareketli-hayat-db/Dokumanlar/Rehberler/Turkiye_Beslenme_Rehber_TUBER_2022_min.pdf

26. Paccagnella A, Baruffi C, Pizzolato D, et al. Home enteral nutrition in adults: a five-year (2001-2005) epidemiological analysis. *Clin Nutr*. 2008;27:378-385. **[Crossref]**
27. Folwarski M, Kłęk S, Zoubek-Wójcik A, et al. Home Enteral Nutrition in Adults-Nationwide Multicenter Survey. *Nutrients*. 2020;12:2087. **[Crossref]**
28. Cawsey SI, Soo J, Gramlich LM. Home enteral nutrition: outcomes relative to indication. *Nutr Clin Pract*. 2010;25:296-300. **[Crossref]**
29. Wong A, Banks MD, Bauer JD. A Survey of Home Enteral Nutrition Practices and Reimbursement in the Asia Pacific Region. *Nutrients*. 2018;10:214. **[Crossref]**
30. Epp L, Lammert L, Vallumsetla N, Hurt RT, Mundi MS. Use of Blenderized Tube Feeding in Adult and Pediatric Home Enteral Nutrition Patients. *Nutr Clin Pract*. 2017;32:201-205. **[Crossref]**
31. Przekop Z, Milewska M, Szostak-Węgierek D, Panczyk M, Sobocki J. GLIM-Defined Malnutrition in Patients with Head and Neck Cancer during the Qualification Visit for Home Enteral Nutrition. *Nutrients*. 2022;14:502. **[Crossref]**
32. Narasimhan R, Patel JM, Velapati SR, Elfadil OM, Hurt RT, Mundi MS. The use of calorically dense enteral formulas in adult home enteral nutrition population in a tertiary care center: A retrospective analysis. *Int J Acad Med*. 2020;6:294. **[Crossref]**
33. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010;39:412-423. **[Crossref]**
34. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48:601. **[Crossref]**
35. Volkert D, Pauly L, Stehle P, Sieber CC. Prevalence of malnutrition in orally and tube-fed elderly nursing home residents in Germany and its relation to health complaints and dietary intake. *Gastroenterol Res Pract*. 2011;2011:247315. **[Crossref]**
36. De Luis DA, Izaola O, Cuellar LA, Terroba MC, Cabezas G, De La Fuente B. Experience over 12 years with home enteral nutrition in a healthcare area of Spain. *J Hum Nutr Diet*. 2013;26(Suppl 1):39-44. **[Crossref]**
37. Kreymann KG, Berger MM, Deutz NEP, et al. ESPEN Guidelines on Enteral Nutrition: Intensive care. *Clin Nutr*. 2006;25:210-223. **[Crossref]**
38. Gao X, Zhang Y, Zhang L, et al. Effect of Home Enteral Nutrition on Nutritional Status, Body Composition and Quality of Life in Patients With Malnourished Intestinal Failure. *Front Nutr*. 2021;8:643907. **[Crossref]**
39. Folwarski M, Kłęk S, Zoubek-Wójcik A, et al. Foods for Special Medical Purposes in Home Enteral Nutrition-Clinical Practice Experience. Multicenter Study. *Front Nutr*. 2022;9:906186. **[Crossref]**
40. Iacone R, Scanzano C, Alfonsi L, et al. Daily macro and micronutrient supply for patients on total enteral nutrition: are they in keeping with new dietary reference intakes for the Italian population? *Nutr Metab Cardiovasc Dis*. 2014;24:e15-e17. **[Crossref]**
41. Villar Taibo R, Martínez Olmos MÁ, Bellido Guerrero D, et al. Epidemiology of home enteral nutrition: an approximation to reality. *Nutr Hosp*. 2018;35:511-518. **[Crossref]**
42. Lim ML, Yong BYP, Mar MQM, et al. Caring for patients on home enteral nutrition: Reported complications by home carers and perspectives of community nurses. *J Clin Nurs*. 2018;27:2825-2835. **[Crossref]**
43. Alivizatos V, Gavala V, Alexopoulos P, Apostolopoulos A, Bajrucevic S. Feeding Tube-related Complications and Problems in Patients Receiving Long-term Home Enteral Nutrition. *Indian J Palliat Care*. 2012;18:31-33. **[Crossref]**
44. Hucl T, Spicak J. Complications of percutaneous endoscopic gastrostomy. *Best Pract Res Clin Gastroenterol*. 2016;30:769-781. **[Crossref]**

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Evaluation of dysphagia in patients with neurological diagnosis with the Turkish EAT-10 questionnaire

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ABSTRACT

Objective: The aim of this study was to assess the prevalence of dysphagia in neurological patients using the Turkish Eating Assessment Tool-10 (EAT-10) screening test. Dysphagia is common in neurovascular, neurodegenerative, and neuromuscular diseases.

Methods: Three hundred neurological patients [stroke, multiple sclerosis (MS), dementia, Guillain Barre Syndrome (GBS), cerebral palsy (CP), myastenia gravis (MG)] were evaluated using the Turkish EAT-10 test. Data were analysed using IBM SPSS21, and $p<0.05$ was considered significant.

Results: The mean EAT-10 score was 6.22, with 69% of patients classified as dysphagic. The prevalence of dysphagia was highest in MG (100%) and dementia (83.32%). The severity of dysphagia was greater in women and patients aged 65+ ($p<0.001$).

Conclusions: Dysphagia is common in neurological patients. Due to the cost and limitations of instrumental methods, the Turkish EAT-10 test is recommended as a practical and reliable alternative for screening. Women and people over 65 may be at higher risk for dysphagia.

Keywords: swallowing, neurological dysphagia, EAT-10

Introduction

Swallowing is the is the process of transferring food from the mouth to the stomach. The swallowing function incvolves both voluntary and involuntary movements. In order for the swallowing function to occur safely, the muscles involved in the swallowing function must be able to produce the appropriate force and contract at the appropriate rate and sequence. To achieve this, processes must occur that ensure harmonious sensorimotor coordination. The anatomical structures involved in swallowing are also related to our breathing and speech. This situation increases the impact of swallowing on vital functions. Swallowing function is closely related to malnutrition, dehydration, choking and quality of life.[1-3]

Swallowing consists of oral, pharyngeal and oesophageal phases. While conscious and unconscious movements are combined in the oral phase, unconscious movements are more dominant in the pharyngeal and oesophageal phases. If the structures cannot safely perform the necessary activities in any phase of these three stages dysphagia, also known as swallowing disorder or difficulty swallowing may occurs. Dysphagia can develop

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due to anatomical problems and damage to areas related to swallowing in the cerebral cortex or neuromuscular transmission.[4]

Swallowing is a very sensitive neurological function and neurogenic dysphagia is a consequence of neurological diseases. Studies have shown that post-stroke dysphagia is associated with increased risk of mortality or dependency, pneumonia, decreased quality of life, prolonged hospital stay, and health care costs.[5,6] Dysphagia may also accompany the neurodegeneration process in Parkinson's patients with bulbar dysfunction. Dysphagia has been associated with malnutrition and aspiration pneumonia in Parkinson's patients.[7] In neurological autoimmune diseases such as multiple sclerosis (MS), myastenia gravis (MG) and Guillain-Barre Syndrome (GBS), dysphagia may develop due to involvement of yhe muscle, brainstem, neuromuscular junction and corticospinal tract.[8]

Causes such as decreased tongue control, failure of the swallow reflex, decreased laryngeal closure and sensory loss have been associated with swallowing problems in people with MS.[9] In cerebral palsy (CP), a neurodevelopmental disorder, impaired neck and trunk stabilisation, muscle weakness and muscle strength imbalance may prevent effective swallowing.[10] In patients with dementia, cumulative changes caused by age-related sensorimotor changes, loss of muscle mass and strength, and loss of connective tissue elasticity may lead to dysphagia.[11] Determining the status dysphagia in the course of neurological diseases is important for managing the prognosis and complications of the disease. It is possible to encounter dysphagia with different aetiologies in the clinic. However, it is diffucult to assess dysphagia with objective tests because it requires specialised equipment and experts. On the other hand, the use of a test with proven validity and reliability, such as the Turkish EAT-10, is valuable for both immediate use and for detecting dysphagia. Although there are many studies on the Turkish EAT-10 test, its use for screening purposes in the clinic is not common. This study supports the use of the Turkish EAT-10 for clinical screening in patients with different neurological diagnoses. Our study aims to integrate the Turkish EAT-10 test into the clinical workflow in dysphagia screening so that dysphagia of different aetiologies can be directed to appropriate treatment and managed. Our study aims to raise awareness of dysphagia and will contribute to the literature in this direction.

Main Points

- Orally fed patients can face significant challenges due to dysphagia symptoms.
- Dysphagia is often observed in neurological patients. Following a neurological diagnosis, patients can be rapidly screened for dysphagia using the Turkish EAT-10 test.
- Risk of dysphagia varies according to gender and age-related factors

Material and Method

For our study, demographic characteristics and the Turkish EAT-10 questionnaire were applied to patients diagnosed with stroke, MS, dementia, GBS, CP, MG based on medical history, clinical examination and laboraty findings (magnetic resonance imaging, electroencephalography, electromyography) in neurological outpatient clinics and neurological intensive care units. The study design was cross-sectional and prevalence-based. We conducted our study between May 2022 and October 2022. Ethical approval for the study was obtained from the Non-invasive Ethics Committee of Dicle University, protocol number 301 dated 14.04.2022.

The EAT-10 questionnaire was used to determine the severity of oropharyngeal dysphagia and its validity and reliability were determined by Belafsky et al.[12] In the EAT-10 test, translated into Turkish by Demir et al., each question is scored between '0' (no problem) and '4' (severe problem). The maximum possible total score is calculated as 40 points.[13] According to the scoring of the test, a score of 3 or more is considered abnormal and the presence of dysphagia should be reported.[14] The internal consistency of the Turkish EAT-10 was found to be high, with a Cronbach's alpha value of 0.90 for test and 0.91 for test-retest repeatability; an alpha value of 0.70 to 0.80 indicates satisfactory consistency, 0.8 to 0.9 good consistency, and a value greater than 0.9 indicates excellent consistency.[13] The sample consisted of patient from the neurology department, neurology intensive care unit patients and neurology outpatient clinic of Dicle University Hospital. For our study, we tried to determine the sample size by using the G-Power 3.1 package program. Accordingly, the study was planned to include a minimum of 200 patients, according to the power analysis performed with a type I error of 0.05, power of 0.80 and effect size of 0.20. Given the missing data, the study was stopped when data were collected from a total of 300 participants.

There was no gender discrimination in the people who participating in the study. As the questions of the EAT-10 test used in the study consist of questions related to swallowing experience, only orally fed individuals were included in the study. In the analysis of the results, the mean ± standard deviation, median, minimum and maximum values were used for the numerical results of the descriptive statistics. The distributions of grouped measurements were assessed using the normality test. Mann-Whitney U test and Kruskal-Wallis test were used to detect differences in numerical results. Values with $p<0.05$ were considered statistically significant.

Criteria for inclusion of volunteers in research:

- 18 years old or over 18 years old
- Oral feeding
- Have one of the following diagnoses; stroke, Parkinson's disease, MS, dementia, GBS, CP, MG
- The volunteer for the study
- Have the cognitive ability to answer the survey questions

Exclusion criteria:

- Feeding by nasogastric (NG) Tube, percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ)
- History of laryngeal surgery
- History of chemotherapy/radiotherapy to the head and neck
- Having at a cognitive level that prevents you from answering survey questions
- Not volunteering for the study

These exclusions were made to ensure the validity of the survey responses, as the Turkish EAT-10 test requires patient participation and understanding and may not be applicable in these populations. In addition, as the data collection tool measured patient-perceived dysphagia based on swallowing experience, patients who were not fed orally could not be included.

Data collection

Patients were informed of the study. After verbal and written informed consent was obtained, a survey form was completed with demographic information about the patient. This form collected baseline information about the patient, including name, age, gender, medical diagnosis, body mass index (BMI), and dietary information. The EAT-10 Swallowing Function Screening Test form was explained to the patient as a swallowing assessment tool, the questions were asked one at a time, and the patient was asked to rate his or her dysphagia from 0 to 4 points for each question, with increasing severity.

Data analysis

Demographic information and EAT-10 data of the patients were analyzed using the IBM SPSS21 package. Mann-Whitney-U test and Kruskal-Wallis test were used to analyse the data for independent group means. Results were presnted as arithmatic mean±standard deviation. $p<0.05$ was considered significant. Normality: Mean ± standard deviation, median, minimum and maximum values were used for numerical results of descriptive statistics in the analysis of the results. The distributions of grouped measurements were assessed using the normality test. Mann-Whitney U test and Kruskal-Wallis test were used to detect differences in numerical outcomes that were not normally distributed. Values with $p<0.05$ were considered statistically significant.

Results

Of the patients who participated in the study, 52% were male. 47.5% of the patients participating in the study were 65 years or older (Table 1). 75.7% of patients in the study had a neurological diagnosis of less than one year. 10% of neurological patients in the study repoted having a history of pneumonia during the course of their illness (Table 2).

When the body mass indexes of the patients included in the study were calculated, 0.3% were underweight (18,5 kg/m^2 and below), 32.6% were normal weight (18,5-24,9 kg/m^2), 40.3% were overweight (25-29,9 kg/m^2), 26% were obese (30-39,9 kg/m^2), 0.7% were morbidly obese (40 kg/m^2) (Figure 1).

Our study includes a diverse cohort of neurological patients with conditions such as stroke, MS, Parkinson' disease, dementia, Guillain-Barre syndrome, CP and MG (Figure 2). The prevalence of dysphagia within these subgroups provides valuable, under-researched insights into specific patient populations.

According to the assessment 69.67% of stroke patients; 80% of Parkinson's patients; 60.8% of MS patients; 83.32%

of dementia patients; 60% of CP patients; 44.4% of GBS patients; 100% of MG patients included in the study were in the dysphagia group (Figure 3). Since a score of 3 or more on the EAT-10 Test is considered abnormal, 69% of the patients scored within the abnormal range. The item with the highest score in the survey was "I have difficulty swallowing solid food", while the item with the lowest score was "I feel pain when swallow".

Changes in the patients' responses to the survey according to demographic characteristics were analysed using the IBM SPSS21 package. According to the results of the normality test applied to the data, it was determined that the data were not normally distributed (Figure 4)

According to the non-parametric test results, the perceived severity of dysphagia was statistically significantly higher in women and those over 65 years of age ($p<0.05$). According to the test results, the time of neurological diagnosis and history of pneumonia were not statistically significantly associated with perceived dysphagia severity ($p>0.05$) (Table 3).

There was no statistically significant difference in the severity of dysphagia as perceived by the test questions according to the patients' body mass index ($p>0.05$) (Table 4).

Table 1. Demographic characteristics

Demographic Category	Number
Gender (Female)	144
Gender (Male)	156
Age (18-64)	157
Age (65+)	143

Table 2. Medical history

Medical Category	Number
Pneumonia Positive	30
Pneumonia Negative	270
Diagnosis <1 year	227
Diagnosis ≥ 1 year	73

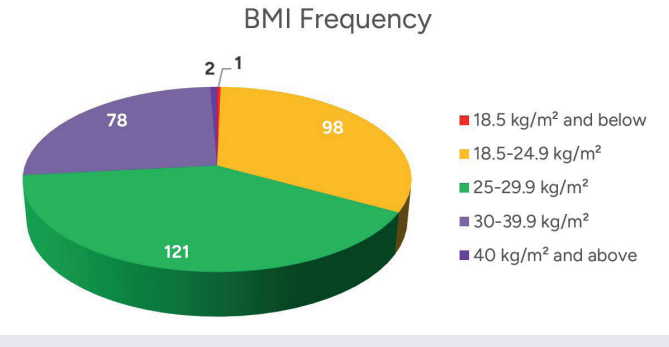

Figure 1. BMI distribution graph of patients included in the study

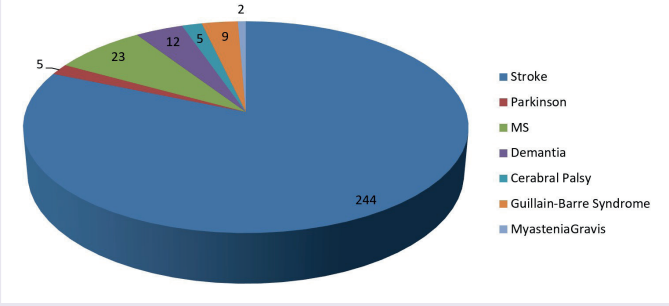

Figure 2. Diagnosis distribution frequency of patients

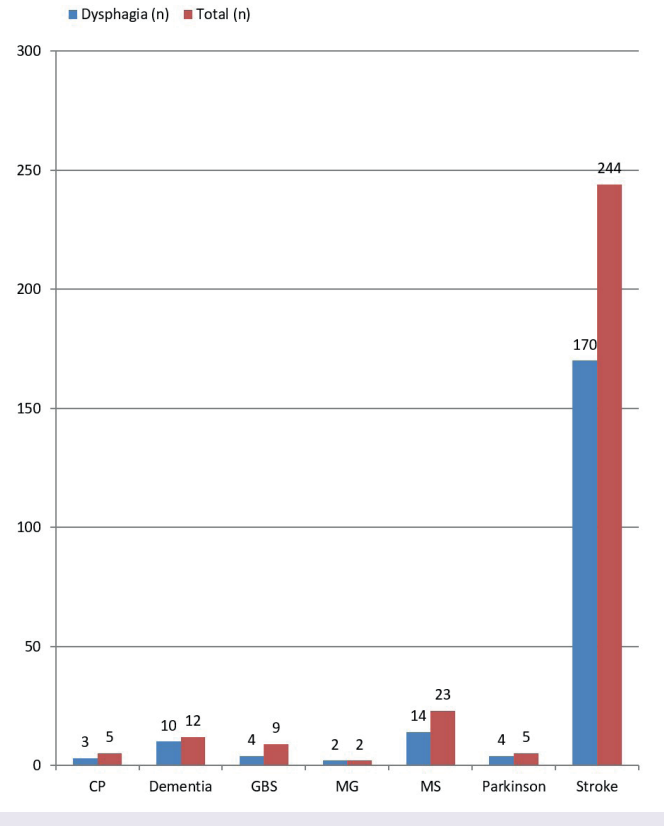

Figure 3. Total number of people according to disease diagnosis and number of people with dysphagia (n)

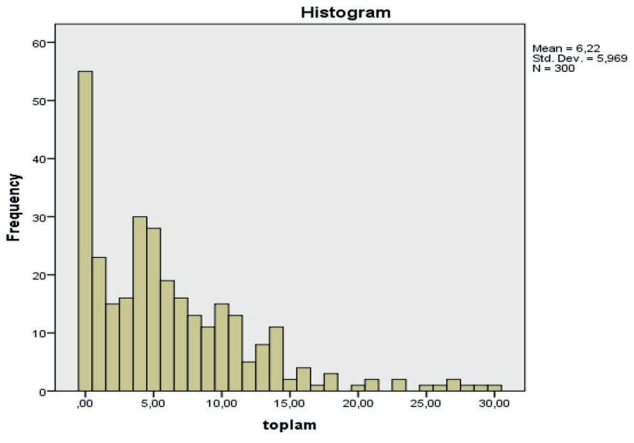

Figure 4. Normality test

As the majority of the sample in our study consisted of stroke patients, we also performed statistical calculations specifically for stroke. According to the normality test performed on the results obtained from the data of the stroke patients, we found that the data were not normally distributed. We therefore used non-parametric tests. 69.7% of the stroke patients were classified as dysphagic because they scored 3 or more points on the Turkish EAT-10 test. According to the data collected from the stroke patients, the severity of dysphagia perceived by the patients was statistically significantly higher in women and participants over 65 years of age ($p<0.05$). The severity of dysphagia perceived by the stroke patients did not show a statistically significant difference according to the time of diagnosis of the disease, the patients' history of pneumonia, and the patients' body mass index ($p>0.05$) (Table 5 and Table 6).

Table 3. Mann-Whitney U Test for responses to the T-EAT-10 Test according to variables such as gender, age, history of pneumonia, and time of diagnosis

	N	U	p
Gender			
Female	144	8810	.001*
Male	156		
Age			
18-64	157	8516	.000*
65 and over	143		
Pneumonia History			
Positive	30	3610	.327
Negative	270		
Time of Diagnosis			
<1 year	227	7244	.105
1 years and above	73		

Table 4. T-EAT-10 test Kruskal-Wallis test result table according to BMI variable

	Sum of Squares	Standard deviation	Mean Square	p
BMI Groups			,120	,585
Within Groups	2,838	4	,361	
Total				

Table 5. Mann-Whitney U test for responses to the T-EAT-10 test according to variables such as gender, age, history of pneumonia and time of diagnosis of stroke patients

	N	U	p
Gender			
Female	118	6154	.02*
Male	126		
Age			
18-64	118	5558	.001*
65 and over	126		
Pneumonia History			
Positive	18	1643	.173
Negative	226		
Time of Diagnosis			
<1 year	207	3318	.19
1 years and above	37		

Table 6. Table of responses given by stroke patients to the T-EAT-10 test according to the Kruskal-Wallis test results according to the BMI variable

	Sum of Squares	Standard deviation	Mean Square	p
BMI Groups			,120	,692
Within Groups	2,239	4	,361	
Total				

Discussion

Dysphagia associated with malnutrition[15] and pneumonia[16] is an important and current problem. Our study used the Turkish EAT-10 test, a non-invasive assessment tool, with attention to contact isolation in accordance with pandemic conditions. The gold standards in the literature for the evaluation of dysphagia are the flexible endoscopic swallowing study and videofluoroscopic evaluation. In the literature, flexible endoscopic swallowing study and videofluoroscopy evaluation have been found to be statistically significantly associated with the EAT-10 test.[17,18] It has become very difficult to use the methods used as the gold standard for assessing dysphagia, which require appropriate equipment and expert support, especially due to the measures brought about by the pandemic conditions. In our study, it was practical and facilitating to use the EAT-10 test, which has known validity and reliability, to assess and manage dysphagia under pandemic conditions. Despite the pandemic conditions, it is believed that the sample size of our study and the diverse cohort of patients included will contribute to the literature.

As 69% of the neurogenic patients participating in the study scored within abnormal limits, they were defined as dysphagic according to the survey results. In the study by Andrade et al., dysphagia screening was carried out on all patients in hospital wards and a prevalence of 10.5% was found in adults and elderly people. Since the group of neurological patients was not specifically selected in this study, it can be said that the rate was low compared to our study.[19] In the study conducted by Abdulmassih et al. to evaluate the development of dysphagia in neurological patients during hospitalisation, 39 patients who were fed orally and in good clinical condition were included and evaluated by videofluoroscopy. The study found that 14 patients had mild dysphagia, 16 patients had moderate dysphagia and 9 patients had severe dysphagia, and the prevalence of dysphagia was 100%.[20] It can be said that the detection rate may be higher if the study is conducted using objective and sensitive tests such as videofluoroscopy. It has been estimated in the literature that neurogenic dysphagia develops in 400,000 to 800,000 people worldwide each year as a result of neurological disorders.[21]

While 69.67% of the stroke patients included in the study were in the dysphagia group, it was noted that the results found in the literature were heterogeneous and generally ranged from 42% and 95%.[22] In the study conducted by Broadley et al.[23], when the dysphagia findings of 149 stroke patients were evaluated, 50% of the patients were classified as dysphagic. This difference may be due to the different sample size of our study and that of Broadley et al.[23] In the study by Tuncay et al.[24], it was determined that 50 stroke patients who were fed orally were divided into two groups according to their dysphagia status, and the degree of stroke was higher in the dysphagia group. In this case, it can be said that the severity of dysphagia is closely related to the severity of the neurological disease.[24]

While 80% of the Parkinson's patients included in the study were in the dysphagia group, it has been reported in the literature that more than 80% of Parkinson's patients may develop dysphagia during the course of the disease.[25] The basal ganglia, which modulate sensory information, provide a response according to the consistency and texture of the bolus. The high rate of dysphagia in Parkinson's disease, which is a disease of the basal ganglia, is not surprising.

While 60.8% of MS patients are in the dysphagia group, the literature has shown that this rate varies between 38% and 81%.[26] While the rate of dysphagia we found in patients with dementia was 83.32%, the estimated frequency of dysphagia in patients with dementia in the literature varied from 7% to 87%.[27] While 60% of patients with CP have dysphagia, the literature suggests that the rate may be as high as 30-40%.[28] 44.4% of GBS patients and 100% of MG patients were in the dysphagia. The literature suggest that dysphagia may occur in approximately 36% of patients with inflammatory myopathy.[8] When comparing the rates obtained, it is possible to see differences due to the size of the sample and the difference in the assessment tool used.

In our study, the item that received the highest score according to the questions of the survey was the item "I have difficulty swallowing solid foods." In the literature, in the study conducted by Bisch et al.[29] in healthy subjects and stroke patients, it was investigated that as the viscosity of the swallowed substance increases, oropharyngeal swallowing efficiency decreases. This was associated with increased viscosity, prolonged oral transit time and prolonged cricopharyngeal patency.[29] This may have been influenced by the fact that the participants in our study gave high scores to this item.

In general, the study found that women had a statistically significantly higher rate of dysphagia than men. On the other hand, people aged 65 and over were significantly more likely to have dysphagia. In the literature, an American study found that people who presented to the hospital with swallowing problems during the year were more likely to be female than male. In addition, the same study found that dysphagia was associated with increasing age, which supports the findings of our study.[30] In the study by Güçmen et al., stroke patients were divided into two groups, with and without according to the EAT-10 scale.[31] While a statistically significant difference was observed between the two groups according to the parameter of age, no statistically significant difference was observed between gender, stroke duration, and BMI.[31] The results of the study support our research except for the parameter of gender.

There are no studies that have used objective tests and biomechanical analysis to investigate the factors that vary by gender and iron deficiency which is one of the predictors of dysphagia. However there are also studies that show a statistically significant relationship between gender and iron deficiency, which is one of the predictors of dysphagia. In a study analysing the prevalence of iron deficiency in adult patients, it was found to be statistically significantly higher in women. The higher prevalence of iron deficiency in women may be an effective factor in the higher prevalence of dysphagia in women.[32] In addition, sarcopenia has been associated with dysphagia in the literature. Sarcopenic dysphagia is known as dysphagia resulting from sarcopenia of the whole body and the muscles involved in swallowing.[33] Sarcopenia is more common in women and in older age.[34] The reason why dysphagia was more common in women in our study may be related to sarcopenia.

Anatomical and physiological problems that develop with age can cause dysphagia. Examples include myosin loss and postural changes that occur over time.[32] The difference in dysphagia between age groups observed in the study is consistent with the literature. Ageing can adversely affect the oral, pharyngeal, and oesophageal phases of swallowing. This may increase the potential for dysphagia in the future. It is estimated by the 2050s, people over the age of 65 will make up approximately 25% of the population in developed countries.[32] This will have an impact on health services.

Dysphagia, which has been associated with aspiration bronchopneumonia and malnutrition in the literature, was not found to be significantly associated with pneumonia and body mass index in our study. This may be due to the fact that the severity of dysphagia in the patients included in the study was not high. In our study, dysphagic patients were not grouped according to the severity of dysphagia. However, the fact that the patients included in the study were fed orally suggests that the severity of dysphagia was not high.

Limitations

During our study, due to the fact that invasive tests were not allowed under pandemic conditions and there was no equipped equipment support, objective dysphagia assessment tests other than the Eat-10 test could not be used. The fact that instrumental tests such as fiberoptic endoscopy and videofluoroscopy were not used is one of the limitations of our study. Studies using objective test will contribute to the literature.

In addition, the inability to distinguish dysphagia from oral, pharyngeal, and oesophageal dysphagia is one of the limitations of our study. Screening with objective tests will contribute to the literature in this direction.

Our study was conducted at a time when it was difficult to conduct research in the hospital under pandemic conditions. The assessment tool we were able to obtain permission to use for the study was the Turkish EAT-10 test. Only people who volunteered to take part and who could experience swallowing in a way that was appropriate to the nature of the test could be included in this test. However, patients from whom we could not obtain consent due to their level of consciousness and patients receiving enteral nutrition, most of whom were in intensive care, could not be included in the study. This situation is the main limitation of our study. Future studies can be extended by including patients with severe dysphagia who were receiving enteral nutrition, using the records of all patient in the hospital.

The hospital was very busy with patients under pandemic conditions. Malnutrition monitoring could not be carried out because there were no suitable conditions for long-term follow-up of participants. Studies comparing the first test and last test and monitoring malnutrition will contribute to the literature.

Ethical approval

This study has been approved by the Non-invasive Ethics Committee of Dicle University (approval date DD.MM.14.04.2022, number 301). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: CG, MUÇ; supervision: CG, MUÇ; data collection: ŞS; analysis and interpretation of results: İY, ŞS; draft manuscript preparation: ŞS; Critical Review: ŞS, CG, MUÇ, İY. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Chen YC, Chen PY, Wang YC, Wang TG, Han DS. Decreased swallowing function in the sarcopenic elderly without clinical dysphagia: a cross-sectional study. *BMC Geriatr*. 2020;20:419. [Crossref]
2. Sayaca Ç. Investigation the effect of proprioceptive neuromuscular facilitation technique in the rehabilitation of swallowing disorders [dissertation]. Ankara: Hacettepe University; 2018.
3. Zevallos JP. International head and neck cancer epidemiology consortium: Update no. 16. *Head Neck*. 2014;36(10):1391. [Crossref]
4. Hall JE. Guyton and Hall Textbook of Medical Physiology. 13th ed. Philadelphia: Elsevier; 2016.
5. Bath PM, Lee HS, Everton LF. Swallowing therapy for dysphagia in acute and subacute stroke. *Cochrane Database Syst Rev*. 2018;10:CD000323. [Crossref]
6. Feng MC, Lin YC, Chang YH, et al. The Mortality and the Risk of Aspiration Pneumonia Related with Dysphagia in Stroke Patients. *J Stroke Cerebrovasc Dis*. 2019;28:1381-1387. [Crossref]
7. Gandhi P, Steele CM. Effectiveness of Interventions for Dysphagia in Parkinson Disease: A Systematic Review. *Am J Speech Lang Pathol*. 2022;31:463-485. [Crossref]
8. Stathopoulos P, Dalakas MC. Autoimmune Neurogenic Dysphagia. *Dysphagia*. 2022;37:473-487. [Crossref]
9. Kalatzi M. Standardization and cultural adaptation of the Greek questionnaire for recording dysphagia phenomena in patients with multiple sclerosis (DYMUS) [master's thesis]. Macedonia: University of Macedonia, Department of Educational and Social Policy; 2018. Available at: https://dspace.lib.uom.gr/bitstream/2159/22018/3/KalaitziMariaMsc2018.pdf
10. Ejraeı N, Yildiz Ozer A. Trunk Stabilization and Its Rehabilitative Effects in Children with Cerebral Palsy. *Abant Tıp Dergisi*. 2022;11:123-131. [Crossref]
11. Sura L, Madhavan A, Carnaby G, Crary MA. Dysphagia in the elderly: management and nutritional considerations. *Clin Interv Aging*. 2012;7:287-298. [Crossref]
12. Belafsky PC, Mouadeb DA, Rees CJ, et al. Validity and reliability of the Eating Assessment Tool (EAT-10). *Ann Otol Rhinol Laryngol*. 2008;117:919-924. [Crossref]
13. Demir N, Serel Arslan S, İnal Ö, Karaduman AA. Reliability and Validity of the Turkish Eating Assessment Tool (T-EAT-10). *Dysphagia*. 2016;31:644-649. [Crossref]
14. Schindler A, de Fátima Lago Alvite M, Robles-Rodriguez WG, Barcons N, Clavé P. History and Science behind the Eating Assessment Tool-10 (Eat-10): Lessons Learned. *J Nutr Health Aging*. 2023;27:597-606. [Crossref]
15. Shimizu A, Fujishima I, Maeda K, et al. Effect of low tongue pressure on nutritional status and improvement of swallowing function in sarcopenic dysphagia. *Nutrition*. 2021;90:111295. [Crossref]
16. Ulukavak Çiftçi T, Mollarecep ER, Ekim N. Aspiration Pneumonia (Report of Seven Cases and a Review of the Literature). *Turk Thorac J*. 2004;5:100-105.
17. Arrese LC, Carrau R, Plowman EK. Relationship Between the Eating Assessment Tool-10 and Objective Clinical Ratings of Swallowing Function in Individuals with Head and Neck Cancer. *Dysphagia*. 2017;32:83-89. [Crossref]
18. Ersöz Ünlü EC, Akın Öçal FC. Can Eating Assessment Tool (EAT-10) Anticipate Objective Findings of Dysphagia Patients? *Kulak Burun Boğaz ve Baş Boyun Cerrahisi Dergisi*. 2020;28:146-151. [Crossref]
19. ndrade PA, Santos CAD, Firmino HH, Rosa COB. The importance of dysphagia screening and nutritional assessment in hospitalized patients. *Einstein (Sao Paulo)*. 2018;16:eAO4189. [Crossref]
20. Abdulmassih EMS, Macedo Filho ED, Santos RS, Jurkiewicz AL. Evolution of Patients with Oropharyngeal Dysphasia in Hospital Environment. *Int Arch Otorhinolaryngol*. 2009;13:55-62.

21. Panebianco M, Marchese-Ragona R, Masiero S, Restivo DA. Dysphagia in neurological diseases: a literature review. *Neurol Sci*. 2020;41:3067-3073. **[Crossref]**

22. Banda KJ, Chu H, Kang XL, et al. Prevalence of dysphagia and risk of pneumonia and mortality in acute stroke patients: a meta-analysis. *BMC Geriatr*. 2022;22:420. **[Crossref]**

23. Broadley S, Cheek A, Salonikis S, et al. Predicting prolonged dysphagia in acute stroke: the Royal Adelaide Prognostic Index for Dysphagic Stroke (RAPIDS). *Dysphagia*. 2005;20:303-310. **[Crossref]**

24. Tuncay F, Taşbaş Ö, Borman P, Geçene M, Coşkun Ö. The Bedside Clinical Evaluation of Swallowing Function of Stroke Patients in Acute Stage. *J PMR Sci*. 2011;14:33-38.

25. Suttrup I, Warnecke T. Dysphagia in Parkinson's Disease. *Dysphagia*. 2016;31:24-32. **[Crossref]**

26. Ansari NN, Tarameshlu M, Ghelichi L. Dysphagia In Multiple Sclerosis Patients: Diagnostic And Evaluation Strategies. *Degener Neurol Neuromuscul Dis*. 2020;10:15-28. **[Crossref]**

27. Wang S, Gustafson S, Deckelman C, et al. Dysphagia Profiles Among Inpatients with Dementia Referred for Swallow Evaluation. *J Alzheimers Dis*. 2022;89:351-358. **[Crossref]**

28. García Ron A, González Toboso RM, Bote Gascón M, de Santos MT, Vecino R, Bodas Pinedo A. Nutritional status and prevalence of dysphagia in cerebral palsy: usefulness of the Eating and Drinking Ability Classification System scale and correlation with the degree of motor impairment according to the Gross Motor Function Classification System. *Neurologia (Engl Ed)*. 2023;38:35-40. **[Crossref]**

29. Bisch EM, Logemann JA, Rademaker AW, Kahrilas PJ, Lazarus CL. Pharyngeal effects of bolus volume, viscosity, and temperature in patients with dysphagia resulting from neurologic impairment and in normal subjects. *J Speech Hear Res*. 1994;37:1041-1059. **[Crossref]**

30. Bhattacharyya N. The prevalence of dysphagia among adults in the United States. *Otolaryngol Head Neck Surg*. 2014;151:765-769. **[Crossref]**

31. Güçmen N, Güçmen B, Koca TT. The Importance of Malnutrition and Dysphage in Patient With Stroke. *Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Dergisi*. 2022;17:182-190. **[Crossref]**

32. Karakuş V, Giden A, Ersil Soysal D, Bozkurt S, Kurtoğlu E. Evaluation of Anemia in Terms of Etiology, Risk Factors, and Relaps in Adult Patients. *Medical Journal of Mugla Sitki Kocman University*. 2016;3:1-6.

33. Fujishima I, Fujiu-Kurachi M, Arai H, et al. Sarcopenia and dysphagia: Position paper by four professional organizations. *Geriatr Gerontol Int*. 2019;19:91-97. **[Crossref]**

34. Sökmen ÜN, Dişçigil G. Sarcopenia in the elderly. *The Journal of Turkish Family Physician*. 2017;8:49-54. **[Crossref]**

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Nutritional risk assessment with NRS-2002 in inpatients hospitalized neurology clinic: A single center cross-sectional study

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ABSTRACT

Objective: Long-term illnesses and hospitalizations can negatively affect the nutritional status of individuals, and have a risk for malnutrition. Nutritional status of patients in clinics are important during the treatment process. The aim of this study was to evaluate the nutritional status of inpatients in a neurology clinic.

Methods: This cross-sectional study was conducted on inpatients receiving treatment in neurology clinic. The characteristics of patients were questioned using a questionnaire form. Anthropometric measurements (body height, body weight, mid-upper arm circumference, and calf circumference) were taken, and nutritional risk assessment (with Nutritional Risk Screening – 2002) and biochemical data (hemoglobin, hematocrit, albumin, and vitamin B12) were evaluated. $p<0.05$ was considered statistically significant.

Results: A total of 100 patients, between the ages of 18-86 years were included. The nutritional risk screening scores of patients who stated they had no appetite and non-smoking patients are higher. As the length of hospital stay increases, risk of malnutrition increases and when modeling according to age, gender, and smoking according to the regression analysis still positively affected. As mid-upper arm circumference and calf circumference decreases, the risk of malnutrition increases. Another results of regression analysis is that as hemoglobin and hematocrit decreases, risk of malnutrition increases.

Conclusion: This study showed that patients at risk of malnutrition had low hematocrit levels and was negatively affected by mid-upper arm circumference and calf circumference. Also malnutrition was negatively affected by hospital length of stay. These results reveal importance of nutritional screening in patients hospitalized in the neurology clinic.

Keywords: malnutrition, neurology, nutritional status, nutrition evaluation, NRS-2002

Introduction

The situation resulting from inadequate and unbalanced intake of energy and protein due to excessive nutritional loss or increased catabolism is defined as malnutrition.[1] European Society for Clinical Nutrition and Metabolism (ESPEN) describes malnutrition: "a nutritional condition that has significant adverse clinical effects on tissue or body (means body shape, size, and composition) and functions due to insufficiency or imbalance of "energy, protein, and other nutrients".[2] Malnutrition is common in patients with severe and chronic diseases, and it can

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increases morbidity, mortality, and reduces the quality of life. Interaction between nutrition and neurology is increasingly the subject of research. Various studies are showing that malnutrition and nutritional deficiencies are the cause and consequence of specific neurological pathologies. Malnutrition has been shown to cause or exacerbate neurological symptoms and disorders. It is also known that some neurological diseases (such as autism spectrum disorders, dementia, Parkinson's disease, and stroke) lead to increased susceptibility to nutritional deficiencies and feeding difficulties.[3]

Malnutrition (disease-related) is a significant health problem for developing countries. Various studies have reported the prevalence of malnutrition as 20-50% in hospitalized patients. Malnutrition has many negative consequences, such as prolonged hospital stays, increased morbidity and mortality, and hospital costs.[4,5] Neurological patients experience feeding difficulties due to various factors such as neurological deficits and age-related problems such as dementia, dysphagia, and edentulism.[4-7] Patients with dementia may lose their ability to feed and maintain regular meal patterns due to cognitive difficulties and memory loss. In the case of paralysis or impairment of voluntary movements, patients may experience severe problems in handling and swallowing food.[4,8] Dysphagia is a condition characterized by difficulty swallowing, is another determining factor in malnutrition, and its prevalence has been shown in various studies to be over 30% in people with neurodegenerative diseases.[9-11] For all these reasons, this patient population may face malnutrition. It is also important to emphasize that neurological deficits are often associated with nutrition and various comorbidities affecting nutritional status.[12] For all these reasons, detection of malnutrition in these patients and early nutritional support, the rate and cost of malnutrition can be reduced, and the hospital length of stay (LOS) of patients can be shortened.

Main Points

- Having no appetite is associated with higher NRS-2002 scores.
- The hematocrit value is significantly higher in patients without malnutrition.
- Lenghth of stay in hospital is related with risk of malnutrition.
- Degrease in mid-upper arm circumference and calf circumference are related with risk of malnutrition.

It was aimed to evaluate the nutritional status of inpatients in a neurology clinic, and also it was aimed to determine potential correlations between malnutrition risk and variables of clinical interest, and LOS in this study.

Materials and Methods

This cross-sectional study was carried on inpatients receiving treatment at Ondokuz Mayıs University Health Application and Research Centre of Neurology Clinic between January 17th and April 25th, 2022. Patients were informed about the study, and their verbal voluntary consent was obtained, and they were included. The characteristics of patients evaluated within the scope of the study were questioned using a questionnaire form. Anthropometric measurements were taken, and nutritional risk assessment and biochemical data were evaluated.

Data collection tools

Patient data were evaluated using a questionnaire form, anthropometric measurements were taken, and hospital records were used to identify biochemical characteristics by researchers.

Questionnaire form

Questions to determine patients' demographic characteristics, disease information, and nutritional habits were asked face to face and using a questionnaire form.

Anthropometric measurements

Anthropometric measurements that is including "body height (m), body weight (kg), mid-upper arm circumference (MUAC-cm), and calf circumference (CC-cm)" were taken. Body mass index (BMI) was used and calculated from weight/height.[2] It was calculated and classified reference of World Health Organization's BMI classification for adults.[13]

Biochemical measurements

Biochemical measurements of the participants were evaluated from hospital records that is the most commonly tested biochemical parameters related to nutritional status in all patients during their hospitalization. No

additional blood samples were taken from the patients. Serum hemoglobin (Hb), hematocrit (Htc), albumin, and vitamin B_{12} were evaluated. These parameters were analyzed with a Roche Diagnostic Cobas 8000 device.

Determination of malnutrition

Nutritional risk screening-2002 (NRS-2002) was performed to determine malnutrition. It is one of the screening tests recommended for hospitalized patients to evaluate malnutrition developed by ESPEN.[14] Weight loss, nutritional intake, BMI, disease severity score are evaluated in NRS-2002, and age correction in patients over 70 years of age. It is classified as without risk of malnutrition (RM) (<3 points), and risk of malnutrition (RM) (≥3 points).[15]

Ethical approval and informed consent statements

The Declaration of Helsinki were complied with in the study, and ethics committee permission dated 08.12.2021 and numbered 2021/629 was obtained from Ondokuz Mayıs University Clinical Research Ethics Committee.

Analysis of data

The data of study was analyzed with Statistical Package Program for Social Science (SPSS) for Windows 21.0 program. Continuous parametric data were presented as mean ($\overline{X}$) and standard deviation (SD), non-parametric data as median (min-max), and categorical data as number (n) and percentage (%). The Kolmogorov-Smirnov test was used to evaluate distribution of normality. Independent Sample T-test between parametric pairs, One Way Anova test between more than two groups; Non-parametric Mann Whitney U test was used between two groups, and Kruskal Wallis test was performed between more than two groups. Linear regression analysis was performed to find the relationship between NRS-2002 socres with length of stay in the hospital and nutritional status, including anthropometric and biochemical measurements. $p<0.05$ was considered statistically significant.

Results

A total of 100 patients, 48 females (48.0%) and 52 males (52.0%) between the ages of 18-86 years were included in this study. The descriptive characteristics are given in Table 1. Their mean age was 56.9±18.8 years. The patients treated in the service for complaints which are cerebrovascular disease (46%), epilepsy (10%), myasthenia gravis (6%), multiple sclerosis (5%), other diseases (33%) (patients with diagnoses and complaints of amyotrophic lateral sclerosis, diplopia, encephalitis, neuromuscular disease, guillain-barre syndrome, encephalopathy, polyneuropathy, ptosis, headache, cerebral hemorrhage, sarcoidosis, myelitis, walking difficulty, weakness, double vision, transient ischemic attack, optic neuropathy, Parkinson's disease, plexopathy, Alzheimer's disease and lumbar disc herniation) were evaluated in this study. The length of hospital stay of patients varied between 1-20 days (Median = 4 days). The nutritional route of patients are oral, parenteral, and enteral (respectively 97%, 2% and 1%). Patients' NRS-

Table 1. Distribution of patients according to descriptive characteristics and NRS-2002 scores of groups

Variables	n	%	NRS-2002 (p)
Gender			0.385*
Women	48	48.0	
Men	52	52.0	
Age groups (years)			0.596**
18-45	25	25.0	
46-64	31	31.0	
> 65	44	44.0	
Education level			0.402**
Not literate	11	11.0	
Primary school	42	42.0	
Secondary school	16	16.0	
High school	23	23.0	
Undergraduate	8	8.0	
Working status			0.909*
Yes	20	20.0	
No	80	80.0	
Marital status			0.207*
Married	71	71.0	
Single	29	29.0	
Mobilization			0.123*
Yes	72	72.0	
No	28	28.0	

NRS-2002: Nutritional risk screening-2002, ᵞ p<0.05, * Mann Whitney U test, **Kruskal Wallis test

2002 scores were between 0-6 and had similar NRS-2002 scores according to gender, age groups, education level, employment status, marital status, presence of chronic disease, and mobilization (p>0.05).

Distribution of patients' eating habits and groups according to NRS-2002 scores is given in Table 2. The NRS-2002 scores do not differ according to drinking alcohol, skipping meals, and BMI. Patients who stated they had no appetite have higher NRS-2002 scores (p<0.05). Also non-smoking patients have higher NRS-2002 score (p<0.05).

A comparison of anthropometric measurements and biochemical values of patients with and without malnutrition is given in Table 3. The BMI, MUAC, and CC measurements did not differ according to malnutrition. Among biochemical measurements, the Htc value was significantly higher in patients without malnutrition (p<0.05).

Table 2. Distribution nutritional habits of patients and groups according to NRS-2002

Variables	n	%	NRS-2002 Median (Min-Max)	p
Smoking				**0.007**$^{*,\gamma}$
Yes	18	18.0	0(0-3)	
No	82	82.0	1(0-6)	
Drinking alcohol				0.462*
Yes	3	3.0		
No	97	97.0		
Meal skipping				0.363**
Yes	49	49.0		
Mid morning	6	12.2		
Lunch	29	59.2		
Afternoon	7	14.4		
Dinner	1	2.0		
Night	6	12.2		
No	51	51.0		
Appetite status (self-reported)				**0.002**$^{*,\gamma}$
Yes	75	75.0	0 (0-5)	
No	25	25.0	2(0-6)	
Body mass index classification				0.076**
Underweight	4	4.0		
Normal	36	36.0		
Overweight	31	31.0		
Obesity	29	29.0		
RM				
Yes	29	29.0		
No	71	71.0		

$^{\gamma}$ p<0.05, * Mann Whitney U test, **Kruskal Wallis test, NRS-2002: nutritional risk screening-2002, RM: risk of malnutrition

Table 3. Anthropometric measurements and biochemical values of patients with and without malnutrition

Variables	PWM	PWNM	p
	$\overline{X}$±SD	$\overline{X}$±SD	
Anthropometric measurements			
BMI	26.7±5.4	26.8±4.9	0.982
MUAC	29.2±5.4	30.9±4.6	0.117
CC	58.2±9.4	60.2±9.1	0.337
Biochemical measurements			
Albumin	3.4(0-5.1)	3.9(0-12.7)	0.534
Hb	12.9±1.6	13.6±1.5	0.096
Htc	36.3±3.9	39.2±4.6	**0.006**ᵞ
Vitamin B_{12}	387(113-1090)	358(162-1381)	0.686

ᵞp<0.05, BMI: body mass index, CC: calf circumference, Hb: hemoglobin, Htc: hematokrit, NRS-2002: nutritional risk screening-2002, PWM: patients with malnutrition risk, PWNM: patients with no malnutrition risk, MUAC: Mid-upper arm circumference

Table 4. Linear regression analysis between NRS-2002 with length of stay in hospital, and nutritional status including anthropometric measurements and biochemical measurements

Variables	n	Crude Model			Adjusted Model		
		Beta	t	p	Beta	t	p
LOS (day)	100	0.246	2.513	**0.014**ᵞ	0.246	2.460	**0.016**ᵞ
BMI (kg/m$^{2)}$	100	-0.143	-1.425	0.157	-0.093	-0.689	0.494
MUAC (cm)	100	-0.263	-2.693	**0.008**ᵞ	-0.246	-2.467	**0.015**ᵞ
CC (cm)	100	-0.197	-1.986	**0.050**ᵞ	-0.192	-1.874	0.064
Albumin (g/dl)	64	0.024	0.193	0.848	-0.030	-0.214	0.831
Hb (g/dl)	80	-0.248	-2.260	**0.027**ᵞ	-0.174	-1.581	0.118
Htc (%)	80	-0.332	-3.113	**0.003**ᵞ	-0.284	-2.637	**0.010**ᵞ
Vitamin B_{12} (pg/ml)	63	-0.013	-0.101	0.920	-0.093	-0.689	0.494

ᵞp<0.05, β: Beta coefficient, BMI: body mass index, CC: calf circumference, Hb: hemoglobin, Htc: hematokrit, LOS: hospital length of stay, MUAC: Mid-upper arm circumference, t: t-statistics, SE: Standard error. Each model is adjusted by age, gender, and smoking. Significant results are shown in bold.

The linear regression analysis of between NRS-2002 score with length of stay in hospital and nutritional status, including anthropometric measurements and biochemical measurements, is given in Table 4. As the LOS increases, RM increases (β=0.246, p=0.014) and when modeling according to age, gender, and smoking according to the regression analysis still positively affected (β=0.246, p=0.016). According to the regression analysis, as MUAC (β=-0.263, p=0.008) and CC (β=-0.197, p=0.050) decreases, the RM increases. The NRS-2002 was still affected by MUAC when modeling according to age, gender, and smoking (β=-0.246, p=0.015). As Hb (β=-0.248, p=0.027) and Htc (β=-0.332, p=0.003) decreases, the RM increases according to the regression analysis. This relationship for Htc was also observed when modeling was performed according to age, gender, and smoking (β =-0.284, p=0.010).

Discussion

Malnutrition is common in hospitalized patients due to various factors, such as underlying diseases and comorbidities that prevent proper nutrition. Malnutrition

is also a common risk in neurological patients due to feeding difficulties and/or inability to communicate or meet nutritional needs, as well as therapeutic interventions.[4] In this study, the risk of malnutrition was detected in 29% of patients hospitalized in the neurology clinic. Similarly, in the study conducted in a neurology clinic, the risk of malnutrition was found to be 28.4%.[16] A retrospective study conducted in the neurology clinic determined that patients faced a 53.8% risk of malnutrition in hospitalization.[17] The different rates of malnutrition risk in the studies may be due to the difference in the scales and sample numbers. It is important to routinely screen hospitalized patients for malnutrition because these patients are at risk for malnutrition. The NRS-2002 is a nutritional screening tool, also recommended by ESPEN, that detects the presence of malnutrition and the risk of malnutrition in the hospital environment. It is a test that questions the severity of the disease and includes age in the scoring, in addition to weight loss, body mass index, and oral intake.[18]

In this study, no significant relationship was found between the risk of malnutrition and demographic information and nutritional habits, except for smoking status. Non-smoking patients have higher NRS-2002 score. Unlike our study, in the literature[19], cigarette consumption is associated with the risk of malnutrition. While finding a different result in our study may be a statistical coincidence, in this study only consumption was questioned and no further evaluation was made to question the duration and amount of smoking. The 25% of the patients declared that their appetite was not good. The percentage of patients with loss of appetite is approximately similar to the percentage of patients with malnutrition risk (PWM) (Table 2). A positive relationship was found between the hospital length of stay and the risk of malnutrition. And according to the regression analysis, the same result was found when modeling was done according to age, gender and smoking status. Similarly, it was conducted on patients hospitalized in the neurology department, a strong correlation was found between the duration of hospital stay and the risk of malnutrition.[1] In neurological diseases, nutritional problems and comorbidities that develop due to the disease may increase the risk of malnutrition. Another factor that may increase the risk of malnutrition in patients may be the hospital diet.

Malnutrition in patients can be assessed through anthropometric measurement and evaluation of nutritional status, muscle function and strength, laboratory tests such as albumin, prealbumin and transferrin, immune and inflammatory biomarkers, and quality of life assessment. Many laboratory parameters such as albumin, prealbumin, Hb, Htc and total protein are used as determinants of malnutrition even in the presence of chronic inflammation.[20] The protein most studied in diagnosing malnutrition is albumin. High or low levels of albumin in the body can be attributed to various factors such as food intake, especially protein, inflammatory response, and malnutrition.[21] Our study found no significant relationship between albumin level and malnutrition risk. Serum albumin has prognostic value only for the prevalence of malnutrition, where there is a relationship between serum albumin levels and malnutrition. Still, it cannot be used as a marker of nutritional status. Albumin is a better indicator of inflammation than nutritional status.[22] The half-life of albumin is 20 days, and a decrease in serum levels can occur in long-term malnutrition, assuming the hydration is kept constant.[23] Many studies in the literature have found that albumin, prealbumin, total protein, hemoglobin and low total cholesterol are associated with the risk of malnutrition.[24] In our study, hematocrit values were higher in patients without malnutrition risk than in those with malnutrition risk. Another study found low albumin, high C-reactive protein, and high creatinine levels in patients at risk of malnutrition.[16] It has been shown that the more severe the degree of malnutrition in cancer patients, the lower the average Hb level.[25] Mid-upper arm circumference is a good indicator of skeletal muscle and protein mass. Reduction in subcutaneous fat and overall body muscle mass is an essential indicator of malnutrition.[26] According to the regression analysis in our study, the risk of malnutrition was negatively affected by MUAC and CC. Another notable finding was that the risk of malnutrition was still affected by MUAC when modelled by age, gender, and smoking. This reflects that malnutrition will reduce lean body mass due to the breakdown of energy reserves from sources other than fat stores.

Studies on the nutrition of hospitalized patients mostly cover intensive care units, oncology, surgery and internal services.[27-30] In addition, it is important to evaluate the nutritional status of patients in other services where there are problems that may affect nutritional intake, such as patients being hungry for examination, presence of infection, hospital psychology, etc., for the success of the treatment. In addition to these features, it may affect the gastrointestinal systems of patients and cause dysfunction due to neurological symptoms, and may affect individuals' appetite and food intake.[31] The results of this study aimed to draw attention to the fact that

patients hospitalized in neurology services may also be at risk of nutritional deficiency and that patients should be regularly screened for nutrition.

This study has some limitations that it was conducted in a single center, not have control group, not evaluated food consumption records, and the disease distribution of patients in the neurology clinic differed. The design of the study is cross-sectional, and a cross-sectional study has limitations. Additionally, another limitation is that we could only use routine biochemistry results. In terms of generalizability of the results, there is a need to increase the number of multicenter samples to evaluate the effect of nutritional support on clinical outcomes.

Conclusion

Malnutrition was detected in approximately one-third of the patients participating in the study. Our research showed that patients at risk of malnutrition had low hematocrit levels. The malnutrition risk was positively affected by hospital length of stay and was negatively impacted by MUAC and CC. Nutritional support appropriate to the needs of the patient and the disease is essential. The presence of malnutrition should be detected at an early stage, which may negatively affect the clinical course of patients, and to establish hospital protocols for using nutritional screening tools during hospitalization as a part of medical treatment. The initiation of diet or nutritional counseling may complement it. To consider food consumption records of patients and if they need additional support to start rigorous nutritional intervention early may also prevent more serious nutritional complications during the disease process.

Ethical approval

This study has been approved by the Ondokuz Mayıs University Clinical Research Ethics Committee (approval date 08.12.2021, number 2021/629). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: ZU, OND; data collection: OND; analysis and interpretation of results: ZU, SK; draft manuscript preparation: ZU, OND, SK. All authors reviewed the results and approved the final version of the article.

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The authors declare that there is no conflict of interest.

References

1. Starace E, De Pasquale G, Morenghi E, et al. Hospital Malnutrition in the Medicine and Neurology Departments: A Complex Challenge. *Nutrients*. 2023;15:5061. **[Crossref]**
2. Lochs H, Allison SP, Meier R, et al. Introductory to the ESPEN Guidelines on Enteral Nutrition: Terminology, definitions and general topics. *Clin Nutr*. 2006;25:180-186. **[Crossref]**
3. Tsalamandris G, Hadjivassiliou M, Zis P. The Role of Nutrition in Neurological Disorders. *Nutrients*. 2023;15:4713. **[Crossref]**
4. Lee H. The Importance of Nutrition in Neurological Disorders and Nutrition Assessment Methods. *Brain Neurorehabil*. 2022;15:e1. **[Crossref]**
5. Uhl S, Siddique SM, Bloschichak A, et al. Interventions for malnutrition in hospitalized adults: A systematic review and meta-analysis. *J Hosp Med*. 2022;17:556-564. **[Crossref]**
6. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr*. 2016;40:159-211. **[Crossref]**
7. Zhu M, Wei J, Chen W, et al. Nutritional Risk and Nutritional Status at Admission and Discharge among Chinese Hospitalized Patients: A Prospective, Nationwide, Multicenter Study. *J Am Coll Nutr*. 2017;36:357-363. **[Crossref]**
8. Herke M, Fink A, Langer G, et al. Environmental and behavioural modifications for improving food and fluid intake in people with dementia. *Cochrane Database Syst Rev*. 2018;7:CD011542. **[Crossref]**

9. Hayashi M, Yahiro A, Sakuragi Y, et al. Impaired Swallowing in Hospitalized Patients: An Observational Study in a Community Hospital in Japan (2012-2014). *Nurs Res*. 2016;65:389-396. **[Crossref]**
10. Panebianco M, Marchese-Ragona R, Masiero S, Restivo DA. Dysphagia in neurological diseases: a literature review. *Neurol Sci*. 2020;41:3067-3073. **[Crossref]**
11. McCarty EB, Chao TN. Dysphagia and Swallowing Disorders. *Med Clin North Am*. 2021;105:939-954. **[Crossref]**
12. Schuetz P, Seres D, Lobo DN, Gomes F, Kaegi-Braun N, Stanga Z. Management of disease-related malnutrition for patients being treated in hospital. *Lancet*. 2021;398:1927-1938. **[Crossref]**
13. World Health Organization (WHO). Global Database on Body Mass Index: BMI classification. 2004.
14. Cederholm T, Bosaeus I, Barazzoni R, et al. Diagnostic criteria for malnutrition - An ESPEN Consensus Statement. *Clin Nutr*. 2015;34:335-340. **[Crossref]**
15. Türkoğlu İ, Ilgaz F, Yalçın T, et al. Hastanede Yatan Yetişkin Hastalarda Malnütrisyon Prevelansı: Dört Farklı Beslenme Tarama Aracının Karşılaştırılması. *Bes Diy Derg*. 2015;43:135-142.
16. Çoban E, Soysal A. The profile of a neurology clinic and malnutrition awareness. *Turk J Neurol*. 2021;27:128-132. **[Crossref]**
17. Ongun N. Nöroloji Kliniği'nde yatan hastalarda nutrisyonel durumun polifarmasi ve hastane yatış süresi ile ilişkisi. *Pamukkale Medical Journal*. 2019;12:467-473. **[Crossref]**
18. Kondrup J, Allison SP, Elia M, Vellas B, Plauth M; Educational and Clinical Practice Committee, European Society of Parenteral and Enteral Nutrition (ESPEN). ESPEN guidelines for nutrition screening 2002. *Clin Nutr*. 2003;22:415-421. **[Crossref]**
19. Lambert C, Nüssler A, Biesalski HK, et al. Age-dependent risk factors for malnutrition in traumatology and orthopedic patients. *Nutrition*. 2017;37:60-67. **[Crossref]**
20. Raiten DJ, Namasté S, Brabin B, et al. Executive summary-Biomarkers of Nutrition for Development: Building a Consensus. *Am J Clin Nutr*. 2011;94:633S-650S. **[Crossref]**
21. Bharadwaj S, Ginoya S, Tandon P, et al. Malnutrition: laboratory markers vs nutritional assessment. *Gastroenterol Rep (Oxf)*. 2016;4:272-280. **[Crossref]**
22. Bullock AF, Greenley SL, McKenzie GA, Paton LW, Johnson MJ. Relationship between markers of malnutrition and clinical outcomes in older adults with cancer: systematic review, narrative synthesis and meta-analysis. *Eur J Clin Nutr*. 2020;74:1519-1535. **[Crossref]**
23. Rzepecki P, Barzal J, Sarosiek T, Szczylik C. Biochemical indices for the assessment of nutritional status during hematopoietic stem cell transplantation: are they worth using? A single center experience. *Bone Marrow Transplant*. 2007;40:567-572. **[Crossref]**
24. Zhang Z, Pereira SL, Luo M, Matheson EM. Evaluation of Blood Biomarkers Associated with Risk of Malnutrition in Older Adults: A Systematic Review and Meta-Analysis. *Nutrients*. 2017;9:829. **[Crossref]**
25. Susetyowati S, Kurniasari FN, Sholikhati AS, Hardianti M, Ekaputra E. Assessment of Nutritional Status in Patients with Head and Neck Cancer Before Radiotherapy: A Single-center, Cross-sectional Study. *Medeni Med J*. 2024;39:24-32. **[Crossref]**
26. Mulasi U, Kuchnia AJ, Cole AJ, Earthman CP. Bioimpedance at the bedside: current applications, limitations, and opportunities. *Nutr Clin Pract*. 2015;30:180-193. **[Crossref]**
27. Braga-da-Silveira J, Baron MV, Carati-da-Rocha GG, Reinheimer IC, Figueiredo AE, Poli-de-Figueiredo CE. Nutritional risk and morbidity and mortality in intensive care unit patients with Coronavirus disease 2019. *Clin Nutr ESPEN*. 2024;60:234-239. **[Crossref]**
28. Şahin Ergül S, Gunes Sahin G, Tugra Ozer N, Kaynar L, Celik S, Gundogan K. Evaluation of refeeding hypophosphatemia frequency, risk factors, and nutritional status during stem cell transplantation in patients with hematologic malignancy. *Clin Nutr ESPEN*. 2022;51:385-390. **[Crossref]**
29. Hiraoka SI, Shimada Y, Kawasaki Y, Akutagawa M, Tanaka S. Preoperative nutritional evaluation, surgical site infection, and prognosis in patients with oral cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2022;134:168-175. **[Crossref]**
30. Girishbhai Patel D, Baral T, Jacob Kurian S, Malakapogu P, Saravu K, Sekhar Miraj S. Nutritional status in patients with tuberculosis and diabetes mellitus: A comparative observational study. *J Clin Tuberc Other Mycobact Dis*. 2024;35:100428. **[Crossref]**
31. Burgos R, Bretón I, Cereda E, et al. ESPEN guideline clinical nutrition in neurology. *Clin Nutr*. 2018;37:354-396. **[Crossref]**

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Characteristics of patients with oropharyngeal dysphagia in a geriatric outpatient clinic

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ABSTRACT

Objective: To describe the characteristics of patients with oropharyngeal dysphagia (OD) presenting to a geriatric outpatient clinic.

Methods: Patients with positive dysphagia screening who presented to the geriatric outpatient clinic of a university hospital through August 2020 to August 2024 were retrospectively analyzed. OD was screened with the Eating Assessment Tool-10. Functionality was assessed with Katz Activities of Daily Living and Lawton Instrumental Activities of Daily Living scales. Nutritional status was evaluated using the Mini-Nutritional Assessment-Short Form and frailty was assessed with the FRAIL scale. Clinical dysphagia evaluation was recorded from patient files.

Results: A total of 87 patients were included. The mean age was 81 ± 7 and 54 (62%) were female. Out of 87 patients, 84 (97%) were frail and 36 (44%) were functionally dependent. Eighty-nine percent of the patients had malnutrition or malnutrition risk. Functionality was the only independent factor associated with frailty in multivariate analysis (OR=1.2, 95% CI 0.78-1.7, p<0.001 for semi-dependency and OR=1.3, 95% CI 0.79-1.7, p<0.001 for dependency, respectively).

Conclusion: Frailty, functional dependency and malnutrition are highly prevalent in older adults with dysphagia.

Keywords: dysphagia, frailty, malnutrition, older adult

Introduction

The global population is aging rapidly and older adults are expected to make up approximately the third of the population by 2050.[1] Oropharyngeal dysphagia (OD), difficulty transferring food from the mouth into the pharynx and esophagus, is a frequent condition among older adults. It has even been recognized as a geriatric syndrome by the European Geriatric Medicine Society.[2] Neurological disorders including stroke, Parkinson's disease and dementia constitute majority of the patients with dysphagia. Advanced age increases OD prevalence with rates between 30% and 40% in independently living older people and 44% in geriatric acute care.[2] In a systematic review, OD prevalence has been reported to reach as high as 72% in community-dwelling older adults.[3] A major cause of mortality and morbidity, OD has been associated with aspiration pneumonia, malnutrition and dehydration.[2,4-7]

Clinical suspicion of OD or a positive screening test warrants affirmative clinical or instrumental assessment. Gold standard instrumental assessment methods include fiberoptic endoscopic evaluation of swallowing (FEES) and video fluoroscopic swallowing study (VFSS). Instrumental tests can even detect silent aspiration that

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may go unnoticed with bedside evaluations and are therefore considered more accurate.[8]

Comprehensive geriatric assessment includes the evaluation of geriatric syndromes such as malnutrition, frailty, functionality and polypharmacy. Malnutrition is defined as decreased nutritional intake leading to impaired mental and physical function.[9] Frailty is another essential geriatric syndrome characterized by reduced physical reserve and increased vulnerability to stressors.[10] Dysphagia, more prevalent among older adults, may be exacerbated by poor nutritional status and frailty, as both syndromes are associated with impaired neuromuscular function.[11] However, there are contradictory findings in the literature regarding the relationship between dysphagia and other geriatric syndromes.[11-13]

Timely recognition and management OD may help prevent the morbidity and mortality related to the syndrome. Therefore, risk stratification of patients, especially among older adults, is of utmost importance. Recognizing factors associated with OD will help clinicians identify high-risk patients and allow for timely intervention. As such, the aim of this study was to describe the characteristics of patients with oropharyngeal dysphagia who presented to a geriatric outpatient clinic.

Methods

Patients who presented to the geriatric outpatient clinic of a university hospital were enrolled in this retrospective cross-sectional study. All patient files through August 2020 to August 2024 were retrospectively analyzed. Patients with positive dysphagia screening were included in the study. Patients who died during clinical follow up were excluded. In the geriatric outpatient clinic where the study was conducted, the Eating Assessment Tool-10 (EAT-10) is used to screen liquid and solid dysphagia.[14] The tool has ten questions and each question is scored between 0 to 4 points. A total score of 3 and above is considered positive, and the patient is referred to the swallowing disorders clinic for detailed evaluation.

Main Points

- Oropharyngeal dysphagia is a common geriatric syndrome.
- Frailty, functional dependency and malnutrition are highly prevalent in older adults with oropharyngeal dysphagia.
- Functional impairment is independently associated with frailty.

Patient demographics, anthropometric measurements, comorbidities, list of medications and serum albumin levels on admission were recorded from patient files. Body mass index (BMI) was calculated as weight (kg) divided by height $(m)^2$. The consultation notes from the swallowing disorders clinic were also recorded.

Functional status was assessed by the Katz Activities of Daily Living Scale-ADL and Lawton Instrumental Activities of Daily Living Scale-IADL.[15,16] While the ADL scale questions basic abilities like getting dressed, locomotion and eating, the IADL scale evaluates the ability to carry out more difficult tasks such as using a telephone, shopping, housekeeping, use of public transportation, managing self-medication, and handling finances. For this study, patients were grouped into three categories by a geriatrician (dependent, semi-dependent and independent) according to their functionality.

Nutritional status was screened with the Mini-Nutritional Assessment-Short Form (MNA-SF).[17] MNA-SF is composed of six questions and scores range between 0 to 14. A score of 0-7 is categorized as “malnutrition”, a score of 8-11 is “at risk of malnutrition”, and a score of 12 and above is “normal nutritional status”.

Frailty was assessed using the FRAIL scale, which questions five domains; Fatigue, Resistance, Ambulation, Illness, and Loss of Weight.[10] A score between 3 and 5 represents frailty and a score of 1 to 2 points represents pre-frailty.

Dementia was diagnosed according to Diagnostic and Statistical Manual of Mental Disorders, 5th edition.[18] Polypharmacy was defined as the use of 5 or more drugs.

The study complies with the Declaration of Helsinki and was approved by Clinical Research Ethics Committee of the university (Approval number: 723, Approval date: June/28/2024).

Statistics

The normality of continuous variables was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For normally distributed data, mean and standard deviation (SD) were reported. Non-normally distributed data were reported as median and range (minimum-

maximum). Group comparisons for normally distributed numerical data were conducted with the independent-samples t-test. Wilcoxon rank sum test was used for non-normally distributed data. Chi-square test was used to analyze categorical variables. For categorical variables with low frequencies, Fisher's Exact test was used. One-way analysis of variance (ANOVA) was used to compare two groups with normally distributed data. Krukal-Wallis test was used to compare groups without a normal distribution. Logistic regression analysis was used to evaluate univariate and multivariate independent variables. All statistical tests were two-tailed. A *p*-value less than 0.05 was considered statistically significant. The study data were analyzed for statistical significance using R software (version 4.3.3).

Results

A total of 87 patients who screened positive for dysphagia were included in the study. The mean age of study participants was 81 ± 7 and 54 (62%) were female. Out of 87 patients, 84 (97%) were frail and 36 (44%) were functionally dependent. All study participants had an EAT-10 score of ≥3. The majority (89%) of the patients with positive dysphagia screening either had malnutrition or malnutrition risk. Table 1 shows the general characteristics of the study population.

Hypertension was the most prevalent comorbidity (61%). With regards to neuromuscular diseases; 38 (44%) patients had dementia, 22 (25%) had Parkinson's disease, 23 (26%) had cerebrovascular disease, 2 had myasthenia gravis and 2 had amyotrophic lateral sclerosis (ALS). Eight patients were diagnosed with cancer (3 prostate cancers, 2 gastric cancers, 1 colorectal cancer, 1 lung cancer and 1 lymphoma). None of the patients had head and neck cancer.

Categories of medications used by the study participants are presented in Table 2. A total of 66 patients (76%) had polypharmacy, defined as using 5 or more drugs.

Factors associated with frailty in the univariate analysis were lower BMI (p = 0.029), functional dependency (p<0.001), low serum albumin (p = 0.033) and statin use (p = 0.041) (Table 3).

Factors that were associated with frailty in univariate analysis (p<0.05) were used as independent factors in multivariate Cox regression analysis. Functionality was the only independent factor associated with frailty in multivariate analysis (OR=1.2, 95% CI 0.78-1.7, p<0.001 for semi-dependency and OR=1.3, 95% CI 0.79-1.7, p<0.001 for dependency, respectively) (Table 4).

Three patients had normal swallowing function documented with VFSS and one patient had normal swallowing function documented with FEES. Rest of the patients were either advised to use thickeners, enrolled in dysphagia therapy or advised to stop oral intake completely. A total of 11 patients were referred to gastroenterology for percutaneous endoscopic gastrostomy (PEG) tube placement.

Table 1. General characteristics of participants

Characteristics	N = 87 Mean ± SD; n (%)
Age (year)	81.3 ± 7.1
Gender (Female) Gender (Male)	54 (62%) 33 (38%)
BMI (kg/m^2)	23.7 ± 4.4
BMI category (kg/m^2)	
<18.5	13 (15%)
18.5-24.9	39 (45%)
25.0-29.9	28 (32%)
≥30.0	7 (8%)
Serum albumin (g/L)	39.3 ± 4.4
Functionality	
Semi-dependent	40 (49%)
Dependent	36 (44%)
FRAIL score	4.0 ± 0.5
FRAIL category	
Robust	0 (0%)
Pre-frail	3 (3%)
Frail	84 (97%)
MNA-SF score	7.8 ± 2.5
MNA-SF category	
Normal	10 (11%)
Malnutrition Risk	40 (46%)
Malnutrition	37 (43%)

BMI= Body Mass Index, MNA-SF= Mini Nutritional Assessment-Short Form

Table 2. Medications used by study participants

Medication Categories	N = 87 n (%)
Steroid	6 (7%)
Antipsychotic	25 (29%)
Antidepressant	26 (30%)
Antiepileptic	12 (14%)
Anti-Dementia	36 (41%)
Antimuscarinic	4 (5%)
Calcium channel blocker	23 (26%)
Beta blocker	33 (38%)
RAS blocker	40 (46%)
OAD / insulin	32 (37%)
Antiplatelet	30 (34%)
Diuretic	26 (30%)
Anti-Parkinson	18 (21%)
Anticoagulant	27 (31%)
PPI	25 (29%)
Statin	19 (22%)
Riluzole	2 (2%)

RAS= Renin Angiotensin Aldosterone System, OAD= Oral Antidiabetic Drug, PPI= Proton Pump Inhibitor

Table 3. Univariate analysis for frailty

Variables	Odds Ratio	95% CI	*p* value
Gender			
Female	—	—	
Male	0.12	-0.10 to 0.35	0.29
BMI (kg/m^2)	-0.03	-0.05 to 0.00	**0.029**
Functionality			
Semi-dependent	1.1	0.75 to 1.5	**<0.001**
Dependent	1.3	0.91 to 1.6	**<0.001**
Serum albumin (g/L)	-0.03	-0.05 to 0.00	**0.033**
Polypharmacy	0.06	-0.20 to 0.32	0.65
Antipsychotic use	0.23	-0.01 to 0.47	0.061
Antidepressant use	-0.21	-0.45 to 0.03	0.091
Statin use	-0.28	-0.54 to -0.02	**0.041**

BMI= Body Mass Index, CI=Confidence Interval

Table 4. Multivariate analysis for frailty

Variables	Odds Ratio	95% CI	*p* value
Gender			
Female	—	—	
Male	0.00	-0.20 to 0.20	0.97
BMI (kg/m^2)	-0.01	-0.04 to 0.01	0.26
Functionality			
Semi-dependent	1.2	0.78 to 1.7	**<0.001**
Dependent	1.3	0.79 to 1.7	**<0.001**
Serum albumin (g/L)	-0.02	-0.04 to 0.01	0.16
Polypharmacy	0.07	-0.20 to 0.33	0.62
Antipsychotic use	0.02	-0.20 to 0.24	0.87
Antidepressant use	-0.10	-0.32 to 0.12	0.37
Statin use	-0.04	-0.28 to 0.19	0.72

BMI= Body Mass Index, CI=Confidence Interval

Discussion

The aim of this study was to describe the characteristics of patients with OD who presented to a geriatric outpatient clinic. The results indicate that frailty, functional dependency and malnutrition are highly prevalent in OD patients. Furthermore, functional impairment is independently associated with frailty.

OD can be defined as difficulty initiating a swallow. It is associated with malnutrition, dehydration, aspiration pneumonia and mortality.[2,4-7] The first step in the assessment of OD is screening, which helps early identification of patients at risk. The EAT-10 is a valid self-reported questionnaire frequently used as part of the comprehensive geriatric assessment.[14] Patients who screen positive for dysphagia with EAT-10 should then be referred for clinical swallowing assessment. Our center has the advantage of performing VFSS and FEES when instrumental assessment is warranted.

Frailty can be defined as increased vulnerability to stressors and multi system dysfunction. A study from Turkiye reported a frailty prevalence of 10% in community dwelling older adults using the FRAIL scale.[19] However, in the present study, nearly all patients who screened positive for dysphagia were frail. The components of frailty consist of exhaustion, decreased muscle strength, low physical activity, and unintentional weight loss. Loss

of muscle strength in frailty may lead to dysphagia, as healthy swallowing involves the collaboration of more than thirty oropharyngeal muscles.[20] Conversely, sarcopenia of the oropharyngeal muscles reduces oral intake and leads to nutritional deficiencies and weight loss, paving the path for frailty and eventually, death.[21,22]

A recent study by Güner et al.[23] showed that dysphagia is associated with frailty (according to the FRAIL scale) independent of age, sex, nutritional status and dementia. However, dysphagia assessment in this study only involved screening. The present study differs from the previous study since clinical evaluation of swallowing was also performed.

The cross-sectional design of the study prevents inference of causality. Hence, OD may be associated with frailty through the neurological comorbidities that cause OD in the first place. However, Bahat et al.[13] revealed an association between dysphagia and frailty independent of comorbidities, age, handgrip strength, nutritional status, polypharmacy. Similar to the previous study, dysphagia was evaluated using the EAT-10 questionnaire. Interestingly, a study that recruited 47 community-dwelling older women aged 85 to 94 failed to show a relationship between frailty and dysphagia, though the small study sample may have accounted for the contradictory findings.[12]

A systematic review has revealed that advanced age could be a dysphagia risk factor.[3] In the present study, all study participants were older adults, which might explain the lack of association between age and dysphagia.

Frailty and malnutrition are closely linked geriatric syndromes with common pathophysiological pathways including chronic inflammation.[24] The prevalence of malnutrition and malnutrition risk among community dwelling older adults in Turkiye were reported to be 13% and 31% respectively.[25] Strikingly, in the present study, malnutrition (43%) and malnutrition risk (46%) were more frequent among older adults with OD. In line with these findings, several studies have linked malnutrition to dysphagia.[5,11,26] Nutritional deficiencies and weight loss brought about by reduced oral intake may cause malnutrition in patients with OD. Malnutrition subsequently results in reduced oropharyngeal muscle mass, starting a vicious cycle. If not treated, malnutrition has been shown to increase mortality in older adults.[27] In our center, we treat all patients with malnutrition and malnutrition risk with energy and protein enriched diet or oral nutritional supplements if the oral route is safe. If the oral route is not safe, we recommend enteral nutrition.

In the current study, the relationship between dysphagia, frailty and malnutrition was still observed after excluding the four patients whose instrumental assessment revealed normal swallowing function, probably because they were the patients with better scores in terms of functionality, nutritional status and frailty.

Similar to the results of this study, OD has been reported to be more prevalent in community dwelling older adults with functional impairments.[28] Neuromuscular disorders frequently encountered in the study population may have caused poor functionality. However, it is of note that functional impairment was independently associated with frailty in the multivariate analysis. Consistent with the study results, functional impairment has been shown to increase proportionally to frailty in a large-scale study recruiting community dwelling older adults.[29] This is probably because components that define frailty such as of exhaustion, decreased muscle strength and low physical activity are interrelated with loss of functionality.

Majority of the patients in the study were diagnosed with a neuromuscular disease, in line with a previous report.[30] Cerebral, cerebellar and brain stem lesions in stroke patients impair various stages of swallowing. Lewy bodies deposited in neurons responsible for the control of swallowing centers may cause dysphagia in Parkinson's disease. As for late-stage dementia, in addition to loss of motor function, malnutrition may also aggravate an existing dysphagia.

Certain medications may affect swallowing function as well.[31] Medications may be the initial cause of dysphagia, or they may be a contributing factor. Medications may alter salivation, impair consciousness or cause dysfunction in the motor coordination of swallowing. Some of the culprit drugs include antipsychotics, anticonvulsants, antidepressants, antimuscarinics, antiarrhythmics, diuretics and angiotensin-converting enzyme inhibitors.[31] In the present study, most of the culprit drugs were used by the study participants, which could be a contributing factor to the development of dysphagia.

Limitations of the study

First, the sample size limits the generalizability of the findings. However, clinical dysphagia assessment was performed for all study patients, which distinguishes the

present study from prior studies in the literature. Second, the study was conducted in a tertiary healthcare setting, which is a referral center for more frail and dependent patients. Hence, this may have caused a selection bias. Third, the cross-sectional design of the study prevents the determination of causality. Prospective studies with larger study samples should be designed to better elucidate the risk factors for dysphagia. As for the strengths of the study, comprehensive geriatric assessment and clinical dysphagia evaluation were performed for all patients, as opposed to previous studies in the literature.

Conclusions

If left untreated, OD has been shown to increase the risk of aspiration pneumonia and mortality. Hospital admissions and mortality may be prevented by detecting OD in the outpatient setting. The present study highlights the characteristics of patients with OD, allowing for a risk stratification and therefore, early detection of swallowing dysfunction in the outpatient setting. Patients with frailty, functional impairment and malnutrition should be carefully assessed for OD and referred for further evaluation.

Ethical approval

This study has been approved by the Marmara University Clinical Research Ethics Committee (approval date 28.06.2024, number 723). Written informed consent was obtained from the participants.

Author contribution

The author declare contribution to the paper as follows: Study conception and design: BC; data collection: BC; analysis and interpretation of results: BC; draft manuscript preparation: BC. The author reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. The Lancet Regional Health-Europe. Securing the future of Europe's ageing population by 2050. *Lancet Reg Health Eur*. 2023;35:100807. [Crossref]
2. Baijens LW, Clavé P, Cras P, et al. European Society for Swallowing Disorders - European Union Geriatric Medicine Society white paper: oropharyngeal dysphagia as a geriatric syndrome. *Clin Interv Aging*. 2016;11:1403-1428. [Crossref]
3. Madhavan A, LaGorio LA, Crary MA, Dahl WJ, Carnaby GD. Prevalence of and Risk Factors for Dysphagia in the Community Dwelling Elderly: A Systematic Review. *J Nutr Health Aging*. 2016;20:806-815. [Crossref]
4. Tagliaferri S, Lauretani F, Pelá G, Meschi T, Maggio M. The risk of dysphagia is associated with malnutrition and poor functional outcomes in a large population of outpatient older individuals. *Clin Nutr*. 2019;38:2684-2689. [Crossref]
5. Carrión S, Cabré M, Monteis R, et al. Oropharyngeal dysphagia is a prevalent risk factor for malnutrition in a cohort of older patients admitted with an acute disease to a general hospital. *Clin Nutr*. 2015;34:436-442. [Crossref]
6. Loeb M, Neupane B, Walter SD, et al. Environmental risk factors for community-acquired pneumonia hospitalization in older adults. *J Am Geriatr Soc*. 2009;57:1036-1040. [Crossref]
7. Cabre M, Serra-Prat M, Palomera E, Almirall J, Pallares R, Clavé P. Prevalence and prognostic implications of dysphagia in elderly patients with pneumonia. *Age Ageing*. 2010;39:39-45. [Crossref]
8. Leder SB, Espinosa JF. Aspiration risk after acute stroke: comparison of clinical examination and fiberoptic endoscopic evaluation of swallowing. *Dysphagia*. 2002;17:214-218. [Crossref]
9. Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr*. 2017;36:49-64. [Crossref]
10. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging*. 2012;16:601-608. [Crossref]
11. Nishida T, Yamabe K, Honda S. The Influence of Dysphagia on Nutritional and Frailty Status among Community-Dwelling Older Adults. *Nutrients*. 2021;13:512. [Crossref]
12. González-Fernández M, Humbert I, Winegrad H, Cappola AR, Fried LP. Dysphagia in old-old women: prevalence as determined according to self-report and the 3-ounce water swallowing test. *J Am Geriatr Soc*. 2014;62:716-720. [Crossref]
13. Bahat G, Yilmaz O, Durmazoglu S, Kilic C, Tascioglu C, Karan MA. Association between Dysphagia and Frailty in Community Dwelling Older Adults. *J Nutr Health Aging*. 2019;23:571-577. [Crossref]
14. Belafsky PC, Mouadeb DA, Rees CJ, et al. Validity and reliability of the Eating Assessment Tool (EAT-10). *Ann Otol Rhinol Laryngol*. 2008;117:919-924. [Crossref]

15. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist*. 1970;10:20-30. **[Crossref]**

16. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9:179-186.

17. Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci*. 2001;56:M366-M372. **[Crossref]**

18. First MB. Diagnostic and statistical manual of mental disorders, 5th edition, and clinical utility. *J Nerv Ment Dis*. 2013;201:727-729. **[Crossref]**

19. Akın S, Mazıcıoglu MM, Mucuk S, et al. The prevalence of frailty and related factors in community-dwelling Turkish elderly according to modified Fried Frailty Index and FRAIL scales. *Aging Clin Exp Res*. 2015;27:703-709. **[Crossref]**

20. Suzuki M, Asada Y, Ito J, Hayashi K, Inoue H, Kitano H. Activation of cerebellum and basal ganglia on volitional swallowing detected by functional magnetic resonance imaging. *Dysphagia*. 2003;18:71-77. **[Crossref]**

21. Tanaka T, Takahashi K, Hirano H, et al. Oral Frailty as a Risk Factor for Physical Frailty and Mortality in Community-Dwelling Elderly. *J Gerontol A Biol Sci Med Sci*. 2018;73:1661-1667. **[Crossref]**

22. Wakabayashi H. Presbyphagia and Sarcopenic Dysphagia: Association between Aging, Sarcopenia, and Deglutition Disorders. *J Frailty Aging*. 2014;3:97-103. **[Crossref]**

23. Güner M, Baş AO, Ceylan S, et al. Dysphagia is closely related to frailty in mild-to-moderate Alzheimer's disease. *BMC Geriatr*. 2023;23:304. **[Crossref]**

24. Wei K, Nyunt MS, Gao Q, Wee SL, Yap KB, Ng TP. Association of Frailty and Malnutrition With Long-term Functional and Mortality Outcomes Among Community-Dwelling Older Adults: Results From the Singapore Longitudinal Aging Study 1. *JAMA Netw Open*. 2018;1:e180650. **[Crossref]**

25. Saka B, Kaya O, Ozturk GB, Erten N, Karan MA. Malnutrition in the elderly and its relationship with other geriatric syndromes. *Clin Nutr*. 2010;29:745-748. **[Crossref]**

26. Serra-Prat M, Palomera M, Gomez C, et al. Oropharyngeal dysphagia as a risk factor for malnutrition and lower respiratory tract infection in independently living older persons: a population-based prospective study. *Age Ageing*. 2012;41:376-381. **[Crossref]**

27. Söderström L, Rosenblad A, Thors Adolfsson E, Bergkvist L. Malnutrition is associated with increased mortality in older adults regardless of the cause of death. *Br J Nutr*. 2017;117:532-540. **[Crossref]**

28. Serra-Prat M, Hinojosa G, López D, et al. Prevalence of oropharyngeal dysphagia and impaired safety and efficacy of swallow in independently living older persons. *J Am Geriatr Soc*. 2011;59:186-187. **[Crossref]**

29. Tchalla A, Laubarie-Mouret C, Cardinaud N, et al. Risk factors of frailty and functional disability in community-dwelling older adults: a cross-sectional analysis of the FREEDOM-LNA cohort study. *BMC Geriatr*. 2022;22:762. **[Crossref]**

30. Kwon S, Cha S, Kim J, Han K, Paik NJ, Kim WS. Trends in the incidence and prevalence of dysphagia requiring medical attention among adults in South Korea, 2006-2016: A nationwide population study. *PLoS One*. 2023;18:e0287512. **[Crossref]**

31. Carl L, Johnson P. Drugs and Dysphagia: How Medications Can Affect Eating and Swallowing. 1st ed. Pro-Ed, Inc; 2006.

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Determining the refeeding syndrome awareness levels of nurses working in intensive care units

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ABSTRACT

Aim: This study was conducted to determine the refeeding syndrome (RFS) awareness levels of nurses working in the intensive care unit.

Methods: A descriptive research design was employed. The study was conducted with nurses working in adult ICUs at Çukurova University Balcalı Hospital.

Results: A total of 73 nurses participated in the study. There was a high-level, statistically significant relationship between participants' education level and giving correct answers to the statement "Only the dietician is responsible for patient nutrition" ($p<0.05$). A statistically significant relationship was found between the level of education and giving correct answers to the questions about "the most common vitamin deficiency" ($p=0.003$) and "the risk of RFS in stroke patients" ($p=0.004$), compared to giving incorrect responses to these items. A statistically significant relationship was detected between the total work experience and giving correct answers to the following questions: "Individuals with low body mass index (BMI) have a risk of developing RFS," "Individuals who develop RFS have normal blood potassium levels," "Only the dietician is responsible for patient nutrition," "The patient's weight is monitored before feeding," and "RFS is an apparent abnormality" ($p<0.05$).

Conclusion: It was determined that nurses who worked in intensive care units and had an undergraduate or above education had better knowledge of RFS than those with an associate degree or below education.

Keywords: refeeding syndrome, nursing, refeeding, intensive care unit, awareness level

Introduction

Refeeding syndrome (RFS) is defined as a series of metabolic and electrolyte changes that occur as a result of the reintroduction and/or increase of calories after a period of reduced or no calorie intake.[1] It was first identified during World War II when prisoners of war experienced unexpected disorders and death after they were fed. Fatal cardiac complications occurred after individuals were rapidly refed.[2]

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RFS was observed in 48% of severely malnourished patients, 34% of intensive care unit (ICU) patients, 33% of patients with anorexia nervosa, 25% of inpatients with cancer, and 9.5% of hospitalized patients in a study.[3] Reported incidence rates vary between 0% and 80%, depending on the recognition of the disease and the patient population studied.[4]

The basic principle in the prevention and treatment of RFS is to identify patients at risk of developing the syndrome and have an experienced multidisciplinary team (physician, nurse, and dietitian) monitor nutritional intake and fluid-electrolyte replacement.[5]

RFS is a potentially life-threatening disease; however, it is largely preventable. To prevent it, patients at risk of developing RFS must be identified, and appropriate protocols must be implemented. Nurses play a critical role in the care of patients at risk of developing RFS who are at high risk of malnutrition, have poor oral intake, or cannot tolerate nasogastric feeding.[6] While providing care for patients, nurses use their knowledge, experience, and critical thinking skills to decide which interventions will benefit the patient the most in line with the nursing process.[7] Therefore, it is very valuable for nurses to know the basics of fluid, electrolyte, and nutrient metabolism as well as metabolic complications to identify patients at risk for metabolic complications due to RFS and to report these findings to their team members.[8] In a study in Israel titled "The Role and Knowledge of Intensive Care Nurses in the Assessment and Management of Hypophosphatemia and RFS," it was revealed that intensive care nurses were unclear about their roles and had little knowledge about nutritional management.[9] A study in Yemen titled "The Assessment of the Level of Knowledge of RFS among Physicians and Nurses in ICUs" indicated that the level of nurses' knowledge was low.[10] In another study at Assiut University Hospital in Egypt titled "The perceptions of intensive care nurses and physicians about RFS," nurses' knowledge levels were found inadequate.[11]

Main Points

- Early recognition and management of refeeding syndrome is of vital importance in terms of improving clinical outcomes.
- This study was conducted to determine the RFS awareness levels of intensive care nurses
- It was determined that nurses who worked in intensive care units and had an undergraduate or above education had better knowledge of RFS than those with an associate degree or below education.

In 2017, the American Society for Parenteral and Enteral Nutrition (ASPEN), Parenteral Nutrition (PN) Safety Committee and Clinical Practice Committee established an interprofessional task force consisting of dietitians, nurses, pharmacists, and physicians, who were commissioned to develop consensus recommendations for screening and managing patients who were at risk for or who had developed RF.[1] The multidisciplinary team, consisting of nurses and other healthcare team members, collaborates in ICUs to manage the care and treatment procedures of patients with RFS.[12] As members of the healthcare team, frequently evaluating patients in terms of all daily living activities and constantly monitoring them and observing potential problems at the earliest, nurses play a critical role in the evaluation, monitoring, and follow-up of many complex processes in the ICU.[9] It has been stated that careful patient monitoring and disciplined team management help to recognize early symptoms of RFS and reduce morbidity and mortality.[13] Therefore, nurses need to be aware of early signs, symptoms, or various clinical features of RFS and to recognize the pathophysiology of this syndrome so that they can monitor early symptoms and implement appropriate interventions in patient care.[7]

A review of the literature indicated that there were no studies in Türkiye to measure the level of ICU nurses' awareness of RFS. Early recognition and management of refeeding syndrome is of vital importance in terms of improving clinical outcomes. In this context, this study was conducted to determine the RFS awareness levels of intensive care nurses. In this context, the research questions were determined as follows.

1. Do nurses working in adult ICUs have awareness of RFS?
2. Do nurses working in adult ICUs have enough knowledge about RFS?

Materials and Methods

Research type

A descriptive and cross-sectional research design was employed.

Setting

This research was conducted with nurses working in adult ICUs at Çukurova University Faculty of Medicine, Balcalı Hospital.

Population and sample

The population of the study consisted of 140 nurses who had been actively working as nurses at Çukurova University Faculty of Medicine, Balcalı Hospital for at least one year. Nurses working in adult ICUs at Balcalı Hospital made up the sample. Inclusion criteria were working as an active nurse in adult ICUs of the Çukurova University Faculty of Medicine, Balcalı Hospital for the past year and volunteering to participate in the study. Considering the inclusion criteria in the study, it was aimed to recruit the entire population without implementing a sampling procedure. Accordingly, all nurses were interviewed, and the study was conducted with those who agreed to participate voluntarily in the study. The participation rate in the study was 52.2% (n=73).

Ethics of the research

At the outset, the approval of the Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee was obtained (Meeting number: 128; Decision Number: 38, 02.12.2022). Participation in the study was voluntary, and individuals who gave consent were informed about the protection of confidentiality and privacy and that they could withdraw from the study at any time.

Data collection tools

1. Personal Information Form: This form was prepared by the researcher. It consists of questions about participants' socio-demographic characteristics (age, gender, marital status, educational status, etc.).
2. RFS Information Form: This form includes statements about nurses' perceptions of their roles in the management of nutritional care, information on the importance of electrolyte monitoring before starting refeeding, and information on RFS.

Statistical analyses

Analyses were performed on the SPSS (IBM SPSS Statistics 27) software. Findings were interpreted through descriptive statistics and frequency tables. "Pearson-X^2" cross tables were employed to study the correlations between two qualitative variables. The p value of <0.05 was considered statistically significant.

Results

Participants' mean age was 30.17±5.71 (years), and 45 (35.0%) of them were in the <30 age group. Fifty-nine of them (80.8%) were female, 50 (68.5%) had an undergraduate degree, and 39 (53.4%) were married. Fifty-eight of the participants (79.5%) liked their job, Total nursing experience was 8.07±6.36 (years), 25 (34.2%) had been nurses for ≥10 years, 55 (75.3%) had not received nutrition education, and 52 (71.2%) worked voluntarily in the ICU (Table 1).

There was a high and statistically significant relationship between the level of education and the rate of correct responses to the item "Only the dietician is responsible for patient nutrition," compared to the rate of incorrect responses ($p<0.001$) (Table 2).

A statistically significant relationship was found between the level of education and the rate of correct responses to the items about "The most common vitamin deficiency" ($p=0.003$)" and "Risk of RFS in stroke patients" ($p=0.004$)," compared to the rate of incorrect responses (Table 3). There was no statistically significant relationship between the level of education and the rate of correct/incorrect responses to other items in the table ($p>0.05$) (Table 3).

The relationship between total work experience groups and the rate of correct responses to the items "Those with low BMI* are at risk for developing RFS" ($p=0.018$), "Those who develop RFS have normal blood potassium levels" ($p=0.048$), "Only the dietician is responsible for patient nutrition" ($p=0.017$) and "The patient's weight is monitored before feeding" was statistically significant ($p=0.002$). There was no statistically significant relationship between total work experience groups and the rate of correct responses to other items in the table ($p>0.05$) (Table 4).

Table 1. Distribution of participant characteristics

Variable (N=73)	n	%
Age groups		
<30	45	61.6
≥30	28	38.4
Gender		
Female	59	80.8
Male	14	19.2
Level of education		
Vocational high school	13	17.8
Associate degree	7	9.6
Undergraduate degree	50	68.5
Master's degree	3	4.1
Marital status		
Married	39	53.4
Single	34	46.6
Status of liking the profession		
Yes	58	79.5
No	15	20.5
Total nursing experience (years)		
<5	24	32.9
5-9	24	32.9
≥10	25	34.2
Having received nutrition education		
Yes	18	24.7
No	55	75.3
*Working voluntarily in the ICU		
Yes	52	71.2
No	21	28.8

*ICU:(Intensive Care Unit)

A statistically significant relationship was found between total work experience groups and the rate of correct responses to the item "RFS is an apparent abnormality" (p=0.021). There was no statistically significant relationship between total work experience groups and the rate of correct/incorrect responses to other items in the table (p>0.05) (Table 5).

Discussion

Nutrition is an interdisciplinary process.[9] A multidisciplinary team approach is vital for the management of RFS. Nurses, who are part of this team, play an important role in the care of patients at risk of developing RFS who have poor oral intake and intolerance to nasogastric intake. They are responsible for the assessment, planning, and implementation of nutrition; therefore, they need to be able to identify the risk factors, pathophysiology, and clinical features of RFS and to report these to appropriate team members.[6] When planning nutritional therapy, experienced clinical nutrition teams should be able to predict the complications that may develop when the patient is refed after a long period of fasting, and they should be able to interpret abnormalities in biochemical findings and the patient's clinical condition and report these to the appropriate team members.[14]

According to the findings of this study, a statistically significant relationship was found between the nurses' education level and the rate of correct/incorrect responses to the statement "Only the dietitian is responsible for patient nutrition." The majority of those who responded to this question accurately had an undergraduate degree or higher education, while all those who answered incorrectly had an associate degree or below education. Contrary to our study, a study in Israel indicated that 91.1% of the nurses participating in the study did not consider nutritional care and follow-up as their responsibility, thinking it only as the responsibility of a dietician.[9] Our study showed that intensive care nurses (with an undergraduate degree or higher education) were aware of their roles and responsibilities among team members in monitoring and managing patients at risk of or with RFS.

In our study, a statistically significant relationship was found between the level of education and the rate of correct/incorrect responses to the statement "The most common vitamin deficiency." It was determined that 49 nurses with an undergraduate degree or higher education (92.5%) had answered the question correctly. The results of the study conducted in Egypt were consistent with our study findings. In the study, 70% of the nurses gave correct answers to the statement "RFS is the most common vitamin deficiency".[11] In another study conducted in Sana, Yemen, the rate of correct responses to the item "RFS is the most common vitamin deficiency" was 26.7%, contrary to our study.[10] Our study revealed that nurses with an undergraduate degree or higher education had better nutrition knowledge.

In our study, a statistically significant relationship was found between the level of education and the rate of correct/incorrect responses to the statement "Risk of RFS in stroke patients." It was determined that 44 people

Table 2. Examination of the relationship between the level of education and knowledge levels about RFS

Level of education / Variable	Associate degree/ below (n=20)		Undergraduate degree/above (n=53)		Statistical analysis*
	n	%	n	%	Probability
"Only the nurse is responsible for diet care monitoring."					
True	20	100.0	51	96.2	X^2=0.776
False	-	-	2	3.8	p=0.378
"Only the nurse is responsible for electrolyte monitoring."					
True	20	100.0	53	100.0	#
"The nurse reports electrolyte abnormalities to the physician."					
True	6	30.0	27	50.9	X^2=2.571
False	14	70.0	26	49.1	p=0.109
"Nutrition should be provided according to RMR* measurement."					
True	5	25.0	11	20.8	X^2=0.153
False	15	75.0	42	79.2	p=0.696
"Those with low BMI* are at risk for developing RFS."					
True	14	70.0	38	71.7	X^2=0.020
False	6	30.0	15	28.3	p=0.886
"Those who develop RFS have normal blood potassium levels."					
True	11	55.0	27	50.9	X^2=0.096
False	9	45.0	26	49.1	p=0.757
"The nurse regularly monitors nutritional status."					
True	17	85.0	50	94.3	X^2=1.679
False	3	15.0	3	5.7	p=0.195
"Only the dietitian is responsible for the patient's nutrition."					
True	16	80.0	53	100.0	X^2=11.214
False	4	20.0	-	-	**p<0.001**
"The nurse monitors blood sugar regularly."					
True	18	90.0	51	96.2	X^2=1.087
False	2	10.0	2	3.8	p=0.297
"Blood electrolytes are checked daily before feeding."					
True	13	65.0	40	75.5	X^2=0.800
False	7	35.0	13	24.5	p=0.371
"The patient's weight is monitored before feeding."					
True	16	80.0	47	88.7	X^2=0.925
False	4	20.0	6	11.3	p=0.336
"Nurses are always aware of RFS*."					
True	11	55.0	39	63.6	X^2=2.324
False	9	45.0	14	26.4	p=0.127
"Updated information and education on nutritional status is provided."					
True	8	40.0	22	41.5	X^2=0.014
False	12	60.0	31	58.5	p=0.907

*RMR (Resting metabolic rate), BMI (Body mass index), RFS (Refeeding syndrome)
*"Pearson-X^2" cross tables were used to examine the relationships between two qualitative variables.

Table 3. Examination of the relationship between the level of education and knowledge levels about RFS

Level of education / **Variable**	**Associate degree/ below (n=20)**		**Undergraduate degree/ above (n=53)**		**Statistical analysis*** **Probability**
	n	**%**	**n**	**%**	
"RFS is the route of feeding."					
True	15	75,0	46	86,8	X^2=1,470
False	5	25,0	7	13,2	p=0,225
"RFS is an apparent abnormality."					
True	12	60,0	31	58,5	X^2=0,014
False	8	40,0	22	41,5	p=0,907
"RFS is the source of electrolyte disturbance."					
True	4	20,0	10	18,9	X^2=0,012
False	16	80,0	43	81,1	p=0,913
"RFS is the most common vitamin deficiency."					
True	13	65,0	49	92,5	X^2=8,551
False	7	35,0	4	7,5	**p=0,003**
"RFS is not a risk factor."					
True	3	15,0	21	39,6	X^2=2,951
False	17	85,0	32	60,4	p=0,086
"Operations increase the risk of RFS."					
True	18	90,0	50	94,3	X^2=0,429
False	2	10,0	3	5,7	p=0,513
"RFS is risky weight loss."					
True	16	80,0	43	81,1	X^2=0,012
False	4	20,0	10	18,9	p=0,913
"Risks in patients receiving CT*"					
True	12	60,0	42	79,2	X^2=1,883
False	8	40,0	11	20,8	p=0,170
"Risk of RFS in stroke patients"					
True	10	50,0	44	83,0	X^2=8,223
False	10	50,0	9	17,0	**p=0,004**
"Ocular disease develops in those with RFS."					
True	4	20,0	13	24,5	X^2=0,167
False	16	80,0	40	75,5	p=0,683
"Distinguishing inaccurate information about RFS"					
True	8	40,0	29	54,7	X^2=1,258
False	12	60,0	24	45,3	p=0,262
"The most important application for RFS"					
True	19	95,0	48	90,6	X^2=0,378
False	1	5,0	5	9,4	p=0,538

*CT(chemotherapy)
*"Pearson-X^2" cross tables were used to examine the relationships between two qualitative variables.

Table 4. Examination of the relationship between total work experience and knowledge levels about RFS

Total work experience / **Variable**	**<5 years (n=24)**		**5-9 years (n=24)**		**≥10 years (n=25)**		**Statistical analysis***
	n	**%**	**n**	**%**	**n**	**%**	**Probability**
"Only the nurse is responsible for diet care monitoring."							
True	22	91.7	24	100.0	25	100.0	X^2=4.198
False	2	8.3	-	-	-	-	p=0.123
"Only the nurse is responsible for electrolyte monitoring."							
True	24	100.0	24	100.0	25	100.0	#
"The nurse reports electrolyte abnormalities to the physician."							
True	11	45.8	10	41.7	12	48.0	X^2=0.204
False	13	54.2	14	58.3	13	52.0	p=0.903
"Nutrition should be provided according to RMR* measurement."							
True	3	12.5	7	29.2	6	24.0	X^2=2.044
False	21	87.5	17	70.8	19	76.0	p=0.360
"Those with low BMI* are at risk for developing RFS."							
True	12	50.0	19	79.2	21	84.0	X^2=8.006
False	12	50.0	5	20.8	4	16.0	**p=0.018**
"Those who develop RFS have normal blood potassium levels."							
True	8	33.3	13	54.2	17	68.0	X^2=6.076
False	16	66.7	11	45.8	8	32.0	**p=0.048**
"The nurse regularly monitors nutritional status."							
True	23	95.8	22	91.7	22	88.0	X^2=0.997
False	1	4.2	2	8.3	3	12.0	p=0.608
"Only the dietitian is responsible for the patient's nutrition."							
True	24	100.0	24	100.0	21	84.0	X^2=8.125
False	-	-	-	-	4	16.0	**p=0.017**
"The nurse monitors blood sugar regularly."							
True	23	95.8	21	87.5	25	100.0	X^2=3.813
False	1	4.2	3	12.5	-	-	p=0.149
"Blood electrolytes are checked daily before feeding."							
True	15	62.5	17	70.8	21	84.0	X^2=2.902
False	9	37.5	7	29.2	4	16.0	p=0.234
"The patient's weight is monitored before feeding."							
True	22	91.7	16	66.7	25	100.0	X^2=12.379
False	2	8.3	8	33.3	-	-	**p=0.002**
"Nurses are always aware of RFS*."							
True	19	79.2	14	58.3	17	68.0	X^2=2.418
False	5	20.8	10	41.7	8	32.0	p=0.299
"Updated information and education on nutritional status is provided."							
True	8	33.3	8	33.3	14	56.0	X^2=3.489
False	16	66.7	16	66.7	11	44.0	p=0.175

*RMR (Resting metabolic rate), BMI (Body mass index), RFS (Refeeding syndrome)

*"Pearson-X^2" cross tables were used to examine the relationships between two qualitative variables.

Table 5. Examination of the relationship between total work experience and knowledge levels about RFS

Total work experience / **Variable**	**<5 years (n=24)**		**5-9 years (n=24)**		**≥10 years (n=25)**		**Statistical analysis*** **Probability**
	n	**%**	**n**	**%**	**n**	**%**	
"RFS is the route of feeding."							
True	19	79.2	21	87.5	21	84.0	X^2=0.612
False	5	20.8	3	12.5	4	16.0	p=0.736
"RFS is an apparent abnormality."							
True	10	41.7	13	54.2	20	80.0	X^2=7.765
False	14	58.3	11	45.8	5	20.0	**p=0.021**
"RFS is the source of electrolyte disturbance."							
True	6	25.0	3	12.5	5	20.0	X^2=1.226
False	18	75.0	21	87.5	20	80.0	p=0.542
"RFS is the most common vitamin deficiency."							
True	22	91.7	20	83.3	20	80.0	X^2=1.375
False	2	8.3	4	16.7	5	20.0	p=0.503
"RFS is not a risk factor."							
True	5	20.8	9	37.5	10	40.0	X^2=2.385
False	19	79.2	15	62.5	15	60.0	p=0.304
"Operations increase the risk of RFS."							
True	21	87.5	22	91.7	25	100.0	X^2=3.122
False	3	12.5	2	8.3	-	-	p=0.210
"RFS is risky weight loss."							
True	20	83.3	19	79.2	20	80.0	X^2=0.151
False	4	16.7	5	20.8	5	20.0	p=0.927
"Risks in patients receiving CT*"							
True	20	83.3	15	62.5	19	76.0	X^2=2.786
False	4	16.7	9	37.5	6	24.0	p=0.248
"Risk of RFS in stroke patients"							
True	19	79.2	16	66.7	19	76.0	X^2=1.055
False	5	20.8	8	33.3	6	24.0	p=0.590
"Ocular disease develops in those with RFS."							
True	6	25.0	7	29.2	4	16.0	X^2=1.247
False	18	75.0	17	70.8	21	84.0	p=0.536
"Distinguishing inaccurate information about RFS"							
True	12	50.0	12	50.0	13	52.0	X^2=0.026
False	12	50.0	12	50.0	12	48.0	p=0.987
"The most important application for RFS"							
True	21	87.5	22	91.7	24	96.0	X^2=1.173
False	3	12.5	2	8.3	1	4.0	p=0.556

*CT(chemotherapy), RFS (Refeeding syndrome)
*"Pearson-X^2" cross tables were used to examine the relationships between two qualitative variables.

with an undergraduate degree or higher education (83.0%) gave correct responses to the item. The majority of those who responded to the item correctly had an undergraduate degree or higher education, while most of those who answered incorrectly had an associate degree or lower education. In contrast to our study, in a study in Egypt, 23.3% of the nurses identified the reason for the increased risk of RFS in stroke patients as dysphagia correctly.[11] In the study conducted in Sana, Yemen, 51.1% of the nurses identified the reason for the increased risk of RFS in stroke patients as dysphagia correctly, while 48.9% gave incorrect answers.[10] According to our study and the literature, nurses with undergraduate and higher education are aware of refeeding syndrome and have more knowledge on this subject.

There was a statistically significant relationship between the total work experience and the rate of correct/incorrect responses to the items "Those with low BMI have a risk of developing RFS," "Those who develop RFS have normal blood potassium levels," and "The patient's weight is monitored before feeding." It was determined that the majority of those who answered the questions correctly had been working for ≥10 years, while most of those who answered them incorrectly had been working for <5 years. The results of a systematic review of the Use of Approved Tools to Determine the Nutrition Knowledge of Physicians and Nurses were consistent with our study. It was stated that the nutritional knowledge of nurses who were specialized in the profession and had more practice experience was higher than the level of those who were not specialized and had less practice experience.[15]

Conclusions and Recommendations

It was determined that intensive care nurses with undergraduate or higher education had better levels of knowledge about refeeding syndrome than those who had associate or below education. It may be recommended that in-service training programs be organized to increase the knowledge of nurses, who are an integral part of a multidisciplinary team in nutritional care, regarding the identification and management of RFS, and that a protocol based on current nutritional guidelines be created to increase awareness of RFS.

Ethical approval

This study has been approved by the Çukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (approval date 02.12.2022, number 38). Written informed consent was obtained from the participants.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: KM, ZE, KA, PYD; data collection: KM; analysis and interpretation of results: KM, ZE, KA, PYD; draft manuscript preparation: KM, ZE, KA, PYD. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Da Silva JS, Seres DS, Sabino K, et al. ASPEN consensus recommendations for refeeding syndrome [published correction appears in *Nutr Clin Pract*. 2020;35(3):584-585.]. *Nutr Clin Pract*. 2020;35:178-195. **[Crossref]**
2. Adkins SM. Recognizing and preventing refeeding syndrome. *Dimens Crit Care Nurs*. 2009;28:53-58. **[Crossref]**
3. Ponzo V, Pellegrini M, Cioffi I, Scaglione L, Bo S. The Refeeding Syndrome: a neglected but potentially serious condition for inpatients. A narrative review. *Intern Emerg Med*. 2021;16:49-60. **[Crossref]**
4. Friedli N, Stanga Z, Sobotka L, et al. Revisiting the refeeding syndrome: Results of a systematic review. *Nutrition*. 2017;35:151-160. **[Crossref]**
5. Koçer E, Gormez A. Refeeding syndrome. *Bezmialem Science*. 2017;5(3):121-125. **[Crossref]**

6. Adam K, Silva AND. Refeeding syndrome: an update and pragmatic approach to management. *Gastrointestinal Nursing*. 2018;16(9):37-42. **[Crossref]**

7. Kebede Y, Korhonen M. Nursing Interventions needed in Preventing Refeeding Syndrome in Anorexia Nervosa Inpatients: Literature Review 2016 [Bachelor's Thesis]. Laurea University of Applied Sciences; 2016.

8. Lauts NM. Management of the patient with refeeding syndrome. *J Infus Nurs*. 2005;28:337-342. **[Crossref]**

9. Ben-Tovim H, Theilla M. Role and knowledge of critical care nurses in the assessment and management of hypophosphataemia and refeeding syndrome. A descriptive exploratory study. *Intensive Crit Care Nurs*. 2021;67:103097. **[Crossref]**

10. Alghabri HM, Abbas NM, Alaghbari WW, et al. Assessment of the knowledge regarding refeeding syndrome among doctors and nurses in the intensive care units and inpatient wards Sana'a, Yemen [Graduation research report]. Republic of Yemen, University of Science and Technology, Faculty of Medicine and Health Sciences; 2023.

11. Mahran GSK, Abdelrahman HA. Critical Care Nurses' and Physicians' Perception about Re-feeding Syndrome. *American Journal of Nursing Research*. 2019;7:179-184.

12. Byrnes MC, Stangenes J. Refeeding in the ICU: an adult and pediatric problem. *Curr Opin Clin Nutr Metab Care*. 2011;14:186-192. **[Crossref]**

13. Crook MA. Refeeding syndrome: problems with definition and management. *Nutrition*. 2014;30:1448-1455. **[Crossref]**

14. Çakır BK, Abbasoğlu O. Beslenme tedavisi alan hastalarda hipofosfatemiye neden olan faktörler. *Turk J Intensive Care*. 2022;20:72-78. **[Crossref]**

15. Zeldman J, Andrade JM. Identifying physicians' and nurses' nutrition knowledge using validated instruments: a systematic narrative. *Int J Nutr Food Sci*. 2020;9:43-53. **[Crossref]**

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Effect of high or low protein nutrition on diaphragm thickness using ultrasonography in mechanically ventilated intensive care patients

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ABSTRACT

Background: Diaphragmatic dysfunction is associated with difficulties from weaning and have worse patient outcomes in intensive care unit (ICU). It is still not clear how to prevent diaphragmatic dysfunction. Protein may be one of the modifiable factors that can prevent diaphragmatic dysfunction. We aimed to compare the effects of low protein and high protein support on diaphragm thickness using ultrasonography in mechanically ventilated patients in the ICU.

Methods: This study was performed in intensive care patients over the age of 18 who were mechanically ventilated and administered enteral nutrition. Patients were randomly (using a computer-generated list: 1/1 block randomization) allocated to low protein group (1.1 g/kg/day) or a high protein group (1.5 g/kg/day). The patients' demographics, diagnosis and comorbidities, length of stay (APACHE II), NRS 2002 scores were recorded on the first day of intubation. Diaphragm thickness and mid arm muscle circumference measurements were taken on the 1st, 7th, and 14th days on mechanically ventilation and day of weaning.

Results: 42 Intubated critically ill patients (age 69 ± 15 years, 12 women/30 men) enrolled in this study. Demographics BMI, Apache II score, duration of mechanical ventilation, length of intensive care stay and hospital stay were not different between groups. The diaphragm thickness measured on the 7th day was 1.81 ± 0.29 mm (n=21) in low protein group and 2.00 ± 0.23 mm (n=21) in the high protein group (p= 0.028). The diaphragm thickness measured on the weaning day were 1.73 ± 0.14 mm (n=9) and 2.01 ± 0.21 mm (n=10) in the low protein group and in the high protein group respectively (p= 0.004).

Conclusions: Large-scale and long-term studies on this subject may help reveal the differences between the high protein and low protein support for ICU patients.

Keywords: diaphragm, malnutrition, mechanical ventilation, nutrition, nutritional assessment, proteins

Introduction

Critical illness is associated with a protein catabolic state, causing in muscle wasting ICU patients. Loss of muscle mass and function during ICU has a negative impact on long-term quality of life as well as short- and long-term outcomes. Mechanical ventilation is one of the most important treatments in ICU. Mechanically ventilated patients have difficulties being weaned from mechanical ventilation when respiratory support is no longer needed.[1] Mechanical ventilation has also negative effects on respiratory muscles that causes atrophy and

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dysfunction in the diaphragm muscle.[2] The diaphragm is the main muscle involved in ventilation, and its dysfunction causes various respiratory complications.[3] Diaphragmatic ultrasonography has recently become a valuable tool in intensive care for the evaluation of diaphragmatic dysfunction.[4]

Insufficient protein intake and increased protein loss cause weakening of the respiratory muscles, especially the diaphragm, and deterioration of their structure and function. Current American and European nutrition guidelines recommend 1.2–2.0 g/kg/day and 1.3 g/kg/day, respectively, for protein support in the absence of high-quality studies.[5,6] In the systematic review and meta-analysis of nineteen randomized controlled trials (n=1731 patients), Lee at al.[7] compared higher vs lower protein delivery (with similar energy delivery between groups) in critically ill patients. The pooled mean protein delivery for the higher versus lower protein group were 1.31 ± 0.48 vs 0.90 ± 0.30 g/kg/day respectively. They reported that a 0.48 g/kg/day higher protein support didn't show any significant effect on mortality and other outcomes. On the other hand, higher protein, was linked to a tendency toward shorter mechanical ventilation and ICU length of stay. Higher protein was related with a shorter duration of mechanical ventilation (0.73 days) and a one-day reduction in the length of stay in the ICU (p = 0.07), in the subset group of trials. Higher protein delivery is associated with a muscle loss attenuation (−3.44% per week, 95% CI −4.99 to −1.90, p<0.0001) in five studies.

In this study, it was aimed to compare low protein and high protein support on diaphragm thickness using ultrasonography in patients undergoing invasive mechanical ventilation in the ICU.

Main Points

- Mechanical ventilation causes atrophy and dysfunction in the diaphragm muscle.
- Diaphragma ultrasonography is a valuable tool in intensive care for the evaluation of diaphragmatic dysfunction.
- Insufficient protein intake and increased protein loss cause weakening of the respiratory muscles, especially in the diaphragm.
- So, nutrition must include adequate provision of protein. This is particularly important for icu patients.

Materials and Methods

After the Local Ethics Committee of the Pamukkale University, Medical School, this study was performed in 42 intensive care patients over the age of 18 who were mechanically ventilated and administered enteral nutrition. Patients with known primary or secondary muscle disease (systemic disorders secondary affect the skeletal muscle manifesting as myositis or rhabdomyolysis) , anatomical diaphragm malformation, chronic obstructive pulmonary disease, severe malnutrition (BMI<18,5 kg/m2 if <70 years old or BMI <20 kg/m2 if >70 years old) advanced organ failure, mechanical ventilation support for more than 24 hours in the ICU in the 6 months prior to inclusion, those who required positive end expiratory pressure ≥ 20 cm H_2O and FiO_2 > 60% during indirect calorimetry measurement, and those whose enteral feeding was discontinued were excluded from the study.

Patients who received enteral nutrition under mechanical ventilation support in the ICU were divided into two groups by randomization using a computer-generated list (1: 1 block randomization), with 21 patients in each group such as low protein group (1.1 g/kg/day) or a high protein group (1.5 g/kg/day).

After the patients admitted the ICU with stable hemodynamics and enteral nutrition was indicated, enteral nutrition was started within 24–48 hours. In the ICU, the intensive care team inserted a 12F feeding tube into the patients.The position of the tube was confirmed by taking a chest radiograph, followed by enteral nutrition with a standard or protein-rich polymeric formula. For the low protein group, Nutrison (Nutricia, Zoetermeer, the Netherlands; 1 mL/kcal; this product provided 20 g protein, 19.5 gr fat, 61.5 gr carbohydrate /500 mL) was used. For the high protein group, Nutrison Protein Plus (Nutricia, Zoetermeer, the Netherlands; 1.25 kcal/1 mL; this product provided 31.5 g protein, 24.5 gr fat, 71 gr carbohydrate /500 mL) was used. Enteral feeding was started at the flow rate of 20 mL/h in the ICU and was increased by 20 mL/h every 6 h, depending on clinical signs of intolerance, until the target calorie rate was reached. Residual gastric volumes was routinely monitored as a measure of digestive intolerance four times daily. Patients who developed high gastric residue (greater than 300ml in 12h) within the first 24h of the enteral nutritional therapy, intravenous metoclopramide were given. In both groups, the resting energy expenditure of the patients was measured daily by indirect calorimetry using the Datex Ohmeda M-CAiOVX module (Datex- Ohmeda, Finland). Actual nutrition delivery was monitored daily

based on the volumes delivered relative to the predefined daily caloric targets. If there was a feeding interruption due to gastric intolerance the delivery rate was not increased after resumption to compensate for the interruption and feeding was resumed at the initial rate after 6 hours without a new episode of intolerance. The rate of administration was not increased to compensate for nutrition not received. For all patients who underwent enteral nutrition, the head of the bed was kept in an upward position of 30–45 degrees.

Diaphragm thickness and mid arm muscle circumference measurements were taken on the 1st, 7th, and 14th days on mechanically ventilation and day of weaning from the ventilator. Mid arm muscle circumference measurements were obtained from the same location using a skin marker. Patient age, gender, body mass index, hospitalisation diagnosis and comorbidities, acute physiology and chronic health evaluation (APACHE II), NRS 2002 scores and daily hemogram, albumin, and total protein values were also recorded. Total protein and albumin values were measured on the 1st day, 7th day, 14th day, and day of weaning from mechanical ventilation. Patients were fed the same enteral nutrition product during mechanical ventilation. Thirteen patients in the low protein group and sixteen patients in the high protein group have 14th day measurements for diaphragm thickness and mid arm muscle circumference. Nine patients in the low protein group and 10 in the high protein group were successfully weaned from mechanical ventilation within 21 days. Measurements were performed in these patients.

Measurements

The diaphragm was visualised by placing the ultrasonography probe vertically between the 9th and 10th ribs between the anterior-mid-axillary lines while the patient was in the supine position. Diaphragm thickness was measured at the end of expiration with ultrasound using a 6–13 MHz linear probe in B mode. Measurement with ultrasound was performed only by the responsible authors.

Indirect calorimetry measurements were started after haemodynamic stability was achieved in the intubated patients who were admitted to our ICU. Indirect calorimetry measurements were performed in the first 24–48 hours after admission to the ICU, with the Datex-Ohmeda M-CAiOVX module (Datex-Ohmeda, Helsinki, Finland) for 24 h without interruption. Average of the measurements was recorded by pressing the "trend" button and enrolled. Measurements were repeated daily by trained staff during mechanical ventilation and enteral nutrition therapy.

Statistical analysis

As a result of the power analysis made hypothetically in the direction of expectations, assuming that a strong degree effect size (d=0.8) will be obtained for the difference to be obtained between the two groups It has been calculated that at least 42 people (21 people for each group) should be included in the study in order to achieve 80% power with 95% confidence. The data were analysed using IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY). Continuous variables were presented using the mean ± standard deviation, median, and minimum–maximum value. The number and percentage calculations were performed for categorical variables. When the parametric test assumptions were met, the independent-samples T test and one-way analysis of variance were used for the enteral nutrition groups to compare the differences between the groups. In cases where the parametric test assumptions were not met, the Mann–Whitney U test and Friedman repeated-measures analysis of variance were used to compare the differences between the enteral nutrition groups. Pearson's chi-square test was applied to compare categorical variables and examine the relationship between the variables of the two groups. Median values were compared to determine statistical significance.

Results

The mean age of 42 patients included in the study was 69.00 ± 15.69 years. The mean height, weight, and body mass index were 164.52 ± 6.61 cm, 67.48 ± 10.35 kg, and 25.54 ± 3.93, respectively. There were 12 women (28.6%) and 30 men (71.4%). Higher NRS 2002 scores were obtained in the high protein group (Table 1). Pneumonia was the most admission diagnosis (31/42 patients). Other reasons for icu admission were pulmonary edema (3/42 patients), massive pulmonary embolism (2/42 patients), diabetic foot ulcer (2/42 patients), acute heart failure (2/42 patients), pneumococcal meningitis (1/42 patients) and acute intraalveolar hemorrhage (1/42 patients).

During the study, the number of patients decreased because there were patients who were extubated, died or transferred to another hospital before the 14th day and the weaning day. There were totally 29 patients on 14th day and 19 patients on the weaning day.

Table 1. Demographic data of the patients and analysis results of some variables according to enteral nutrition status

Parameters	Low Protein (n=21)	High Protein (n=21)	p
Age (Year)	64.38 ± 18.16	73.62±11.41	0.055
Sex (F/M)	8 (%38.1)	4 (%19)	0.153
Height (cm)	163.33 ± 7.80	165.71±5.07	0.248
Weight (kg)	65.10 ± 9.47	69.86±10.87	0.138
BMI	24.33 ± 2.75	25.38±4.20	0.347
NRS 2002	3.81 ± 0.60	4.29 ± 0.46	0.006
APACHE 2	13.62 ± 3.81	15.05 ± 2.50	0.158
Energy requirement (kcal)	1877.71 ± 154.19	1900±64.67	0.541
MV time (day)	24 ± 25.48	21.48±12.69	0.687
Length of ICU stay (day)	27.33 ± 24.06	25.43±11.34	0.744
Length of hospital stay (day)	32.33 ± 26.58	30.71±11.98	0.801

*p<0.05, statistically significant difference; mean; SD: standard deviation

Table 2. Diaphragm thickness measurements on day 1, day 7, day 14, and on the day of weaning from mechanic ventilation

	Low Protein n=21		High Protein n=21		p value
	Mean ± SD (mm)	Median (Min–max)	Mean ± SD (mm)	Median (Min–max)	
Day 1	1.94 ± 0.27	1.80 (1.70–2.90)	2.10 ± 0.23	2.20 (1.7–2.50)	0.054
Day 7	1.81 ± 0.29	1.70 (1.50–2.90)	2.00 ± 0.23	2.00 (1.70–2.40)	0.028
Day 14	1.80 ± 0.33 (n=13)	1.70 (1.50–2.80)	1.86 ± 0.25 (n=16)	1.95 (1.50–2.30)	0.628
Day of weaning	1.73 ± 0.14 (n=9)	1.70 (1.60–2.00)	2.01 ± 0.21 (n=10)	2.00 (1.70–2.40)	0.004

*p<0.05 statistically significant difference; SD, standard deviation; Min–max, minimum and maximum values

Diaphragm thickness measurements on the first day and 14th day did not show a statistically significant difference between groups. There was a statistically significant difference in diaphragm thickness measurements on the 7th day and on the day of weaning from mechanical ventilation between the groups (Table 2). Diaphragm thicknesses of the patients showed a significant difference within groups on 7th day, 14th day, and day weaning from mechanical ventilation for both groups. Diaphragm thickness levels tended to decrease with time in both groups (Table 3). We found that the decrease in diaphragm thickness in the first 7 days was 0.10 mm in the high protein group and 0.13 mm in the standard protein group.

Mid arm muscle circumferences data did not show statistically significant difference between groups (Table 4). Measured energy expenditure data did not different between groups (Table 1). There was not any difference between groups according to the total protein and albumin levels (Table 5, Table 6). No statistically significant differences in protein and albumin levels were found within the groups. (Table 5, Table 6). Duration of ICU stay; mechanical ventilation time and hospital stay of the groups were similar

Discussion

In this study, it was compared high protein (1.5 g/kg per day) enteral nutrition with low protein enteral nutrition (1.1 g/kg per day) on diaphragm thickness using ultrasonography and outcomes in patients undergoing invasive mechanical ventilation in ICU. There was no statistically significant difference between groups in the first and 14th day control measurements of diaphragm thickness. This may be related to the low number of intubated patients on the 14th day. On the 14th day, the

Table 3. Changes in diaphragm thicknesses measurements within group

Group	Measurement	Mean ± SD	Median (Min–max)	P	Difference
Low Protein	Day 1	1.94 ± 0.27	1.80 (1.70–2.90)	0.000* §	1 – 2* ‡
	Day 7	1.81 ± 0.29	1.70 (1.50–2.90)		1 – 3* ‡
	Day 14	1.80 ± 0.33 (n=13)	1,70 (1,50 – 2,80)		1 – 4* ‡
	Day of weaning	1.73 ± 0.14 (n=9)	1.70 (1.60–2.00) (n=10)		2 – 3* ‡
					2 – 4* ‡
High Protein	Day 1	2.10 ± 0.23	2.20 (1.7–2.50)	0.000* §	1 – 2* ‡
	Day 7	2.00 ± 0.23	2.00 (1.70–2.40)		1 – 3* ‡
	Day 14	1.86 ± 0.25 (n=16)	1.95 (1.50–2.30)		1 – 4* ‡
	Day of weaning	2.01 ± 0.21 (n=10)	2.00 (1.70–2.40)		2 – 3* ‡
					2 – 4* ‡

*p<0.05 statistically significant difference; SD: standard deviation; Min–max: minimum and maximum values; 1: day 1; 2: day 7; 3: day 14; 4: day of weaving from mechanical ventilation; §: Wilcoxon repeated two-measure difference test; ‡: Friedman repetitive ANOVA.

Table 4. Mid arm muscle circumference measurements on day 1, day 7, day 14, and on the day of weaning from mechanic ventilation

	Mid arm muscle circumference Low Protein n=21		High Protein n=21		P value
	Mean ± SD (cm)	Median (Min–max)	Mean ± SD (cm)	Median (Min–max)	
Day 1	25,31±3,60	26 (18 – 30)	23,66±3,89	27 (19,5-31,5)	0.470
Day 7	24,38±3,55	25 (17 – 28)	23,70±6,68	26 (18,5-30)	0.583
Day 14	24,46±3,38(n=13)	24 (16 – 28)	23,66±3,89 (n=16)	23,75 (17-29	0.562
Day of weaning	23,67±3,95(n=9)	23,5 (18 – 28)	23,70±3,68 (n=10)	23,25 (19-29)	0.985

*p<0.05 statistically significant difference; SD, standard deviation; Min–max, minimum and maximum values.

Table 5. Blood total protein levels of the groups

	Low Protein (n=21)		High Protein (n=21)		P
	Mean ± SD	Median (Min–max)	Mean ± SD	Median (Min–max)	
Day 1	5.46 ± 0.71	5.60 (4.10–6.50)	5.66 ± 0.91	5.70 (3.59–7.30)	0.430
Day 7	5.35 ± 0.81	5.30 (3.60–6.70)	5.40 ± 0.70	5.50 (4.01–6.75)	0.834
Day 14	5.07 ± 0.68 (n=13)	5.01 (3.59–6.10)	5.32 ± 0.64 (n=16)	5.25 (4.40–6.60)	0.322
Day of weaning	5.97 ± 0.53 (n=9)	6.07 (4.90–6.70)	5.54 ± 0.74 (n=10)	5.90 (3.90–6.10)	0.181

*P<0.05 statistically significant difference; SD: standard deviation; Min–max: minimum and maximum values.

number of intubated patients was 29. However, there was a statistically significant difference between the two groups in the measurements on the 7th day and the day of weaning from the mechanical ventilator. Diaphragm thickness decreased as the measurement period progressed in both the groups. In addition, in our study, we found that the decrease in diaphragm thickness in the first 7 days was 0.10 mm in the high protein group and 0.13 mm in the low protein group. It caught our attention that the difference of 0.03 mm was in favour of the high protein group, but we could not find any statistical significance.

A protein catabolic condition associated with critical illness causes significant muscle atrophy when a patient is in the ICU. It has been observed that ICU patients lose

Table 6. Blood albumin levels of the groups

	Low Protein (n=21)		High Protein (n=21)		P
	Mean ± SD	Median (Min–max)	Mean ± SD	Median (Min–max)	
Day 1	3.05 ± 0.5	3.03 (2.06–3.80)	3.01 ± 0.57	3.17 (1.56–3.87)	0.810
Day 7	2.80 ± 0.52	2.87 (1.89–3.83)	2.62 ± 0.38	2.53 (2.06–3.38)	0.217
Day 14	2.73 ± 0.53	2.92 (1.76–3.83)	2.56 ± 0.57	2.61 (1.68–3.53)	0.311
Day of weaning	2.81 ± 0.57	2.94 (1.94–3.70)	2.54 ± 0.67	2.62 (1.61–3.57)	0.209

*p<0.05, statistically significant difference; mean mean; SD: standard deviation; Med: median; min–max: minimum and maximum values.

about 10% of muscle mass during the first 10 days of ICU admission.[8] Attenuating the catabolic state during critical illness could be one way to improve quality of life and post-ICU functional recovery while also slowing down the amount of muscle loss. For healthy individuals, maintaining muscle mass is crucial and requires dietary protein, which is a significant anabolic stimulation. Multinational, registry-based, randomised, single-blind, research was conducted in 85 ICU in sixteen countries. In order to compare the prescription of high-dose protein (≥2.2 g/kg per day) with usual dose protein (≤1.2 g/kg per day), they enrolled nutritionally high-risk adults (≥18 years) undergoing mechanical ventilation. The nutrition was started within 96 hours of ICU admission and continued for up to 28 days, or until death or the start to oral feeding. There were no differences in 60-day mortality or time-to-discharge-alive between the groups in their study. They suggested that excessive protein may be detrimental to patients who are admitted to the ICU and who have acute renal injury.[9]

Recent meta-analysis was published by van Ruijven et al.[10] was included 29 studies written between 2012 and 2022 were included. They included that studies including patients ≥18 years with an ICU stay of ≥2 days and a administered mean amount of protein ≥1.2 g/kg as compared to <1.2 g/kg. They reported outcomes such as ICU and hospital length of stay, ICU, hospital, 28-day, 30-day, 42-day, 60-day, 90-day and 6-month mortality, length of mechanical ventilation, gastric residual volume, vomiting, diarrhoea, infections, nitrogen balance, destination at hospital discharge, changes in muscle mass, physical performance and psychological status. Muscle mass changes were measured between baseline and five weeks after admission. They showed differences between groups in favour of high protein support for sixty-day mortality, nitrogen balance and changes in muscle mass. Muscle mass changes was reported in six studies which included total of 187 patients. They reported a significant difference between groups in favour of high protein. We could not find a difference for diaphragm thickness in our study. This may be since our study was a shorter study than their study or may be the different muscle mass.

In critical illness, diaphragmatic dysfunction and muscle wasting are recognised to be associated with each other and bigger catabolic activity may be seen in the diaphragm after only fifteen h of mechanical ventilation.[11] Animal and human studies in recent years have shown that also mechanical ventilation causes diaphragm dysfunction and atrophy of the respiratory muscles. Levine et al.[12] conducted a similar study in humans and showed that there was significant atrophy of myofibrils in the patient group that underwent 18–69 hours of mechanical ventilation and related diaphragm inactivity. The course of diaphragmatic atrophy in mechanically ventilated patients was evaluated using the ultrasound, and it was shown that mechanical ventilation causes atrophy in the diaphragm, decreases in diaphragm muscle thickness, and the greatest decrease in diaphragm thickness occurs during the first 72 h of mechanical ventilation.[13] In addition, the degree of atrophy was associated with the duration of mechanical ventilation. Similarly, the decrease in diaphragm thickness was directly proportional to time, and the mean diaphragm thickness decreased as the measurement days progressed in our study.

In the multicentre observational study, it was aimed search modifiable risk factors for loss of diaphragmatic function during mechanical ventilation. They studied one hundred and twenty-six critically ill patients who were ventilated for at least forty eight h and used ultrasound imaging to prospectively identify patients who experienced diaphragmatic dysfunction. They reported that patients who experienced diaphragmatic dysfunction were two times more likely to die, eight times more likely to develop extubation failure and required longer ICU stays. Amino acid intake during the first 24 h of ICU admission found the only significant independent

predictors of diaphragmatic dysfunction. Amino acid intake during the first 24 h of ICU stay might reduce the relative risk of developing diaphragmatic dysfunction (10 to 48%) and might reduce the relative risk of mortality (25 to 73%).[14] In our study, diaphragm thickness decreased as the measurement period progressed in both the groups. Although the 0.03 mm difference for diaphragm thickness in favour of the high protein group, we were unable to determine any statistical significance.

In a randomised controlled study by Nakamura et al.[15], patients in ICU were divided into two groups, and the same calorie target was achieved with high-protein nutrition in one group and standard protein nutrition in the other. Patients in both groups underwent rehabilitation with electrical muscle stimulation throughout the treatment, and femoral muscle volume was evaluated using computed tomography on the 1st and 10th days. The decrease in the femoral muscle volume was lower in the high-protein group. Albumin levels were compared on the 10th day, and no significant differences were observed. Albumin levels of the patients did not show a statistically significant difference between the groups in our study.

In a meta-analysis published in 2017, the amount of protein administered to intensive care patients and its effects on mortality, hospital stay, mechanical ventilation, and infection incidence were investigated. It showed that administration of different amounts of protein to patients had no effect on mortality. In addition, there was no significant difference between the patient groups receiving high protein and low protein in terms of length of hospital stay, duration of mechanical ventilation, and incidence of new pneumonia and bacteraemia.[16] We also found no statistically significant difference between the groups in terms of APACHE II score, mechanical ventilation time, length of ICU stay, and length of hospital stay.

Mid arm circumference measurement is considered as a useful indicator of muscle mass and nutritional status.[17] In our study, mid arm muscle circumference measurements did not show statistically significant difference between groups. This may be related to preexisting protein-energy malnutrition, sarcopenia, immobility, and disuse-related muscle atrophy in all patients.[18]

The NRS 2002 screening test is related to the degree of malnutrition. Although our patients in the protein rich group were at risk of severe malnutrition, we observed less thinning in the diaphragm thickness in this group in our study. High protein nutritional support may have affected this result.

Our study has some limitations. First, this study involved a small number of participants. Furthermore, a follow-up period of more than 14 days and a larger number of patients may be needed to show the effect of high protein nutrition on diaphragmatic thickness. We also did not record the presence of sepsis, steroid use, vasopressor use, or their effects on the diaphragm, which may have caused diaphragmatic dysfunction. Protein dosing may not be achieved reasonable between-group separation of actual protein dose delivered. We did not calculate the actually delivered protein doses. We provided the nutrition required to reach the target calories by using enteral products with high or standard protein content. The NRS 2002 scores were not the same between the groups, which may have affected the study results.

Conclusion

In this study, we found statistically significant difference between the two groups in the measurements on the 7th day and the day of weaning from the mechanical ventilator. But there was no statistically significant difference between groups in the first and 14th day control measurements of diaphragm thickness. Also, there was no significant difference between the two enteral nutrition groups in terms of diaphragm mid arm muscle circumference measurements, duration of mechanical ventilation, length of hospital stays and length of stay in the ICU. Large-scale and long-term studies on this subject may help reveal the differences between the high protein and low protein support for ICU patients.

Ethical approval

This study has been approved by the Pamukkale University Faculty of Medicine (approval date 30.08.2018, number 03). Informed consent was obtained from patients' relatives.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: DH, HS; data collection:

DH, HS; analysis and interpretation of results: DH, HS; draft manuscript preparation: DH, HS. All authors reviewed the results and approved the final version of the article.

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References

1. Peñuelas O, Frutos-Vivar F, Fernández C, et al. Characteristics and outcomes of ventilated patients according to time to liberation from mechanical ventilation. *Am J Respir Crit Care Med*. 2011;184:430-437. **[Crossref]**
2. Supinski GS, Morris PE, Dhar S, Callahan LA. Diaphragm dysfunction in critical illness. *Chest*. 2018;153:1040-1051. **[Crossref]**
3. Hudson MB, Smuder AJ, Nelson WB, Bruells CS, Levine S, Powers SK. Both high level pressure support ventilation and controlled mechanical ventilation induce diaphragm dysfunction and atrophy. *Crit Care Med*. 2012;40:1254-1260. **[Crossref]**
4. Francis CA, Hoffer JA, Reynolds S. Ultrasonographic evaluation of diaphragm thickness during mechanical ventilation in intensive care patients. *Am J Crit Care*. 2016;25:e1-e8. **[Crossref]**
5. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr*. 2019;38:48-79. **[Crossref]**
6. Compher C, Bingham AL, McCall M, et al. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. *JPEN J Parenter Enteral Nutr*. 2022;46:12-41. **[Crossref]**
7. Lee ZY, Yap CSL, Hasan MS, et al. The effect of higher versus lower protein delivery in critically ill patients: a systematic review and meta-analysis of randomized controlled trials. *Crit Care*. 2021;25:260. **[Crossref]**
8. Puthucheary ZA, Rawal J, McPhail M, et al. Acute skeletal muscle wasting in critical illness. *JAMA*. 2013;310:1591-1600. **[Crossref]**
9. Heyland DK, Patel J, Compher C, et al. The effect of higher protein dosing in critically ill patients with high nutritional risk (EFFORT Protein): an international, multicentre, pragmatic, registry-based randomised trial. *Lancet*. 2023;401:568-576. **[Crossref]**
10. van Ruijven IM, Abma J, Brunsveld-Reinders AH, et al. High protein provision of more than 1.2 g/kg improves muscle mass preservation and mortality in ICU patients: A systematic review and meta-analyses. *Clin Nutr*. 2023;42:2395-2403. **[Crossref]**
11. Hussain SN, Mofarrahi M, Sigala I, et al. Mechanical ventilation-induced diaphragm disuse in humans triggers autophagy. *Am J Respir Crit Care Med*. 2010;182:1377-1386. **[Crossref]**
12. Levine S, Nguyen T, Taylor N, et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. *N Engl J Med*. 2008;358:1327-1335. **[Crossref]**
13. Schepens T, Verbrugghe W, Dams K, Corthouts B, Parizel PM, Jorens PG. The course of diaphragm atrophy in ventilated patients assessed with ultrasound: a longitudinal cohort study. *Crit Care*. 2015;19:422. **[Crossref]**
14. Pu H, Doig GS, Lv Y, et al. Modifiable risk factors for ventilator associated diaphragmatic dysfunction: a multicenter observational study. *BMC Pulm Med*. 2023;23:343. **[Crossref]**
15. Nakamura K, Nakano H, Naraba H, et al. High protein versus medium protein delivery under equal total energy delivery in critical care: A randomized controlled trial. *Clin Nutr*. 2021;40:796-803. **[Crossref]**
16. Davies ML, Chapple LAS, Chapman MJ, Moran JL, Peake SL. Protein delivery and clinical outcomes in the critically ill: a systematic review and meta-analysis. *Crit Care Resusc*. 2017;19:117-127.
17. Akın S, Mucuk S, Öztürk A, et al. Muscle function-dependent sarcopenia and cut-off values of possible predictors in community-dwelling Turkish elderly: calf circumference, midarm muscle circumference and walking speed. *Eur J Clin Nutr*. 2015;69:1087-1090. **[Crossref]**
18. Hoffer LJ, Dickerson RN, Martindale RG, McClave SA, Ochoa Gautier JB. Will we ever agree on protein requirements in the intensive care unit? *Nutr Clin Pract*. 2017;32(Suppl 1):94-100.

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Gut-brain axis: The role of gut microbiota in energy balance and body weight regulation

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ABSTRACT

Obesity currently represents a major societal and health problem worldwide. Its prevalence has reached epidemic levels, and trends continue to increase; This, in turn, reflects the need for more effective preventive measures. Dietary composition is one of the main factors that modulate the structure and function of the gut microbiota. Therefore, abnormal dietary patterns or unhealthy diets can alter gut microbiota-diet interactions and alter nutrient availability and/or microbial ligands that transmit information from the gut to the brain in response to nutrient intake, thereby disrupting energy homeostasis. Accordingly, this review aims to examine how dietary composition modulates the gut microbiota and thus the potential effects of these biological products on energy homeostasis through gut-brain based mechanisms. It also assesses the knowledge gaps and advances needed to clinically implement microbiome-based strategies to improve gut-brain axis function and therefore combat obesity.

Keywords: microbiota, gut-brain axis, energy balance, obesity

Introduction

According to the World Atlas of Obesity 2023 report, 38% of the world's population is overweight or obese. It is predicted that this rate will reach 51% by 2035.[1] Despite the urgent need for prevention and cure of obesity and obesity-related metabolic diseases, there are few successful treatment options available. Gut microbial modulation has emerged as a potential therapeutic approach in the treatment of obesity.[2] The gut microbiota is a complex community of microorganisms that live in the gastrointestinal tract and have established a close symbiotic relationship with the human host. It plays a very important role in maintaining health, allowing the metabolism of indigestible dietary components and the synthesis of certain vitamins, preventing pathogen colonization and contributing to the development of the immune system. The human gut microbiota is mostly made up of two dominant bacterial phyla, Firmicutes and Bacteroidetes, representing more than 90% of the total population, and other subdominant phyla including Proteobacteria, Actinobacteria, and Verrucomicrobia. It is reported that a higher rate of Firmicutes and a decreased population of Bacteroidetes are often observed in obese individuals, so an increased Firmicutes/Bacteroidetes ratio is reported as a marker of obesity.[3] This microbial imbalance can lead to changes in host metabolism, ultimately leading to body weight gain. In other words, the composition of the microbiota both can be a risk factor for obesity and lifestyle factors that cause the development of obesity can affect the composition of the microbiota.[2]

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The gut-brain axis, on the other hand, is a two-way hormonal and neural signal pathway. There are several mechanisms that connect the gut to the brain in the regulation of metabolic homeostasis. Classically, signals from the gut in response to food intake during meals are transmitted to the brain, and the central nervous system (CNS) is informed about the size and composition of food.[4] The brain, specifically the hypothalamus, combines these gut-derived signals with others to coordinate the regulation of food intake, energy expenditure, and glucose homeostasis. Accordingly, in this review, it is aimed to provide an overview of how the gut-brain axis contributes to energy balance and body weight regulation.

Gut-Brain Axis in Energy Balance

Increased intake of high-energy-density, palatable foods disrupts brain circuits that control energy homeostasis; inadequate response of these circuits to food signals alters feeding behavior, which in turn contributes to an individual's body weight gain. Accordingly, the restoration of nutrient signaling via the gut-brain axis represents a promising strategy to improve the central control of energy homeostasis in response to meals, thereby helping to combat obesity.[5,6] The gut microbiota is a biological factor that can directly or indirectly influence nutrient perception, and theoretically, modulation of it could help restore gut-brain communication and maintain energy homeostasis.[2,4]

Main Points

- The gut microbiota produces metabolites and microbial products such as short-chain fatty acids and secondary bile acids that regulate the host's energy balance and body weight regulation.
- The gut microbiota metabolites act as signaling molecules that regulate energy intake and storage and energy expenditure by affecting the gut-brain axis and interact with the host in multiple ways.
- Enteroendocrine cells in the intestinal epithelium perceive nutritional and microbial signals and can regulate enteric and vagal neuronal pathways in response to microbial signals, thereby contributing to energy balance and body weight regulation.

Major mediators of the gut-brain axis

The intestinal wall is the largest surface barrier between the human body and the outside world. The components of this barrier include microbiota, mucus, epithelial monolayers, and immune cells. Intestinal epithelial cells consist of apical and basolateral area. Immune cells are located in the lamina propia.[7] Bidirectional communication between the brain and gut microbiota is mediated by various pathways, including the immune system, neuroendocrine system, enteric nervous system (ENS), circulatory system, and vagus nerve.[8] Signals from the brain are transmitted to the gut mainly through the autonomic nervous system and the hypothalamic-pituitary axis to regulate many physiological processes.[9] The vagus nerve is called the "wandering nerve" because of its long extensions that originate from the brain stem and stimulate many internal organs. Inside the intestine, the vagal afferent ends are scattered in different layers. The physiological function of a large number of vagal afferent neurons, *which are important for the regulation of energy and glucose homeostasis*, is that they contain receptors for intestinal peptides released by enteroendocrine cells (EECs).[10] Intestinal epithelial cells, EECs, neuropod cells, and enterochromaffin cells (ECs) secrete intestinal peptides, including *glucagon-like peptide-1 (GLP-1), Cholecystokinin* (CCK), *glucose-dependent insulinotropic polypeptide (GIP),* and *Peptide YY* (PYY) on the basolateral side.[6,8] These intestinal peptides are released in the immediate vicinity of vagal afferent neurons that connect the intestinal mucosa to the nervous system and activate these neurons. Vagal afferent neurons send signals to the nucleus tract solitarius (NTS), which can send signals to high-grade brain regions such as the curved nucleus (ARC).[4] ARC includes two subpopulations of neurons; αα those expressing anorexigenic propiomelanocortin (POMC), α precursor to melanocyte-stimulating hormone (α-MSH), and cocaine and amphetamine-regulated transcript (CART); and neurons expressing the agouti gene-related peptide (AgRP) and neuropeptide Y (NPY). Vagal afferent neurons are also activated through the ENS, known as the "second brain," which can regulate GI function independently of CNS action; this system can be activated by the release of gut-derived neurotransmitters such as 5-HT from ECs and intraganglionic laminar endings that sense gut tension.[5,7]

How does food sensing occur by enteroendocrine cells?

Different macronutrients act through alternative pathways to drive the release of the gut peptide.[10] Fatty acids can signal through multiple receptors on both the apical and basolateral membranes. Signaling in the basolateral membrane requires the uptake and packaging of fats into chylomicrons in enterocytes, followed by the release and breakdown of these chylomicrons on the basolateral surface.[11,12] Fatty acids bind to their receptors on enteroendocrine cells, and these activate a downstream signaling cascade that leads to the fusion of vesicles containing the gut peptide and the release of their contents across the basolateral membrane.[13]

Glucose sensing occurs in the apical membrane of an EEC and requires its uptake into the cell along with Na^+ via the Sodium/glucose cotransporter 1 (SGLT-1). Na^+ entry into EEC causes depolarization followed by activation of Ca^{2+} channels, resulting in vesicle fusion and intestinal peptide release.[14]

Amino acid signaling in the enteroendocrine cell involves the uptake of peptides and Na^+ via peptide transporter 1 (PepT1) in the apical membrane. This Na^+ can depolarize cells, but research is still needed to determine the exact mechanism of action. Amino acids are transported outside the cell via the basolateral membrane, where they can activate the calcium-sensing receptor (CaSR), leading to Ca^{2+} release and vesicle fusion. CaSR may also be present in the apical membrane, but research is still needed to elucidate the exact mechanism of protein-derived intestinal peptide release.[15,16]

Effect of intestinal peptides on energy balance and regulation of body weight

Activation of the nutrient sensors of EECs initiates the secretion of gut peptides, and these peptides trigger downstream processes that are essential for maintaining post-meal energy homeostasis.[17] The gut peptides that have been studied most extensively are cholecystokinin which is secreted mainly in the upper part of the intestine, GIP, and glucagon-like peptide-1, which is secreted mainly in the distal part, and the peptide tyrosine tyrosine.[18]

*Incretins;*The 2 hormones responsible for increasing insulin secretion after oral food intake are intestinal peptides, *GLP-1* and *GIP*.[19] *GLP-1* can also modulate satiety: Chronic treatment with Glucagon-like peptide-1 receptor (GLP1R) agonists (compounds that bind to cell receptors to create a response in the cell) in the long-term control of food intake serves to suppress food intake and promote weight loss.[6] Suppression of food intake with the GLP-1R agonist requires GLP-1R expression on glutamatergic neurons of the CNS.[20] However, prolonging the half-life of endogenous GLP-1 by inhibiting dipeptidylpetidase-4 (DPP4) is also reported to be ineffective in modifying food intake, although it potentiates the incretin effect of endogenous GLP-1.[21]

Intestinal GIP is secreted from K cells in the duodenum and proximal jejunum in response to food intake and by acting as an incretin, increases glucose-dependent insulin release from pancreatic β cells and contributes to the normalization of postprandial plasma glucose and thus energy balance.[19]

Peptide YY (PYY) is a 36-amino acid gastrointestinal hormone secreted predominantly by intestinal L cells.[22] PYY, or more specifically its active form PYY3-36, is known for its role in the "ileal break," which slows the passage of chyme to ensure adequate digestion in the proximal intestine.[23] In addition to its satiety-enhancing effect through ileal break, PYY3-36 may also reduce food intake through independent mechanisms without reducing intestinal motility. PYY exerts an anorexigenic effect through vagal afferents and crossing the blood-brain barrier.[24] PPYY3-36 also directly and indirectly stimulates POMC activity through inhibition of NPY neurons and nerve terminals that activate adjacent POMC neurons and induces prolonged upregulation of POMC mRNA expression.[25] In this respect, PYY analogues, together with GLP-1 receptor agonists, are reported as a promising therapeutic approach for obesity with their beneficial effects on energy balance and food intake preference.[26]

Microbial metabolites mediating energy balance and body weight regulation

Gut microbiota is reported as an environmental factor that regulates the host's energy balance.[2] It increases the host's ability to obtain energy from food and produces metabolites and microbial products such as short-chain fatty acids, secondary bile acids, and lipopolysaccharides. These metabolites and microbial products act as signaling molecules that regulate appetite, intestinal motility, energy intake and storage, and energy expenditure.[8,10]

Short chain fatty acids

Adding fermentable carbohydrates, including dietary fibers and resistant starch, to the diet reduces food intake and body weight gain and improves glucose metabolism in rodents and humans.[25] It has been stated that these effects are partly mediated by short-chain fatty acids (SCFAs). SCFAs are produced in a fermentation process from carbohydrates (resistant starch, dietary fiber, and other low-digestible polysaccharides) that cannot be digested by the microbiota in the colon and distal small intestine. Acetate, propionate, and butyrate are the predominant SCFAs in the intestinal lumen in humans and rodents.[27]

SCFAs are known to regulate food intake by modulating hypothalamic function, reaching the systemic circulation to the brain, or directly through food signaling mediated by GLP-1 and PYY produced/released in EECs, or through vagal afferents (such as activating adipose tissue to release leptin hormone).[28] Its microbial-derived SCFAs are absorbed into the bloodstream and affect whole-body physiology through mechanisms that may include G protein-coupled receptors (GPCRs), also called free fatty acid receptors (FFARs).[29] Among SCFAs, acetate appears to reach the brain through systemic pathways, while propionate and butyrate mainly activate nutrient sensing pathways in the gut. Of these SCFAs, propionate, in particular, is reported to centrally control intestinal gluconeogenesis, a process that confers metabolic benefits, including reduced endogenous glucose production, independent of insulin.[30] Furthermore, like acetate, elevated plasma propionate levels promote hypothalamic anorexigenic neuronal activation by inducing leptin release from adipocytes through FFARs-dependent mechanism. Butyrate, on the other hand, is reported to be the most potent stimulant of anorexigenic peptides and the most potent suppressor of food intake.[27] Intestinal butyrate can transmit satietogenic signals by stimulating GLP-1 and GIP secretion in L cells and K cells, respectively, and these effects are potentiated by ghrelin inhibition.[31] These fatty acids also increase insulin sensitivity and mitochondrial function in muscle cells, support pancreatic function, including insulin secretion and beta cell activity, and reduce lipid accumulation and glucose production in the liver.[28] Gut bacterial SCFA-activated free fatty acid receptors 2 and 3 (FFAR2/3) modulate adipose tissue physiology of the host by activating AMP-activated protein kinase (AMPK) in white adipose tissue (BAD), inhibiting cyclic adenosine monophosphate (cAMP) activation, adipogenesis, activation of UCP-1, and browning by increasing fatty acid oxidation, thereby reducing body weight and whole-body metabolic It regulates homeostasis.[29]

The mechanism involving the production of leptin, the satiety hormone derived from adipose tissue, under the influence of SCFAs, is the most studied mechanism.[32] It has been reported that leptin binds to receptors in the brain and inactivates NPY and AgRP in normal physiological conditions, suppressing appetite, as well as inducing POMC mRNA expression.[33] The released leptin is transported across the blood-brain barrier (BBB) to perform its function, and Leptin Receptor-a (LepRa) is needed in this process.[34]

Pathologically, in obese individuals, an excessively high level of leptin in plasma causes saturation of LepRa and thus leads to leptin resistance reducing the rate of leptin transport across the blood-brain barrier (BBB). A number of factors and specific mechanisms underlying the development of this condition are linked to cellular signaling of leptin.[35] Two points are emphasized regarding the disruption of leptin cellular signaling. First, neurons expressing LepR are not sensitive enough to measure circulating leptin levels, which reduces the effectiveness of leptin's binding to LepR. Second, the signaling ability of LepR-expressing cells is impaired. For example, it has been reported that proinflammatory factors such as IL-6 may increase with intestinal dysbiosis and indirectly affect leptin secretion and functionality, and their importance in energy metabolism and body weight regulation has been reported.[33] In addition, circulating leptin-binding proteins such as plasma-soluble LepR and C-reactive protein bind competitively to leptin and promote the development of leptin resistance. Binding of leptin to circulating leptin-binding proteins inhibits leptin transport to the CNS, suppresses the interaction between leptin and LepR neurons, and induces phenotypes associated with leptin resistance. Leptin resistance develops not only in the brain but also in peripheral tissues such as skeletal muscle, adipose tissue, and liver, which may provide new perspectives on obesity treatment.[36]

Microbial metabolites of bile acids

Bile acids (BA) are steroid acids synthesized from cholesterol in the liver, conjugated to taurine or glycine, and released in the duodenum after food intake to facilitate the absorption of dietary lipids and fat-soluble vitamins.[37,38] The majority of primary BA secreted in the gut is actively reabsorbed in the ileum and transported back to the liver via the portal circulation.[39] The remaining

small portion of the primary BA is deconjugated and dehydroxylated by gut bacteria in the ileum and colon and converted into secondary BAs.[37,40] Bacterial bile salt hydrolases (BSH) are enzymes required for the deconjugation of primary BAs to secondary BAs. BAs have also been shown to play a role in the regulation of glucose and lipid metabolism and energy expenditure through activation of BA receptors in the liver, intestine, and peripheral tissues. The effect of secondary BAs resulting from gut microbiota activity on the brain is still poorly studied, but current studies report that secondary BAs can potentially modulate food intake and energy homeostasis through afferent pathways through TGR5-GLP-1 and/or 5-HT gut sensing pathways.[41,42] Specifically, secondary bile acids stimulate GLP-1 secretion by activating G protein-coupled receptors (TGR5) on L cells, and thus its role in stimulating saturation in vagal afferent neurons has been demonstrated.[43] TGR5 receptors are also found in skeletal muscle and brown adipose tissue, where they increase energy expenditure promoting the conversion of inactive thyroxine (T4) to active thyroid hormones (T3).[44] Bile acids have been shown to act on farnesoid X receptors (FXR). Insulin release increases during BA binding of FXR to pancreatic β cells. Bile acid activation of intestinal FXR-containing cells stimulates the secretion of fibroblast growth factor-19 (FGF-19), a protein that contributes to the improvement of peripheral glucose excretion and lipid homeostasis, increasing metabolic rate, and reducing weight. FGF-19 may improve glucose tolerance by regulating insulin-independent glucose flow and hepatic glucose production.[45] Thus, secondary bile acids exert potential effects on the host's energy balance, glucose homeostasis, and body weight regulation.

Amino acid-derived metabolites

Also known as serotonin, 5-HT is synthesized from tryptophan, an important amino acid derived from dietary proteins in the gut as well as in the brain. 5-HT is released from enterochromaffin cells upon intraluminal pressure and leads to activation of receptors and peristaltic action.[46] Derived from the intestines, 5-HT has also been shown to be important for starvation-induced adaptation by promoting lipolysis in adipose tissue and gluconeogenesis in the liver, thereby increasing energy availability for other organs in the body.[47] 5-HT receptors are expressed in many cell types in the gut, including enterochromaffin cells, goblet cells, enterocytes, vagal and spinal afferent nerves, and enteric nerves. The gut microbiota, through its metabolites, is reported to induce the release of 5-HT in the colon and indirectly in the small intestine by stimulating GLP-1 secretion.[42]

Tryptophan can be fermented into indole, a ligand of the arylhydrocarbon receptor (AHR), a transcription factor that regulates gene expression. In vitro assay with GLUTag cell lines shows that activation of AHR with an agonist increases GLP-1 secretion as well as proglucagon expression.[48] Obesity in mice has been associated with an increase in gut IDO1, an enzyme that catalyzes the breakdown of tryptophan via the kynura pathway, thereby limits bacterial indole production from tryptophan and increases its derivatives such as kynurinin and kyuronic acid.[49] Intraperitoneal administration of kynuronic acid in mice has been shown to induce energy expenditure without affecting food intake.[50]

To date, studies on the effect of γ-Aminobutyric acid (GABA), which is produced by the gut microbiota from the dietary amino acid glutamate, on gut-brain communication and thus the control of energy homeostasis are insufficient. GABA is the main inhibitory neurotransmitter in the central nervous system. Peripheral GABA cannot cross the blood-brain barrier, but it has been reported to activate nutrient sensing signaling pathways in the gut.[51] However, more studies are needed to understand its contribution to energy homeostasis and the regulation of body weight.

The Effect Of Diets' Macronutrient Ratio Changes On Energy Balance and Body Weight Regulation Through Microbiota-Gut-Brain Communication

Dietary interventions, such as high-protein or high-fat diets, which are characterized by large differences in macronutrient ratios, affect the composition and function of the gut microbiota.[52] The composition in the macronutrients of these diets exerts a significant influence on the availability of gut microbiota-derived ligands, luminal content, which can control food intake and energy metabolism. The availability of these ligands depends on many biological processes, including microbiota-mediated catabolism of digested nutrients and their absorption by enterocytes.[10,17]

It has been reported that in normal-weight or obese individuals, high-protein meals provide the most satiety compared to isocaloric diets containing high carbohydrates or fats, and this effect is due to PYY,

the secretion of which is preferentially increased by proteins.[7,8] In addition to gut peptides, high-protein diets modulate the gut-brain axis to control food intake and energy metabolism by stimulating gut gluconeogenesis from the postprandial to postabsorption periods.[53] Peptides digested in the small intestine antagonize μ-opioid receptors in the spinal and vagal afferents of the portal vein, whic is a signal that centrally activates intestinal gluconeogenesis. In addition, enriched protein meals are a source of gluconeogenesis substrates such as glutamine and glutamate for the intestines. Compared to carbohydrates and fats, proteins also have the highest effect on triggering thermogenesis. Although the underlying mechanisms need to be elucidated specifically for proteins, thermogenesis-dependent gut-brain axis mechanisms mediated by gut hormones have been identified.[54] For example, GLP-1 centrally enhances thermogenesis through sympathetic efferents, and the duodenal hormone secretin activates thermogenesis postprandial to induce satiety.[55] High-protein diets also increase the amount of amino acids that can be fermented by the gut microbiota in the colon to obtain energy and produce nutrient-sensing ligands. These include amino acid-derived SCFAs, branched-chain fatty acids, and other molecules derived from tryptophan or glutamate. Compared to carbohydrates, fermentation of proteins produces less SCFA, but still contributes significantly to the production of microbial organic acids. However, there are few studies that address the relational or causal links between gut microbiota and high-protein diets on the control of food intake and energy homeostasis via the gut-brain axis. Furthermore, additional studies are needed to evaluate the risks and benefits of high-protein dietary interventions in improving metabolic health. There are studies reporting that such dietary interventions reduce butyrate production and increase the levels of mucosal and renal toxic compounds.[56,57]

Low-carbohydrate diets, on the other hand, have been reported to have a lower capacity to stimulate brain regions associated with food intake, compared to diets high in carbohydrates.[58,59] However, the exact mechanisms underlying the satiety effects caused by these diets, particularly those dependent on the gut microbiota, still remain unclear. Some studies suggest that diet-induced ketogenesis mediates decreased circulating ghrelin levels associated with decreased appetite in overweight/obese individuals following a low-energy diet, although ketone bodies inhibit GLP-1 release by EECs and directly activate orexigenic hypothalamic pathways in the brain.[60,61] Similar to SCFAs, ketone bodies have also been reported to initiate GPR41 and GPR43 signaling to control energy metabolism.[62] To date, it has not been investigated how these ketone bodies affect the hypothalamus via GPR41/43, and more research is needed.

Conclusion

The gut microbiota plays a crucial role in maintaining energy balance and glucose homeostasis. EECs in the GI tract can sense nutrients and release a variety of gut peptides to affect both energy balance and glucose homeostasis. However, more studies are needed to fully understand the mechanisms by which various nutrients activate EECs and release gut peptides. The hypothalamic circuits, which control energy balance in response to food intake, need to be studied further in terms of body weight management.

Author contribution

The authors declare contribution to the paper as follows: Review conception and design: GPT; literature review: GPT; draft manuscript preparation: GPT, ÖB, AD. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Lobstein T, Jackson-Leach R, Powis J, Brinsden H, Gray M. World obesity atlas 2023. Available at: https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2023 (Accessed on May 8, 2023).
2. Saravanan D, Khatoon BS, Winner GJ. Unraveling the Interplay: Exploring the Links Between Gut Microbiota, Obesity, and Psychological Outcomes. *Cureus*. 2023;15:e49271. **[Crossref]**

3. Magne F, Gotteland M, Gauthier L, et al. The Firmicutes/Bacteroidetes Ratio: A Relevant Marker of Gut Dysbiosis in Obese Patients? *Nutrients*. 2020;12:1474. [Crossref]
4. de Lartigue G, Diepenbroek C. Novel developments in vagal afferent nutrient sensing and its role in energy homeostasis. *Curr Opin Pharmacol*. 2016;31:38-43. [Crossref]
5. Clemmensen C, Müller TD, Woods SC, Berthoud HR, Seeley RJ, Tschöp MH. Gut-Brain Cross-Talk in Metabolic Control. *Cell*. 2017;168:758-774. [Crossref]
6. Drucker DJ. Mechanisms of Action and Therapeutic Application of Glucagon-like Peptide-1. *Cell Metab*. 2018;27:740-756. [Crossref]
7. Fan J, Yang Y, Ma C, et al. The effects and cell barrier mechanism of main dietary nutrients on intestinal barrier. *Curr Opin Food Sci*. 2022;48:100942. [Crossref]
8. Liu L, Huh JR, Shah K. Microbiota and the gut-brain-axis: Implications for new therapeutic design in the CNS. *EBioMedicine*. 2022;77:103908. [Crossref]
9. Goldstein N, McKnight AD, Carty JRE, Arnold M, Betley JN, Alhadeff AL. Hypothalamic detection of macronutrients via multiple gut-brain pathways. *Cell Metab*. 2021;33:676-687.e5. [Crossref]
10. Wachsmuth HR, Weninger SN, Duca FA. Role of the gut-brain axis in energy and glucose metabolism. *Exp Mol Med*. 2022;54:377-392. [Crossref]
11. Psichas A, Larraufie PF, Goldspink DA, Gribble FM, Reimann F. Chylomicrons stimulate incretin secretion in mouse and human cells. *Diabetologia*. 2017;60:2475-2485. [Crossref]
12. Lu WJ, Yang Q, Yang L, Lee D, D'Alessio D, Tso P. Chylomicron formation and secretion is required for lipid-stimulated release of incretins GLP-1 and GIP. *Lipids*. 2012;47:571-580. [Crossref]
13. Christensen LW, Kuhre RE, Janus C, Svendsen B, Holst JJ. Vascular, but not luminal, activation of FFAR1 (GPR40) stimulates GLP-1 secretion from isolated perfused rat small intestine. *Physiol Rep*. 2015;3:e12551. [Crossref]
14. Gorboulev V, Schürmann A, Vallon V, et al. Na(+)-D-glucose cotransporter SGLT1 is pivotal for intestinal glucose absorption and glucose-dependent incretin secretion. *Diabetes*. 2012;61:187-196. [Crossref]
15. Modvig IM, Kuhre RE, Holst JJ. Peptone-mediated glucagon-like peptide-1 secretion depends on intestinal absorption and activation of basolaterally located Calcium-Sensing Receptors. *Physiol Rep*. 2019;7:e14056. [Crossref]
16. Mace OJ, Schindler M, Patel S. The regulation of K- and L-cell activity by GLUT2 and the calcium-sensing receptor CasR in rat small intestine. *J Physiol*. 2012;590:2917-2936. [Crossref]
17. Gribble FM, Reimann F. Function and mechanisms of enteroendocrine cells and gut hormones in metabolism. *Nat Rev Endocrinol*. 2019;15:226-237. [Crossref]
18. Barakat GM, Ramadan W, Assi G, Khoury NBE. Satiety: a gut-brain-relationship. *J Physiol Sci*. 2024;74:11. [Crossref]
19. Holst JJ, Rosenkilde MM. GIP as a Therapeutic Target in Diabetes and Obesity: Insight From Incretin Co-agonists. *J Clin Endocrinol Metab*. 2020;105:e2710–e2716. [Crossref]
20. Adams JM, Pei H, Sandoval DA, et al. Liraglutide Modulates Appetite and Body Weight Through Glucagon-Like Peptide 1 Receptor-Expressing Glutamatergic Neurons. *Diabetes*. 2018;67:1538-1548. [Crossref]
21. Cheng W, Ndoka E, Hutch C, et al. Leptin receptor-expressing nucleus tractus solitarius neurons suppress food intake independently of GLP1 in mice. *JCI Insight*. 2020;5:e134359. [Crossref]
22. Chen W, Binbin G, Lidan S, Qiang Z, Jing H. Evolution of peptide YY analogs for the management of type 2 diabetes and obesity. *Bioorg Chem*. 2023;140:106808. [Crossref]
23. Maljaars PW, Peters HP, Mela DJ, Masclee AA. Ileal brake: a sensible food target for appetite control. A review. *Physiol Behav*. 2008;95:271-281. [Crossref]
24. Larraufie P, Martin-Gallausiaux C, Lapaque N, et al. SCFAs strongly stimulate PYY production in human enteroendocrine cells. *Sci Rep*. 2018;8:74. [Crossref]
25. Brooks L, Viardot A, Tsakmaki A, et al. Fermentable carbohydrate stimulates FFAR2-dependent colonic PYY cell expansion to increase satiety. *Mol Metab*. 2016;6:48-60. [Crossref]
26. Oertel M, Ziegler CG, Kohlhaas M, et al. GLP-1 and PYY for the treatment of obesity: a pilot study on the use of agonists and antagonists in diet-induced rats. *Endocr Connect*. 2024;13:e230398. [Crossref]
27. Goswami C, Iwasaki Y, Yada T. Short-chain fatty acids suppress food intake by activating vagal afferent neurons. *J Nutr Biochem*. 2018;57:130-135. [Crossref]
28. Mazhar M, Zhu Y, Qin L. The Interplay of Dietary Fibers and Intestinal Microbiota Affects Type 2 Diabetes by Generating Short-Chain Fatty Acids. *Foods*. 2023;12:1023. [Crossref]
29. May KS, den Hartigh LJ. Gut Microbial-Derived Short Chain Fatty Acids: Impact on Adipose Tissue Physiology. *Nutrients*. 2023;15:272. [Crossref]
30. De Vadder F, Kovatcheva-Datchary P, Goncalves D, et al. Microbiota-generated metabolites promote metabolic benefits via gut-brain neural circuits. *Cell*. 2014;156:84-96. [Crossref]
31. Yadav H, Lee JH, Lloyd J, Walter P, Rane SG. Beneficial metabolic effects of a probiotic via butyrate-induced GLP-1 hormone secretion. *J Biol Chem*. 2013;288:25088-25097. [Crossref]
32. Rastelli M, Knauf C, Cani PD. Gut Microbes and Health: A Focus on the Mechanisms Linking Microbes, Obesity, and Related Disorders. *Obesity (Silver Spring)*. 2018;26:792-800. [Crossref]
33. Rehman Khan A, Awan FR. Leptin Resistance: A Possible Interface Between Obesity and Pulmonary-Related Disorders. *Int J Endocrinol Metab*. 2016;14:e32586. [Crossref]
34. Izquierdo AG, Crujeiras AB, Casanueva FF, Carreira MC. Leptin, Obesity, and Leptin Resistance: Where Are We 25 Years Later? *Nutrients*. 2019;11:2704. [Crossref]

35. Liu J, Lai F, Hou Y, Zheng R. Leptin signaling and leptin resistance. *Med Rev (2021)*. 2022;2:363-384. **[Crossref]**

36. Pena-Leon V, Perez-Lois R, Villalon M, et al. Novel mechanisms involved in leptin sensitization in obesity. *Biochem Pharmacol*. 2024;223:116129. **[Crossref]**

37. Ringseis R, Gessner DK, Eder K. The Gut-Liver Axis in the Control of Energy Metabolism and Food Intake in Animals. *Annu Rev Anim Biosci*. 2020;8:295-319. **[Crossref]**

38. Romaní-Pérez M, Bullich-Vilarrubias C, López-Almela I, Liébana-García R, Olivares M, Sanz Y. The Microbiota and the Gut-Brain Axis in Controlling Food Intake and Energy Homeostasis. *Int J Mol Sci*. 2021;22:5830. **[Crossref]**

39. Dawson PA, Karpen SJ. Intestinal transport and metabolism of bile acids. *J Lipid Res*. 2015;56:1085-1099. **[Crossref]**

40. Lund ML, Egerod KL, Engelstoft MS, et al. Enterochromaffin 5-HT cells - A major target for GLP-1 and gut microbial metabolites. *Mol Metab*. 2018;11:70-83. **[Crossref]**

41. Monteiro-Cardoso VF, Corlianò M, Singaraja RR. Bile Acids: A Communication Channel in the Gut-Brain Axis. *Neuromolecular Med*. 2021;23:99-117. **[Crossref]**

42. Mertens KL, Kalsbeek A, Soeters MR, Eggink HM. Bile Acid Signaling Pathways from the Enterohepatic Circulation to the Central Nervous System. *Front Neurosci*. 2017;11:617. **[Crossref]**

43. Chiang JYL, Ferrell JM. Bile Acids as Metabolic Regulators and Nutrient Sensors. *Annu Rev Nutr*. 2019;39:175-200. **[Crossref]**

44. Fang S, Suh JM, Reilly SM, et al. Intestinal FXR agonism promotes adipose tissue browning and reduces obesity and insulin resistance. *Nat Med*. 2015;21:159-165. **[Crossref]**

45. Sun L, Xie C, Wang G, et al. Gut microbiota and intestinal FXR mediate the clinical benefits of metformin. *Nat Med*. 2018;24:1919-1929. **[Crossref]**

46. Tian P, O'Riordan KJ, Lee YK, et al. Towards a psychobiotic therapy for depression: Bifidobacterium breve CCFM1025 reverses chronic stress-induced depressive symptoms and gut microbial abnormalities in mice. *Neurobiol Stress*. 2020;12:100216. **[Crossref]**

47. Reigstad CS, Salmonson CE, Rainey JF, et al. Gut microbes promote colonic serotonin production through an effect of short-chain fatty acids on enterochromaffin cells. *FASEB J*. 2015;29:1395-1403. **[Crossref]**

48. Natividad JM, Agus A, Planchais J, et al. Impaired Aryl Hydrocarbon Receptor Ligand Production by the Gut Microbiota Is a Key Factor in Metabolic Syndrome. *Cell Metab*. 2018;28:737-749.e4. **[Crossref]**

49. Laurans L, Venteclef N, Haddad Y, et al. Genetic deficiency of indoleamine 2,3-dioxygenase promotes gut microbiota-mediated metabolic health. *Nat Med*. 2018;24:1113-1120. **[Crossref]**

50. Agudelo LZ, Ferreira DMS, Cervenka I, et al. Kynurenic Acid and Gpr35 Regulate Adipose Tissue Energy Homeostasis and Inflammation. *Cell Metab*. 2018;27:378-392.e5. **[Crossref]**

51. Inotsuka R, Uchimura K, Yamatsu A, Kim M, Katakura Y. γ-Aminobutyric acid (GABA) activates neuronal cells by inducing the secretion of exosomes from intestinal cells. *Food Funct*. 2020;11:9285-9290. **[Crossref]**

52. Cabrera-Mulero A, Tinahones A, Bandera B, Moreno-Indias I, Macías-González M, Tinahones FJ. Keto microbiota: A powerful contributor to host disease recovery. *Rev Endocr Metab Disord*. 2019;20:415-425. **[Crossref]**

53. Soty M, Gautier-Stein A, Rajas F, Mithieux G. Gut-Brain Glucose Signaling in Energy Homeostasis. *Cell Metab*. 2017;25:1231-1242. **[Crossref]**

54. Hall KD, Guo J. Obesity Energetics: Body Weight Regulation and the Effects of Diet Composition. *Gastroenterology*. 2017;152:1718-1727.e3. **[Crossref]**

55. Li Y, Schnabl K, Gabler SM, et al. Secretin-Activated Brown Fat Mediates Prandial Thermogenesis to Induce Satiation. *Cell*. 2018;175:1561-1574.e12. **[Crossref]**

56. Blachier F, Beaumont M, Portune KJ, et al. High-protein diets for weight management: Interactions with the intestinal microbiota and consequences for gut health. A position paper by the my new gut study group. *Clin Nutr*. 2019;38:1012-1022. **[Crossref]**

57. Portune K, Beaumont M, Davila AM, Tomé D, Blachier F, Sanz Y. Gut microbiota role in dietary protein metabolism and health-related outcomes: The two sides of the coin. *Trends in Food Science & Technology*. 2016;57:213-232. **[Crossref]**

58. Holsen LM, Hoge WS, Lennerz BS, et al. Diets Varying in Carbohydrate Content Differentially Alter Brain Activity in Homeostatic and Reward Regions in Adults. *J Nutr*. 2021;151:2465-2476. **[Crossref]**

59. Skytte MJ, Samkani A, Astrup A, et al. Effects of carbohydrate restriction on postprandial glucose metabolism, β-cell function, gut hormone secretion, and satiety in patients with Type 2 diabetes. *Am J Physiol Endocrinol Metab*. 2021;320:E7-E18. **[Crossref]**

60. Carneiro L, Geller S, Fioramonti X, et al. Evidence for hypothalamic ketone body sensing: impact on food intake and peripheral metabolic responses in mice. *Am J Physiol Endocrinol Metab*. 2016;310:E103-E115. **[Crossref]**

61. Wallenius V, Elias E, Elebring E, et al. Suppression of enteroendocrine cell glucagon-like peptide (GLP)-1 release by fat-induced small intestinal ketogenesis: a mechanism targeted by Roux-en-Y gastric bypass surgery but not by preoperative very-low-calorie diet. *Gut*. 2020;69:1423-1431. **[Crossref]**

62. Miyamoto J, Igarashi M, Watanabe K, et al. Gut microbiota confers host resistance to obesity by metabolizing dietary polyunsaturated fatty acids. *Nat Commun*. 2019;10:4007. **[Crossref]**

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Nutritional management in MNGIE disease: A case report

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ABSTRACT

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is a rare autosomal recessive metabolic disorder characterized by thymidine phosphorylase deficiency. The progressive course of MNGIE increases the importance of early diagnosis and supportive treatment approaches. The disease usually presents with gastrointestinal dysmotility, neuropathy, hearing loss, cachexia, and nutritional disorders. In this case report, we present the nutritional management and follow-up of a 16-year-old male patient with MNGIE disease. The patient presented with a loss of nearly 40% of his total body weight, a BMI of 9.4 kg/m2 and severe nutritional deficiencies. Total parenteral nutrition was initiated in the first phase of nutritional treatment and then gradually transitioned to enteral nutrition. The patient's nutritional status was improved with peptide-based formulas and pancreatic enzyme support. During the treatment process, energy and protein requirements were nearly met, weight gain was achieved and biochemical parameters were improved.

Keywords: enteral, malnutrition, mitochondrial neurogastrointestinal encephalopathy syndrome, nutrition, parenteral

Introduction

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is a rare autosomal recessively inherited metabolic disorder caused by thymidine phosphorylase (TP) deficiency due to biallelic pathogenic variants in thymidine phosphorylase (*TYMP*) gene. Mutations in *TYMP* gene led to toxic levels of plasma thymidine accumulation, deoxyribonucleoside imbalance, impairment in DNA replication, and eventually mitochondrial disfunction. Approximately 550 cases of MNGIE cases were reported.[1,2]

Although the disease has a progressive and a fatal course, the quality of life demands basically on nutrition aids and other supportive measurements. Behind the several therapeutic approaches targeting enzyme increment such as TP infusions, hematopoietic stem cell transplantation (HSCT), and orthotopic liver transplantation (OLT), a curative solution is not available. The timing of HSCT and OLT is very critical, as the severity of gastrointestinal (GI) symptoms affects treatment success. Gene therapy is considered as a possible treatment option as it has shown efficacy in preliminary clinical studies.[3]

Clinically, MNGIE is characterized by neurological involvement manifestations such as ptosis, external ophthalmoplegia, peripheral neuropathy and leukoencephalopathy. Additionally, dramatic gastrointestinal signs and symptoms of dysmotility, abdominal pain, nausea, dysphagia, attacks of pseudoobstruction, and diarrhea led to severe malnutrition and cachexia. Dysphagia both prevents adequate oral intake and also can lead to aspiration and

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lower respiratory system infections. Different studies put forward that nutritional treatment in pediatric age group provides benefits in terms of clinical course and quality of life. It has been reported that 29-48% of patients with mitochondrial diseases have gastrointestinal involvement and 52% have growth retardation.[3-5] Therefore, clinical nutritional treatment is of great importance in MNGIE disease, although there is not a standard approach. Here, we want to share our nutritional management protocol, as it has been succeded in a MNGIE patient.

Case Report

A 16-year-old male patient was admitted to Çukurova University Division of Pediatric Metabolism and Nutrition Department with complaints of GIS dismotility, severe wait loss, and symptoms of malnutrition together with peripheric neuropathy and hearing loss. Family history was unremarkable and there was no consanguinity between the parents. His mental, motor development and physical growth was normal in the first 15 years of life. Only bilateral sensorineural hearing loss was detected at the age of 7 years. Recurrent vomiting attacks, resistant diarrhea and swallowing difficulties due to muscle weakness, which had been began in the last 6 months caused a 15 kg weight loss and severe malnutrition of the patient (Figure 1). He was hospitalized several times with a need of intravenous fluid support. After excluding common causes of these GIS symptoms such as obstructive lessions, inflamatory bowel diseases, and infections concomitant neurological findings led a suspicion of MNGIE disease. A pathogenic variant detected in *TYMP* gene confirmed the prediagnosis of MNGIE disease.

On admission his weight was 22 kg (-8.09 SDS), height was 153 cm (-3.1 SDS), and body mass index (BMI) was 9.4 kg/m^2 (-10.92 SDS). He had bilateral senseronoral hearing loss, and polyneuropaty. He had also difficulty in swallowing solid foods. Initial hematological and biochemical parameters revealed low levels of hemoglobin, hematocrit, total protein, albumin, sodium, potassium, chloride, iron, calcium, phosphorous, and magnesium (Table 1). During the patient's hospitalization erythrocyte and albumin infusions were given together with vitamin, mineral, and trace elements supplementations.

Figure 1. General appearance of the patient

Evaluation of his 24 hours nutritional record with STRONGkids screening tool (5 point), it was found that the patient was in the high-risk group in terms of malnutrition. Then, oral nutrition was stopped and total parenteral nutrition (TPN) was initiated to come over the severe gastric dismotility and secondary malabsorbsition. Our patient was observed to have gastrointestinal symptoms such as diarrhea 5-6 times/day, vomiting and distension 2-3 times/day. The daily energy and protein intake targets were 440-550 kcal (20-25 kcal/kg/day) and 26 g/day (1.2 g/kg actual body weight), respectively. Energy intake was gradually increased to prevent refeeding syndrome (Table 2). On the 10th day of hospitalization, a nasogastric tube was inserted for transition to enteral nutrition and TPN was gradually tapered and terminated 14th day. Pancreatic enzyme supplementation (600U lipase and amylase per 1 gram fat in diet) was started with enteral formula (16x10 ml)

Main Points

- Severe gastrointestinal dysmotility and malnutrition are common in patients with MNGIE.
- Nutritional treatment is essential to decrease mortality and improve quality of life in MNGIE disease.
- Severe gastrointestinal dysmotility and malnutrition in MNGIE can be effectively managed with a combination of parenteral and enteral nutrition.

Table 1. Laboratory data of the patient.

Parameter	Reference Range	Before Nutritional Treatment (First day)	After Nutritional Treatment (Day 30)
Hemoglobin (g/dL)	12.6-17	6	11.1
Hematocrit (%)	38-49	21.7	32.3
MCV (fl)	79-95	128.2	96
BUN (mg/dL)	8-20	14.06	13
Creatine (mg/dL)	0.3-1	0.4	0.39
Iron (µg/dL)	65-175	10	32
Ferritin (ng/mL)	24-336	67	139.6
Sodium (mmol/L)	136-144	127	137
Potassium (mmol/L)	3.6-5.1	3.3	3.9
Chloride (mmol/L)	101-111	91	104
Calcium (mg/dL)	8.9-10.3	7.6	9.28
Phosphorous (mg/dL)	2.4-4.7	2.35	2.94
Magnesium (mg/dL)	1.8-2.5	1.57	1.92
AST (U/L)	13-38	22	25
ALT (U/L)	8-39	9	10
Triglycerides (mg/dL)	<129	62	117
Total protein (g/dL)	61-79	34.9	67.8
Albumin (g/L)	35-48	21.4	39.88
B12 (pg/mL)	126-505	246	505
Folate (ng/mL)	3.1-19.9	7.74	14.98

Table 2. Nutritional Treatment

Day	Way of nutrition therapy	Energy intake
1-3	TPN-380 mL	220 kcal
4-6	TPN-760 mL	440 kcal
7-9	TPN-950 mL	550 kcal
10-14	TPN-535 mL + EN-160 mL	550 kcal
14-26	Oral nutrition (ON)-Regimen 1-2 + EN-350 mL	660 kcal
27-30	ON-Regimen 2 + EN-400 mL	720 kcal

containing peptide-based medium-chain triglycerides and glutamine (2x5 g-0,5 g/kg/day) was added to the diet. Enteral formula was gradually increased with an average 10-20% increase in each visit. The patient was discharged on the 27th day of hospitalization with NG removal and 8x50 ml oral nutritional treatment and glutamine in addition to regimen 2 (yoghurt, soup, compote etc.-soft and easily digestible diet) feeding. The patient came for outpatient clinic control on the 15th day of discharge, and his current weight was 24 kg (-7.37 SDS) and his body mass index was 10.25 kg/m^2 (-9.23 SDS). He had tolerable gastrointestinal symptoms and signs. Biochemical parameters albumin, total protein, magnesium and calcium levels increased.

Discussion

Due to the rarity and multisystemic involvement of MNGIE, patients have a history of uncountable admissions to different specialties before a specific diagnosis is confirmed. Furthermore, progressive nature of the disease also led to irreversible complications and a poor prognosis.[2]

Severe weight loss and cachexia related to gastrointestinal dysmotility is one of the main problems that are observed in MNGIE. Therefore, nutritional treatment is essential to decrease mortality and improve quality of life in these patients. Nutritional treatment in patients with MNGIE aims to increase nutrient intake with enteral/parenteral nutrition. Feeding tubes are used in cases where necessary. Nutritional treatment has beneficial effects on both decreasing the severity of malnutrition and the other complications. TPN together with enteral nutrition generally prevents refractory cachexia and helps to achieve some weight gain. Although metabolic problems such as hypokalemia, elevated liver function tests and sepsis are the probable side effects associated with TPN, both in the long or short term of MINGIE management TPN is still a gold standard in nutritional treatment.[1] In patients with limited oral intake due to gastrointestinal symptoms, enteral tube feeding may improve quality of life and growth failure. In our patient, reduction in gastrointestinal symptoms and recurrent vomiting attacks, weight gain and improvement in quality of life were observed after tube feeding treatment. There are very limited numbers of case reports about the nutritional management of MNGIE patients. It was notified that a 23-year-old female MNGIE patient with a BMI of 15 kg/m^2 was treated with a hypercaloric diet containing 55% carbohydrate, 16% protein and 29% fat. Initially the patient was unable to finish this diet due to early feeling of satiety and anorexia, however she gradually reached the recommended energy intake. At the end of the first year of follow-up with this diat, the patient's BMI was increased to 16.9 kg/m^2 and muscle strength which was measured by hand grip improved. Also, a significant improvement in biochemical parameters was observed.[6] Another hopeful report of a 36-year-old severely malnutreted MNGIE patient who had recurrent diarrhea, the initial BMI of 11.9 kg/m^2 was improved to 12.7 kg/m^2 in the first year of total parenteral nutrition. On the last visit the patient was 43 years old and has been receiving home nutrition therapy with an acceptable quality of life for more than 6 years.[7] Similar to the cases reported in the literature, the body mass index of our patient increased from 9.4 kg/m^2 (-10.92 SDS) to 10.25 kg/m^2 (-9.23 SDS) with nutritional treatment. So, until a curative treatment option is available, one of the most important goals should be to alleviate the symptoms and increase the resilience of MNGIE patients, thereby improving their quality of life, even if only slightly, and ensuring survival.

Limitations

The fact that nutritional laboratory parameters such as prealbumin and transferrin were not examined and that anthropometric measurements or body composition other than body weight were not taken were counted as limitations.

Conclusion

Nutritional treatment has a critical role in MNGIE disease management. The combined usage of parenteral and enteral nutrition is a relatively effective treatment approach, especially in cases of severe gastrointestinal dysmotility and malnutrition. The case that we reported demonstrated the positive effect of diet on quality of life and somehow in prognosis.

Ethical approval

Written consent was obtained from the patient's parents.

Author contribution

The authors declare contribution to the paper as follows: Study conception and design: TK, SU, İK, FDB, DK, NOM; data collection: TK, SU, İK, FDB, DK, NOM; analysis and interpretation of results: TK, SU, İK, FDB, DK, NOM; draft manuscript preparation: TK, SU, İK, FDB, DK, NOM. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

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References

1. Kasti A, Nikolaki M, Pyrousis I, Synodinou K, Oikonomopoulos N, Triantafyllou K. Intensive nutrition support may benefit patients with a rare mitochondrial disorder. *Nutr Clin Pract*. 2022;37:361-365. **[Crossref]**
2. Redha N, Al-Sahlawi Z, Hasan H, Ghareeb S, Humaidan H. Meningoencephalitis in a novel mutation in MNGIE (mitochondrial neurogastrointestinal encephalomyopathy) ending a familial diagnostic odyssey: A case series report. *J Cent Nerv Syst Dis*. 2024;16:11795735241241423. **[Crossref]**
3. Hirano M, Carelli V, De Giorgio R, et al. Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE): Position paper on diagnosis, prognosis, and treatment by the MNGIE International Network. *J Inherit Metab Dis*. 2021;44:376-387. **[Crossref]**
4. Wang J, Chen W, Wang F, et al. Nutrition Therapy for Mitochondrial Neurogastrointestinal Encephalopathy with Homozygous Mutation of the TYMP Gene. *Clin Nutr Res*. 2015;4:132-136. **[Crossref]**
5. Choi HS, Lee YM. Enteral Tube Feeding in Paediatric Mitochondrial Diseases. *Sci Rep*. 2017;7:16909. **[Crossref]**
6. Paolini B, Ciondolo ID, Lapini E, et al. Nutritional treatment in a patient affected by Mithochondrial Neuro-Gastrointestinal Encephalomyopathy (MNGIE). *Med J Nutrition Metab*. 2014;7:173-179. **[Crossref]**
7. Barisic A, Ljubas Kelecic D, Vranesic Bender D, et al. Case report: A patient with mitochondrial neurogastrointestinal encephalomyopathy and chronic intestinal failure. *Front Nutr*. 2022;9:983873. **[Crossref]**