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AIMS AND SCOPE

Clinical Science of Nutrition (Clin Sci Nutr) is an international, scientific, open Access periodical published in accordance with independent, unbiased, and double-blinded peer-review principles. The journal is the official publication of the Society of Clinical Enteral Parenteral Nutrition – Turkey, and it is published tri-annually in April, August, and December. The publication language of the journal is English.

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.

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ORIGINAL ARTICLES

CLINICAL SCIENCE OF NUTRITION Original Article Clin Sci Nutr 2022;4(1):1-7 • DOI: 10.54614/ClinSciNutr.2022.21515

Investigation of Gastrointestinal Complications in Patients Given Enteral Nutrition

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ABSTRACT

Objective: While deciding on the route of nutritional support therapy, the cost-effective enteral route that preserves the integrity of the gastrointestinal system and supports immune functions should be the first choice. During enteral nutrition, many complications that may lead to the interruption of nutrition may develop. This study was conducted to examine the gastrointestinal complications that developed in patients who received enteral nutrition.

Methods: 300 enterally fed patients who were treated in intensive care unit and wards were included in the study. Patients' age, gender, concomitant disease, diet, duration, type and amount of product, energy value, feeding route and developing gastrointestinal complications were recorded. Gastrointestinal complications and related factors in patients were investigated.

Results: Of the patients included in the study, 53.7% (n=161) were male, 35.7% (n=107) were between the ages of 66-79 years, and 92% (n=276) had at least one diagnosed disease. 77.7% (n=233) of the patients were fed by nasogastric (NG) tube, 50.6% (n=152) were fed by continuous infusion. It was determined that gastrointestinal complications developed in 40.7% (n=122) of the patients during the enteral feeding process, and diarrhea and high gastric residual volume were the most common complications. Aspiration and ileus did not develop in any of the patients. A significant difference was found between feeding time, daily amount, route of administration and infusion method, and gastrointestinal complications ($P < .001$; $P = .041$; $P = .003$; $P = .005$). No relationship was found between gastrointestinal complications and gender, age group, comorbid disease status, and the type of nutritional product according to energy content.

Conclusion: Gastrointestinal complications may frequently develop while patients are given enteral nutrition, which should be the first choice of nutritional support. The most common gastrointestinal complications encountered in this study were diarrhea and high gastric residual volume. It is thought that the duration of feeding, the amount, the route of administration and the infusion method may affect the development of gastrointestinal complications. Patients should be followed closely for complications.

Keywords: Complication, enteral nutrition, gastrointestinal system, nutritional support.

INTRODUCTION

Malnutrition is a common clinical condition that causes measurable adverse effects on the body as a result of a lack of nutrients such as protein and energy.[1] Malnutrition causes many negative consequences such as prolonged hospitalization, increased costs, and increased mortality and morbidity rates.[2] It is known that adequate nutrition has a significant effect on patients' response to medical treatment.[3,4] Although enteral nutrition is a cost-effective way that preserves the integrity of the gastrointestinal tract, supports immune functions, and prevents malnutrition, various complications may develop during the feeding process.[5,6]

Complications that may develop during the enteral feeding process are divided into three groups as mechanical, gastrointestinal and metabolic. The most common complications are thought to be related to gastrointestinal function.[7] Gastrointestinal complications are diarrhea, nausea, vomiting, abdominal distention, aspiration, high gastric residual volume, constipation, and ileus.[7-10] Factors such as the product used, the route and duration of administration, the number and amount of doses may affect the incidence of gastrointestinal complications.[11] This study was conducted to evaluate the gastrointestinal complications and related factors in patients undergoing tube enteral nutrition.

METHODS

This descriptive and retrospective study was conducted in order to evaluate the gastrointestinal complications developed in patients fed with enteral tubes and followed by the nutrition support unit of Kutahya Health Sciences

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University Evliya Celebi Training and Research Hospital. Ethics committee approval was received from the Kutahya Health Sciences University Non-Invasive Clinical Research Ethics Committee (Date: December 16, 2020, Decision No: 2020/17-12).

The study included 300 patients older than 18 years, who were followed by the nutrition support unit of Kütahya Health Sciences University Evliya Çelebi Training and Research Hospital between November 2018 and November 2020 and fed with enteral tube in the intensive care unit (intensive care units for internal medicine, general, coronary, cardiovascular surgery) and wards (palliative care, internal medicine, general surgery, cardiac and vascular surgery). Patients younger than 18 years of age, who received oral enteral nutrition support and who were fed in combination with enteral and parenteral routes, were excluded from the study.

The data were obtained retrospectively from the existing records with the "Information form for patients with tube enteral feeding" prepared by the researcher in line with the literature. This form contains information on the general characteristics of individuals (age, gender, diagnosis of disease), tube feeding (duration of enteral nutrition, type, amount and energy value of enteral nutrition product, feeding route, infusion method) and developing gastrointestinal complications.

Enteral nutrition products are divided into three groups in terms of energy content in the form. Those containing less than 0.9 kilocalories (kcal) of energy in one milliliter (mL) of nutritional solution are classified as hypocaloric, those containing energy of 0.9-1.2 kcal in one mL as isocaloric, and those containing more than 1.2 kcal in one mL as a hypercaloric product.[12]

Main Points

- Enteral nutrition is the first way to be preferred in patients who cannot be adequately fed orally.
- Some complications may develop in the patient during the enteral feeding process. One of them is the complications of the gastrointestinal system.
- In this study, gastrointestinal complications in patients fed enterally with tubes were examined.
- It was determined that gastrointestinal complications developed in 40.7% of the patients during the enteral feeding process, and diarrhea and high gastric residual volume were the most common complications.
- Patients given enteral nutritional support should be followed closely for gastrointestinal complications.

Enteral feeding applications are divided into four as continuous, intermittent, overnight and bolus feeding. Nutrition solution is given continuously in continuous feeding; in 24 hours with rest intervals in intermittent feeding; during whole night in overnight feeding; and at certain time intervals in bolus feeding for 6-8 times a day with the help of an injector.[13] This option was not included in the form as there was no overnight feeding in our hospital. Nutritional solution was given by feeding bag and pump in continuous and intermittent feeding.

When the patient had >200 g/day (or >250 mL/day volume) liquid or soft stool mass and at least 3 stools per day,[14] it was accepted as diarrhea; When there was no stool output for 3 days, it was considered as constipation.[15]

Since the European Society for Parenteral and Enteral Nutrition (ESPEN) recommends delaying enteral feeding when the gastric residual volume is above 500 mL/6 hours in enterally fed patients,[16] the high gastric residual volume limit was accepted as 500 mL/6 hours in this study.

Data were evaluated via the Statistical Package for the Social Sciences version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) using the chi-square and Mann-Whitney U tests. Descriptive statistics were given as number, percentage, median, and minimum-maximum. A $P < .05$ was considered statistically significant in all evaluations.

RESULTS

Data on the general characteristics of the patients are given in Table 1. The median age of the patients (min-max) was 74 (19-99) years, 53.7% were male, 35.7% were 66-79 years old, and 92% had at least one diagnosed disease, and the most commonly encountered diseases were hypertension (26.7%) and diabetes (20.7%), respectively. Other diseases include Alzheimer's, coronary artery disease, epilepsy, Parkinson's, cerebral palsy, liver cirrhosis, Behçet's, rheumatoid arthritis, short bowel syndrome, and amyotrophic lateral sclerosis.

The median of the amount of nutritional product given in the first 24 hours after the start of feeding and the enteral feeding time are given in Table 2.

Isocaloric product was used in 79.3% of the patients, and it was determined that 23.3% were fed enterally for 4-7 days and 8-14 days. 77.7% of the patients were fed by nasogastric tube and 50.6% by continuous infusion. It was reported that gastrointestinal complications developed in 40.7% (122 patients) of the patients during the enter-

Table 1. General Characteristics of Patients (n=300)

General characteristics of patients	Number (n)	Percentage (%)
Gender		
Female	139	46.3
Male	161	53.7
Age (year) median (minimum-maximum)	74 (19-99)	
Age group		
18-65 years	90	30.0
66-79 years	107	35.7
80 years and above	103	34.3
Disease status		
Yes	276	92.0
None	24	8.0
Diagnosed chronic diseases*		
Hypertension	144	26.7
Diabetes	112	20.7
Renal failure	69	12.8
Chronic obstructive pulmonary disease	67	12.4
Heart failure	46	8.5
Cancer	46	8.5
Cerebrovascular diseases	40	7.4
Other	16	3.0

*More than one choice was marked

Table 2. Enteral Nutrition Product Amount, Energy and Feeding Time

	Median	Minimum-maximum
The amount of product given in the first 24 hours (mL/day)	400	160-960
Amount of product delivered in 24 hours (mL/day)	1500	200-2400
Daily energy (kilocalories) delivered by enteral nutrition	1600	200-2400
Enteral feeding duration (day)	9,5	1-130

mL: milliliter

Table 3. Enteral Feeding Features

	Number (n)	Percentage (%)
Type of nutritional product by energy content		
Hypocaloric	2	0.7
Isocaloric	238	79.3
Hypercaloric	60	20.0
Enteral feeding time distribution		
1-3 days	56	18.7
4-7 days	70	23.3
8-14 days	70	23.3
15-21 days	43	14.3
22 days and above	61	20.4
Route of administration of enteral nutrition product		
Nasogastric tube	233	77.7
Percutaneous endoscopic gastrostomy tube	60	20.0
Nasojejunal tube	1	0.3
Percutaneous endoscopic jejunostomy tube	6	2.0
Enteral nutrition infusion way		
Continuous infusion	152	50.6
Intermittent infusion	65	21.7
Bolus feeding	83	27.7
Gastrointestinal complication during enteral feeding process		
Yes	122	40.7
None	178	59.3
Complications that developed*		
Diarrhea	65	46.1
High gastric residual volume	36	25.5
Nausea-vomiting	25	17.7
Abdominal distention	10	7.1
Constipation	5	3.6

*More than one choice was marked.

al feeding process, and diarrhea (46.1%) and high gastric residual volume (25.5%) were the most common complications. Aspiration and ileus did not develop in any of the patients (Table 3).

When the general characteristics and enteral nutrition status of the patients were evaluated according to the development of gastrointestinal complications, no significant relationship was found between the type of nutritional

Table 4. Comparison of Patients According to The Presence of Complications

Variables	No complication		Complication available		X^2	*P*
	n	%	n	%		
Gender					0.340	.560
Female	80	57.6	59	42.4		
Male	98	60.9	63	39.1		
Age group					1.233	.540
18-65 years	55	61.1	35	38.9		
66-79 years	59	55.1	48	44.9		
80 years and above	64	62.1	39	37.9		
Disease status					2.654	.103
Yes	160	58.0	116	42.0		
None	18	75.0	6	25.0		
Type of nutritional product by energy content					0.108	.948
Hypocaloric	1	50.0	1	50.0		
Isocaloric	142	59.7	96	40.3		
Hypercaloric	35	58.3	25	41.7		
Enteral feeding time distribution					24.777	< .001**
1-3 days	42	75.0	14	25.0		
4-7 days	47	67.1	23	32.9		
8-14 days	47	67.1	23	32.9		
15-21 days	18	41.9	25	58.1		
22 days and above	24	39.3	37	60.7		
Route of administration					11.934	.003*
Nasogastric tube	149	63.9	84	36.1		
Percutaneous endoscopic gastrostomy tube	28	46.7	32	53.3		
Nasojejunal tube and percutaneous endoscopic jejunostomy tube	1	14.2	6	85.8		
Infusion way					10.802	.005*
Continuous infusion	104	68.4	48	31.6		
Intermittent infusion	31	47.7	34	52.3		
Bolus feeding	43	51.8	40	48.2		
Chi-square test was performed.						

*P < .05, **P < .001

Table-5. The Relationship Between the Development of Gastrointestinal Complications and Nutritional Characteristics

Variables	No complication		Complication available		Z	*P*
	Median	Min-max	Median	Min-max		
Feeding day	8	1-55	15	1-130	-4.537	< .001**
Amount given on the first day (mL/day)	400	160-960	390	160-840	-1.255	.210
Daily amount of feeding (mL/day)	1525	200-2200	1440	240-2400	-2.047	.041*
Daily amount of energy (kilocalorie/day)	1600	200-2340	1572	240-2400	-1.828	.067

Mann-whitney U test was performed.
Min-max: Minimum-maximum, mL: milliliter
*$P < .05$, **$P < .001$

product and the development of complications according to gender, age group, disease status, and energy content ($P > .05$).

The duration of feeding was found to be associated with the development of gastrointestinal complications ($X^2=24.777$, $P < .001$). It was determined that the risk of developing gastrointestinal complications was higher in patients who were given nutritional support for 22 days or more (60.7%).

In terms of the route and speed of administration of the nutritional solution, the incidence of gastrointestinal complications in patients given nutritional support with NG tube is lower than in those fed with percutaneous endoscopic gastrostomy (PEG) tube, percutaneous endoscopic jejunostomy (PEJ) tube, and nasojejunal (NJ) tube ($X^2=11.934$, $P < .01$), the incidence of complications was found to be lower in the group given nutritional support with continuous infusion ($X^2=10.802$, $P < .01$) (Table 4).

A significant correlation was found between the development of gastrointestinal complications in the patients and the number of days on which nutritional support was given and the maximum amount of enteral product given in 24 hours ($Z=4.537$, $P < .001$; $Z=2.047$, $P < .05$). The number of days on which nutritional support was given was higher in the group developing complication and the maximum amount of enteral product given in 24 hours was less (Table 5).

DISCUSSION

In this study, it was determined that gastrointestinal complications developed in approximately half of the patients during enteral feeding, and diarrhea and high gastric residual volume were the most common complications. Aspiration and ileus did not develop in any of the patients. Enteral nutrition is the route that should be preferred because it ensures the continuity of the gastrointestinal system function.[17] In the study of Gök Metin and Özdemir[18] on enterally fed individuals, the incidence of complication development was found to be 27.5%. The most common complication was abdominal distension, while diarrhea and aspiration were reported to be the least.[18] Reintam et al.[19] reported that gastrointestinal complications developed in 59.1% of the patients, Demiray et al.[20] reported that none of the patients given enteral nutrition support developed any complications. This may be because the study only covered the three-day feeding period. The risk of developing complications during enteral nutrition varies depending on the selection of the nutritional product, its temperature, application rate and amount, and the expertise of the person who administers it.[8] Gök Metin and Özdemir[18] reported in their study that there was no relationship between age, gender, feeding time, amount, enteral feeding way and complication development. Parallel to this, in our study, it was determined that there was no relationship between gender, age, concomitant disease status, type of nutritional product and complication development status.

The possibility of change of the NG tube location is higher compared to the PEG tube, and this may lead to the interruption of feeding.[21] In addition, there are studies reporting that giving enteral nutritional support through NG tube has a higher risk of aspiration compared to giving with a PEG tube.[17,22] Unrelated to the feeding route, aspiration was not observed in any patient in our study. Contrary to the literature, it was found that the incidence of gastrointestinal complications was lower in patients fed with NG tube. It is known that post pyloric feeding reduces gastrointestinal complications such as aspiration risk and gastric intolerance.[16] Post pyloric placement of NG feeding tube in some patients may have reduced the rate of complication development in this patient group.

It is also thought that some patients with PEG may have developed more complications since the PEG tube was surgically placed.

In this study, it was determined that the rate of development of gastrointestinal complications was higher in patients who were given enteral nutrition support for 22 days or more. In a study, it was shown that the rate of complication development increased as the number of days given nutritional support increased.[18] In addition, it was determined that the maximum amount of nutritional product given in 24 hours to the group with complications was less. The reason for this may be the interruption of enteral nutrition due to complications and inadequate increases of nutritional dose.

It has been reported in the literature that the administration of enteral nutritional support by continuous infusion may be associated with less complication development.[23] In a meta-analysis, it was reported that the risk of feeding intolerance was lower in patients fed with continuous infusion compared to those fed with intermittent infusions.[24] In other studies, it has been reported that continuous or bolus administration of nutritional support does not make a significant difference in terms of aspiration, vomiting, diarrhea, and high gastric residual volume development.[25,26] In our study, fewer gastrointestinal complications were observed in the group fed with continuous infusion. This result is thought to be due to the fact that continuous administration of the nutritional product at low doses via the infusion pump increases patient tolerance.

In addition to the beneficial effects of enteral nutrition, close follow-up of patients is of great importance due to complications that may develop during the feeding process.[27] Although gastrointestinal complications may develop in a successful enteral feeding, it has been reported in studies to ensure that the patient continues enteral feeding for as long as possible without interruption by taking appropriate precautions.[28,29] After excluding infectious causes and deciding that diarrhea is related to nutrition in patients who develop diarrhea, antidiarrheal drugs[14,30] are recommended and initiation of motility-enhancing drugs is offered to patients with high gastric residual volume.[31]

The main limitations of the study are that it was conducted in a single-center, it was retrospective, and sufficient information was not available on the use of drugs, mobilizations, and operations of the patients.

In conclusion, enteral nutrition is the first choice for all hospitalized patients. In terms of complications that may develop, patients should be followed closely and tried to be prevented, and when they develop, they should be treated in the early period.

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REFERENCES

1. National Collaborating Centre for Acute Care. *Nutrition support for adults: Oral nutrition support, enteral tube feeding and parenteral nutrition*. London: The Royal College of Surgeons of England; 2006:20. Accessed April 12, 2022. https://www.ncbi.nlm.nih.gov/books/NBK49269/pdf/Bookshelf_NBK49269.pdf.
2. Kozeniecki M, Fritzshall R. Enteral nutrition for adults in the hospital setting. *Nutr Clin Pract.* 2015;(30):634-651. [Crossref]
3. O'Leary-Kelley C, Bawel-Brinkley K. Nutrition support protocols: enhancing delivery of enteral nutrition. *Crit Care Nurse.* 2017;37(2):15-23. [Crossref]
4. Elke G, Felbinger TW, Heyland DK. Gastric residual volume in critically ill patients: a dead marker orstillalive? *Nutr Clin Pract.* 2015;30(1):59-71. [Crossref]
5. Delgado SA. Nutrition is critical. *Am J Crit Care.* 2018;27(2):144. [Crossref]
6. Aktaş H, Bozbay S, Kayhan O, Demirkıran O. Yoğun bakım ünitesindeki kritik hastalarda enteral beslenme hedefi. *Cerrahpaşa Med J.* 2019;43(3):92-96.
7. Bodoky G, Kent-Smith L. Basics in clinical nutrition: Complications of enteral nutrition. e-SPEN. *Eur E J Clin Nutr Metab.* 2009;4:e209-211. [Crossref]
8. Blumenstein I, Shastri YM, Stein J. Gastroenteric tube feeding: Techniques, problems and solutions. *World J Gastroenterol.* 2014;(20):8505-8524. [Crossref]
9. Özyurt Y, Erkal KH, Yıldırım M, Arıkan Z. Total enteral beslenme. *Kartal Eğit. Araşt. Hast. Tıp Derg.* 2000;11(3):950-953.
10. Metin ZG, Özdemir L. Enteral beslenme komplikasyonları ve hemşirelik bakım uygulamaları. *Sağlık ve Toplum Dergisi.* 2015;25(3):28-32.

11. Wanden-Berghe C, Patino-Alonso MC, Galindo-Villardón P, Sanz-Valero J. Complications associated with enteral nutrition: CAFANE study. *Nutrients*. 2019;11(9):2041. [Crossref]
12. 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(2):180-186. [Crossref]
13. De Van Der Schueren MAE. Enteral tüp ile beslenme uygulaması. In: Sobotka L, ed. *Klinik Nütrisyonun Temelleri*. Miki Matbaacılık; 2021:p.300-301.
14. Pirlich M, Bodoky G, Kent-Smith L. Enteral nütrisyonun komplikasyonları. In: Sobotka L, ed. *Klinik Nütrisyonun Temelleri*. Miki Matbaacılık; 2021:p.319-320.
15. Pancorbo-Hidalgo PL, García-Fernandez FP, Ramírez-Pérez C. Complications associated with enteral nutrition by nasogastric tube in an internal medicine unit. *J Clin Nurs*. 2001;10(4):482-490. [Crossref]
16. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr.* 2019;38(1):48-79. [Crossref]
17. Akıncı İÖ, Özcan P, Tuğrul S, et al. Yoğun bakım ünitesinde perkutan endoskopik gastrostomi. *Ulus Travma Derg*. 2000;6(4):281-283.
18. Gök ZM, Özdemir L. Yoğun bakımda enteral pompa ile beslenen hastalarda gelişen komplikasyonlar ve etkileyen faktörlerin belirlenmesi. *HUHEMFAD*. 2015;2:20-29.
19. Reintam A, Parm P, Kitus R, Kern H, Starkopf J. Gastrointestinal symptoms in intensive care patients. *Acta Anesthesiologica Scandinavica*. 2009;(53):318-324. [Crossref]
20. Demiray A, Kuzyaka İ, Açıl A, İlaslan N. Enteral beslenen yoğun bakım hastalarının beslenme süreci ve gelişebilecek komplikasyonlar açısından değerlendirilmesi. *DÜ Sağ Bil Enst Derg*. 2020;10(3):289-96. [Crossref]
21. Pearce CB, Duncan HD. Enteral feding: Nasogastric, nasojejunal, percutaneous endoscopic gastrostomy, or jejunostomy: its indications and limitations. *PMJ*. 2002;78:198-204. [Crossref]
22. Ikenaga Y, Kusunoki T, Yamaguchi H. Percutaneous endoscopic gastrostomy reduces aspiration pneumonia rate in stroke patients with enteral feeding in convalescent rehabilitation wards. *Prog Rehabil Med*. 2021;7(6):1-10. [Crossref]
23. Williams TA, Leslie GD, Leen T, Mills L, Dobb GJ. Reducing interruptions to continuous enteral nutrition in the intensive care unit: a comparative study. *J. Clin. Nurs*. 2013;22(19):2838-2848. [Crossref]
24. Ma Y, Cheng J, Liu L, et al. Intermittent versus continuous enteral nutrition on feding intolerance in critically ill adults: A meta-analysis of randomized controlled trials. *Int J Nurs Stud*. 2021;113:1-29. [Crossref]
25. Kadamani I, Itani M, Zahran E, Taha N. Incidence of aspiration and gastrointestinal complications in critically ill patients using continuous versus bolus infusion of enteral nutrition: A pseudo-randomised controlled trial. *Aust Crit Care*. 2014;24(4):188-193. [Crossref]
26. Serpa LF, Kimura M, Faintuch J, Ceconello I. Effects of continuous versus bolus infusion of enteral nutrition in critical patients. *Rev Hosp Clin*. 2003;58(1):9-14. [Crossref]
27. Çelebi D, Yılmaz E. Cerrahi hastalarda enteral ve parenteral beslenmede kanıta dayalı uygulamalar ve hemşirelik bakımı. *IGUSABDER*. 2019;7:714-731. [Crossref]
28. Tatsumi H. Enteral tolerance in critically ill patients. *J Intensive Care*. 2019;7(30):1-10. [Crossref]
29. Maltseva LO, Mishchenko OO, Kutovyi AB, Mosentsev MF, Lisnycha VM, Kazimirova NA. Enteral tolerance in critically ill patients (literature review). *Emerg Med*. 2020;16(1):36-44. [Crossref]
30. Majid HA, Emery PW, Whelan K. Definitions, attitudes, and management practices in relation to diarrhea during enteral nutrition: A survey of patients, nurses, and dietitians. *Nutr Clin Pract*. 2012;27(2):252-260 [Crossref]
31. Taylor BE, McClave SA, 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.). *Crit Care Med*. 2016;44:390-438. [Crossref]

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Assessment of Nutrition-Related Complications in Hospitalized Patients with Tube Enterostomy

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ABSTRACT

Objective: Malnutrition is an important problem that increases mortality and morbidity in hospitalized patients. If enteral nutrition is expected to be long-term, gastrostomy and jejunostomy should be preferred. In our study, we aimed to examine the nutritional-related complications of patients with nutritional osteomy.

Methods: Patients followed by Hacettepe University Faculty of Medicine Adult Hospital, Clinical Nutrition Unit and fed from gastrostomy or jejunostomy were included in the retrospective study. The clinical demographic information of the patients, indications for feeding ostomy and ostomy methods were evaluated. Nutrition-related complications were divided into three as gastrointestinal, mechanical and metabolic.

Results: A total of 404 patients were included in the study. The median age of the patients was 70 (18-94) and 187 (46.3%) were women. Three hundred fourty seven (85.9%) patients were fed from gastrostomy and 57 (14.1%) patients from jejunostomy. Diarrhea was observed in 36 (8.9%) patients, aspiration pneumonia in 19 (4.7%) patients, vomiting in 13 (3.2%) patients, and regurgitation in 13 (3.2%) patients. The rate of ostomy infection is 5.9%, and the rate of refeeding syndrome is 12.5%. In multivariate regression analysis, weight [OR=0.967, 95% CI:0.938-0.996; *P* = .027] and COPD [OR=4.889, 95% CI:1.754-13.63; *P* = .002] was associated with ostomy infections, independent of all other parametric values. Age [OR=1.040, 95% CI: 1.007- 1.073; *P* = .016], weight [OR=0.959, 95% CI: 0.928-0.992; *P* = .014] and dementia [OR=3.535 95% CI: 1.302-9.597; *P* = .013] are also associated with refeeding syndrome, independent of all other causes.

Conclusion: As a result, close follow-up and early treatment of nutrition-related complications is a priority in patients fed through ostomy.

Keywords: Enteral, Feeding jejunostomy, Malnutrition, Percutaneous endoscopic gastrostomy; Refeeding syndrome.

INTRODUCTION

Malnutrition in hospitalized patients is an important problem characterized by prolonged hospital stay, increased cost, morbidity and mortality. The prevalence of malnutrition in hospitalized patients varies between 20-50%.[1] In a study conducted with the participation of 12 centers in Turkey, the prevalence of malnutrition with MUST was found to be 44.2% in hospitalized patients. According to Balcı C et al., the prevalence of malnutrition in hospitalized patients due to acute illness is 35.9% according to GLIM criteria, 38% according to NRS-2002 and 37.2% using SGA.[2]

A third of the patients without malnutrition before hospitalization and more than half of the patients with malnutrition may have worsening in their nutritional status during their hospitalization.[3] The nutritional status of hospitalized patients should be evaluated at regular intervals and nutritional therapy should be started in the early period in patients with malnutrition.[4] Enteral nutrition therapy should be started in patients who cannot take enough calories and protein orally. If treatment is expected to be longer than 4-6 weeks, gastrostomy or jejunostomy should be preferred as the access route. Tube enterostomies can be placed in the gastrointestinal tract by surgical, endoscopic, or radiological methods.[5]

Mechanical, infectious, gastrointestinal and metabolic complications can be seen in patients fed by tube enterostomy. Mechanical complications include tube oc-

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clusion, malposition of the feeding tube, tube breakage, tube leakage, and accidental tube extrusion.[6]

Periostomal infections are also among the important complications and their incidence varies between 4-30%. Prophylactic antibiotics are recommended prior to tube placement to reduce infectious complications. Diabetes mellitus, long-term hospitalization, low serum albumin levels, malignancy and severe malnutrition have been found to be associated with infectious complications.[7, 8]

Gastrointestinal complications are nausea and vomiting, diarrhea, constipation, cramps, bloating and aspiration. Diarrhea may be seen in approximately 30% of patients admitted to internal and surgical services and approximately 80% of patients in the intensive care unit. Infectious causes, drugs and nutritional solutions are among the causes of diarrhea.[9]

Electrolytic disorders, hypernatremia, hypokalemia, hypomagnesemia, hypo and hyperglycemia and refeeding syndrome are metabolic complications. In the literature, the definition of refeeding syndrome shows heterogeneity. There are different definitions, including only low phosphorus or abnormalities in fluid balance, severe electrolyte imbalance and organ dysfunctions.[10] In the consensus report prepared by the American Society for Parenteral and Enteral Nutrition (ASPEN) in 2020 for refeeding syndrome; body mass index (BMI) of 18.5 kg/m2, 5% weight loss in last 1 month, no oral intake for 5–6 days, or less than 75% of estimated energy need for more than 7 days during an acute illness or injury, or taking less than 75% of the estimated energy need for more than 1 month, low potassium, magnesium and phosphorus levels, decrease in subcutaneous fat and muscle mass, and high-risk co-morbidities are determined as risky conditions for refeeding syndrome.[11]

In our study, we aimed to examine the complications related to nutrition therapy in patients who were followed by the Hacettepe University Faculty of Medicine Adult Hospital, Clinical Nutrition Unit and fed from the ostomy.

Main Points

- Malignancies, neurological diseases, and dementia are the most common indications for feeding with gastrostomy and jejunostomy.
- Feeding ostomy complications which are categorized gastrointestinal, mechanical, and metabolic are still important problems for nutrition.
- Low weight and chronic obstructive pulmonary disease are risk factors for ostomy infection in addition to that age, low weight and dementia are an independent predictors for refeeding syndrome.

METHODS

Patients and Study Design

The patients followed by the Hacettepe University Faculty of Medicine Adult Hospital, Clinical Nutrition Unit were evaluated retrospectively. Patients fed from gastrostomy or jejunosomy were included in the study. Age, gender, height, weight, BMI, NRS-2002, and accompanying co-morbidities of the patients were evaluated. Feeding ostomy opening indications and ostomy opening ways were evaluated. Nutrition-related complications were divided into three as gastrointestinal, mechanical and metabolic. Gastrointestinal complications were determined as diarrhea, regurgitation, vomiting and aspiration pneumonia, and mechanical complications as ostomy infection, tube occlusion and medicine leakage and metabolic complications as refeeding syndrome (serum phosphorus level below 2.5 mg/dL), hypokalemia and hypernatremia.

Ethics committee approval of the study was received by the Hacettepe University Ethics Committee (Date: March 19, 2019, Decision No: 2019/08-02).

Statistical analysis

Descriptive statistics were expressed as mean ± standard deviation if numerical variables fit the normal distribution, if not, as median and minimum-maximum values and as numbers and percentages for categorical variables. Comparisons between groups were made with t-test or Mann Whitney U test according to normal distribution for numerical variables and chi-square test for categorical variables. In multivariate analysis, factors that were determined in univariate analyzes were put into the model, and the factors that would predict ostomy infection and refeeding syndrome were determined, and model fit was evaluated using the Hosmer-Lemeshow test. For $P < .05$, the results were considered statistically significant. Statistics of the study were carried out by using th Statistical Package for the Social Sciences version 23.0 (IBM SPSS Corp.; Armonk, NY, USA).

RESULTS

A total of 404 patients were included in the study. The median age of the patients was 70 (18-94) and 187 (46.3%) were women. Three hundred fourty seven (85.9%) patients were fed from gastrostomy and 57 (14.1%) patients from jejunostomy. Percutaneous endoscopic gastrostomy (PEG) (n=292, 84.1%) was used most frequently among the gastrostomy opening methods. Percutaneous radiological gastrostomy was performed in 48 (13.9%) patients, and gastrostomy was performed in 7 (2%) patients by open surgery. Open surgery was performed in 38 (66.7%) patients with jejunostomy, and

Table 1: Demographic and Clinical Characteristics of the Patients

	n= 404
Age, years	70 (18-94)
Sex (female)	187 (46.3%)
Weight (kg)	63.1 ± 15.2
Height (meter)	1.64 ± 1.01
BMI (kg/m²)	23.19 ± 5.3
NRS-2002	5 (3-7)
Follow up time, days	17 (1-364)
Gastrostomy (n,%)	347 (85.9)
Percutaneous Endoscopic Gastrostomy	292 (84.1)
Percutaneous Radiologic Gastrostomy	48 (13.9)
Open Gastrostomy	7 (2)
Jejunostomy (n,%)	57 (14.1)
Open Gastrojejunostomy	38 (66.7)
Percutaneous Endoscopic Jejunostomy	19 (33.3)
Ostomy Indications (n,%)	
Malignancy	175 (43.3)
Stroke and other neurological diseases	103 (25.5)
Dementia	64 (15.8)
Prolonged Enteral Tube Feeding	35 (8.7)
Others	27 (6.7)
Co-morbidities	
Hypertension	85 (36.6)
Diabetes Mellitus	110 (27.2)
Malignancy	86 (21.3)
Coronary Artery Disease	72 (17.8)
Chronic Obstructive Pulmonary Disease	33 (8.2)

Table 2: Complications of Enterostomy Tube Feeding

Gastrointestinal complications	Mechanical complication	Metabolic complications
Diarrhea 36 (8.9%)	Ostomy infection 24 (5.9%)	Refeeding syndrome 50 (12.5%)
Regurgitation 13 (3.2%)	Tube Clogging 14 (3.5%)	Hypokalemia 11 (2.8%)
Vomiting 13 (3.2%)	Tube Leakage 4 (2.7%)	Hypernatremia 6 (1.5%)
Aspiration pneumonia 19 (4.7%)		

Table 3: Clinical Characteristics of the Patients with Ostomy Infection

	Ostomy infection (n=24)	Control (n=380)	*P*
Age	72.5 (20-93)	70 (18-94)	.848
Sex (female)	11 (45.8%)	176 (46.3%)	.963
Weight (kg)	56.89 ± 15.69	63.53 ± 15.18	.039
Height (meter)	1.61 ± 1.06	1.65 ± 1.06	.105
BMI (kg/m²)	21.59 ± 4.98	23.29 ± 5.31	.128
NRS-2002	4.5 (3-7)	5 (3-7)	.901
Follow up time, days	26 (6-202)	16 (1-364)	.029
Diabetes Mellitus	9 (37.5%)	101 (26.6%)	.244
Hypertension	6 (33.3%)	79 (36.9%)	.762
Chronic Obstructive Pulmonary Disease	6 (25%)	27 (7.1%)	.009
Malignancy	2 (8.3%)	84 (22.1%)	.110

percutaneous endoscopic jejunostomy was performed in 19 (33.3%) patients. Malignancies, stroke and other neurological diseases, dementia, prolonged enteral tube feeding and other causes (burn, cystic fibrosis, etc.) are listed among the indications for ostomy opening. Demographic and clinical characteristics of the patients are shown in Table 1.

The incidence of gastrointestinal complications was diarrhea in 36 (8.9%) patients, aspiration pneumonia in 19 (4.7%) patients, vomiting in 13 (3.2%) patients, and regurgitation in 13 (3.2%) patients. The ostomy infection rate is 5.9%. During the follow-ups, tube obstruction was observed in 14 (3.5%) patients and tube leakage was observed in 4 (2.7%) patients. Refeeding syndrome was observed in 50 (12.5%) patients, hypokalemia was observed in 11 (2.8%) patients, and hypernatremia was observed in 6 (1.5%) patients. Complication rates of the patients are shown in Table 2.

Compared with the control group without ostomy infection, 24 patients with ostomy infection were low weight (56.89 ± 15.69 vs. 63.53 ± 15.18, $P = .039$) and had longer follow-up times [26 (6-202) vs 16 (1-364), $P = .029$]. Demographic and clinical information of patients with and without ostomy infection are shown in Table 3.

The median age of 50 patients with refeeding syndrome was 77 (32-93), and that of the control group was 68 (18-94) ($P = .001$). Four patients were excluded from this anal-

Table 4: Clinical Characteristics of the Patients with Refeeding Syndrome

	Refeeding syndrome (n= 50)	Control (n= 350)	*P*
Age	77 (32-93)	68 (18-94)	.001
Weight (kg)	59.44 ± 13.77	63.73 ± 15.49	.064
Height (meter)	1.61 ± 0.09	1.65 ± 0.01	.011
BMI (kg/m²)	22.63 ± 4.69	23.25 ± 5.44	.447
NRS-2002	5 (3-7)	5 (3-7)	.717
Follow up time, days	18 (1-364)	17 (1-206)	.639
Diabetes Mellitus	23 (46%)	87 (24.9%)	.002
Hypertension	15 (57.7%)	70 (34%)	.018
Chronic Obstructive Pulmonary Disease	6 (12%)	26 (7.4%)	.266
Dementia	16 (32%)	48 (13.7%)	.001
Malignancy	11 (22%)	72 (20.6%)	.816

*4 patients have been excluded from the analysis because of missing data.

Table 5: Multivariate Regression Analysis for Ostomy Infection and Refeeding Syndrome

Ostomy infection#	OR	95 % CI	*P*
Weight (kg)	0.967	0.938- 0.996	.027
Chronic Obstructive Pulmonary Disease	4.889	1.754- 13.63	.002
#Independent variables: Age, Weight, Diabetes Mellitus, Chronic Obstructive Pulmonary Disease			
Refeeding#	**OR**	**95 % CI**	***P***
Age	1.040	1.007- 1.073	.016
Weight (kg)	0.959	0.928- 0.992	.014
Dementia	3.535	1.302- 9.597	.013
# Independent variables: Age, Weight, Follow up time, Diabetes Mellitus, Hypertension, Dementia			

ysis due to missing data. Considering the co-morbidities of the patients, hypertension [15 (57.7%) vs 70 (34%), *P* = .018], diabetes mellitus [23 (46%) vs 87 (24.9%), *P* = .002] and dementia [16 (32)] %) vs 48 (13.7 %), *P* = .001] is more common in patients with refeeding syndrome (Table 4).

In the multivariate regression analysis, after putting age, weight, diabetes mellitus, and coronary obstructive pulmonary disease (COPD) in the model, weight [OR=0.967, 95% CI:0.938-0.996; *P* = .027] and COPD [OR=4.889, 95% CI:1.754-13.63; *P* = .002] were associated with ostomy infections, independent of all other parametric values. Age [OR=1.040, 95% CI: 1.007-1.073; *P* = .016], weight [OR=0.959, 95% CI: 0.928-0.992; *P* = .014] and dementia [OR=3.535 95% CI: 1.302-9.597; *P* = .013] are associated with refeeding syndrome, independent of all other causes (Table 5).

DISCUSSION

In our study, we retrospectively evaluated the ostomy indications and nutrition-related complications of patients fed by tube enterostomy. Age, low weight and presence of dementia for refeeding syndrome; and age and presence of COPD for ostomy infections were associated with complications independent of all other causes.

In our study, the indications for ostomy opening were listed as malignancies with a frequency of 40%, stroke and other neurological diseases with 25%, and dementia with 15%. In a study by Aksoy E et al., the most common indications for PEG were dementia (28.6%) after stroke with a frequency of 34%, malignancies (10.8%) and other causes (15.8%).[12] In another study in which 119 patients were evaluated, PEG opening indications were listed as head and neck tumors (47.9%), neurological diseases (29.4%) and esophageal diseases (9.3%).[13] In our study, ostomy opening indications were similar to the literature.

Ostomy infections occur at a rate of 4-30% and are among the important complications. In a study in which 73 patients with nutritional jejunostomy were evaluated, the rate of infection was 1.3% in the early period, while this rate increased to 4.1% in the late period [14]. In our study, the rate of ostomy infection was 5.9%. In local infections, the technique of opening the osteoma, whether antibiotic prophylaxis is given beforehand, and nursing care are important. In addition, patient-related factors such as DM, malignancy, malnutrition, obesity, and chronic corticosteroid use play an important role.[6,15] The European Society of Gastrointestinal Endoscopy (ESGE) Guidelines recommend the administration of prophylactic single-dose beta-lactam antibiotics to reduce the risk of wound infection after endoscopic enteral tube placement.[16,17] In our study, age and presence of COPD were found to be associated with ostomy infections. While COPD is particularly associated with infections in the respiratory system, an increase in extra-pulmonary infections (including skin infections) was not observed in a study.[18] The reason for the increased risk of ostomy infection in patients with COPD may be related to hospitalization with acute exacerbations and long-term steroid therapy.

Refeeding syndrome is a metabolic shift process characterized by a decrease in insulin secretion and an increase in glucagon secretion, in which protein and fat are used as energy sources after muscle mass loss instead of glucose. It is presented with low levels of intracellular vitamins and minerals, especially phosphate, potassium, and magnesium. Edema can result in death as well as respiratory and heart failure. In a systematic review and meta-analysis, the frequency of refeeding syndrome varies between 0-62%. The reason for this change in incidence rates may be related to differences in definition. While the incidence is reported to be lower when both clinical and electrolyte disturbances are used in the diagnosis, this rate is higher in older patients with malnutrition, inpatients in the intensive care unit, or in studies using higher electrolyte threshold values for the diagnosis of refeeding syndrome.[19] In our study, the refeeding syndrome was accepted as hypophosphatemia, serum phosphorus level being below 2.5 mg/dL[20] and the frequency of refeeding syndrome was found as 12.5%.

In a study evaluating 967 hospitalized patients with malnutrition, the frequency of refeeding syndrome was found to be 14.6% and appetite loss, cancer and hypertension were observed more frequently in patients with refeeding syndrome. Refeeding syndrome increased mortality 1.53 times.[21] In patients with low phosphorus before endoscopic gastrostomy, mortality was higher both in the 1st week and in the 1st month.[22] In our study, age, low weight and dementia were found to be associated with the refeeding syndrome. Dementia patients and advanced age are among the important risk factors for both malnutrition and refeeding syndrome. However, there is no clear data that nutritional support reduces mortality in patients with advanced dementia, and it is even thought that it may increase fatal outcomes due to refeeding syndrome.[23]

Tube leakage was observed in 12.5% and tube occlusion in 2.5% of mechanical complications. In a study evaluating patients with jejunostomy, the rate of tube occlusion in late complications was 8.2%, and tube leakage was 1.3%.[14] In a study by Saka B et al., the rate of tube occlusion among PEG-related complications was 4.9%.[24] In the literature, tube occlusion is a common problem with a rate of 25-35% and improper administration of drugs from the tube is one of the most important causes.[25] The reason for our lower tube occlusion rates may be that we had an experienced clinical pharmacist in our team who evaluated drug administration methods and drug interactions.

Although enteral nutrition is blamed as an important cause of diarrhea in hospitalized patients, drugs, infectious causes and underlying diseases should be primarily evaluated.[26] In our study, the frequency of diarrhea was found to be 8.9% in patients who received enteral nutrition from an ostomy.

The strength of our study is the evaluation of enteral nutrition-related complications in patients who underwent gastrostomy and jejunostomy with different modalities (endoscopic, radiological and surgical). Our complication rates are similar to the literature. The retrospective design of our study and the fact that tube enterostomies were not performed in a single center can be listed among our limitations.

CONCLUSION

Malnutrition is still an important problem in hospitalized patients and if enteral nutrition therapy is expected to be long-term, tube enterostomy should be chosen. Close follow-up and treatment of nutrition-related complications by experienced clinical nutrition teams should be a priority.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Hacettepe University. (Date: March 19, 2019, Decision No: 2019/08-02)

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - P.Ü., M.H.; Design: P.Ü., K.A., M.H.; Supervision – M.H.; Resources – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Materials – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Data Collection and/or Processing – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Analysis and/or Interpretation – P.Ü., B.K.Ç., M.H.; Literature Search – P.Ü., M.H.; Writing Manuscript – P.Ü., M.H.; Critical Review - M.H.

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REFERENCES

1. Kang MC, Kim JH, Ryu SW, et al. Prevalence of malnutrition in hospitalized patients: A multicenter cross-sectional study. *J Korean Med Sci*. 2018;33(2):1-10. [Crossref]
2. Balci C, Bolayir B, Esme M, et al. Comparison of the efficacy of the global leadership initiative on malnutrition criteria, subjective global assessment, and nutrition risk screening 2002 in diagnosing malnutrition and predicting 5-year mortality in patients hospitalized for acute illnesses. *J Parenter Enteral Nutr*. 2021;45(6):1172-1180. [Crossref]

3. Kabashneh S, Alkassis S, Shanah L, Ali H. A Complete guide to identify and manage malnutrition in hospitalized patients. *Cureus*. 2020;12(6):1-8. [Crossref]
4. Thibault R, Abbasoglu O, Ioannou E, et al. ESPEN guideline on hospital nutrition. *Clin Nutr.* 2021;40(12):5684-5709. [Crossref]
5. Pearce CB, Duncan HD. Enteral feeding. Nasogastric, nasojejunal, percutaneous endoscopic gastrostomy, or jejunostomy: its indications and limitations. Postgrad Med J. 2002;78(918):198-204. [Crossref]
6. Blumenstein I, Shastri YM, Stein J. Gastroenteric tube feeding: techniques, problems and solutions. *World J Gastroenterol*. 2014;20(26):8505-8524. [Crossref]
7. Vizhi K, Rao HB, Venu RP. Percutaneous endoscopic gastrostomy site infections-Incidence and risk factors. *Indian J Gastroenterol*. 2018;37(2):103-107. [Crossref]
8. Mundi MS, Seegmiller S, Davidson J, Schneckloth J, Saied J, Hurt RT. Prospective assessment of peristomal infections using objective criteria. *J Parenter Enteral Nutr*. 2018;42(5):877-884. [Crossref]
9. Adeyinka A, Rouster AS, Valentine M. *Enteric Feedings*. In: StatPearls. Treasure Island (FL): StatPearls Publishing; November 3, 2021.
10. 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(1):49-60. [Crossref]
11. da Silva JSV, Seres DS, Sabino K, et al. ASPEN consensus recommendations for refeeding syndrome. *Nutr Clin Pract*. 2020;35(2):178-195. [Crossref]
12. Aksoy EK, Sapmaz F, Akpinar M, Goktas Z, Uzman M, Nazligul Y. Long-term follow-up results of patients with percutaneous endoscopic gastrostomy and factors affecting survival. *J Ankara Univ Fac Med*. 2019;72(2):179-184. [Crossref]
13. Schneider AS, Schettler A, Markowski A, et al. Complication and mortality rate after percutaneous endoscopic gastrostomy are low and indication-dependent. *Scandinavian J of Gastroenterol*. 2014;49(7):891-898. [Crossref]
14. Okida LF, Salimi T, Ferri F, et al. Complications of feeding jejunostomy placement: a single-institution experience. *Surg Endosc*. 2021;35(7):3989-3997. [Crossref]
15. Loser C, Aschl G, Hebuterne X, et al. ESPEN guidelines on artificial enteral nutrition--percutaneous endoscopic gastrostomy (PEG). *Clin Nutr.* 2005;24(5):848-861. [Crossref]
16. Arvanitakis M, Gkolfakis P, Despott EJ, et al. Endoscopic management of enteral tubes in adult patients - Part 1: Definitions and indications. *Endoscopy*. 2021;53(1):81-92. [Crossref]
17. Gkolfakis P, Arvanitakis M, Despott EJ, et al. Endoscopic management of enteral tubes in adult patients - Part 2: Peri- and post-procedural management. *Endoscopy*. 2021;53(2):178-195. [Crossref]
18. Lange P. Chronic obstructive pulmonary disease and risk of infection. *Pneumonol Alergol Pol*. 2009;77(3):284-288.
19. Cioffi I, Ponzo V, Pellegrini M, et al. The incidence of the refeeding syndrome. A systematic review and meta-analyses of literature. *Clin Nutr.* 2021;40(6):3688-3701. [Crossref]
20. Akçay K, Ayhan H, Çakır BK, Abbasoğlu O. Beslenme tedavisi alan hastalarda hipfosfatemiye neden olan faktörler. *Turk J Intensive Care*. 2021;*[e-Pub]* [Crossref]
21. Friedli N, Baumann J, Hummel R, et al. Refeeding syndrome is associated with increased mortality in malnourished medical inpatients: Secondary analysis of a randomized trial. *Medicine*. 2020;99(1):1-9. [Crossref]
22. Nunes G, Brito M, Patita M, Santos CA, Fonseca J. Hypophosphatemia before endoscopic gastrostomy predicts higher mortality during the first week and first month post-gastrostomy: a risk marker of refeeding syndrome in gastrostomy-fed patients. *Nutr Hosp*. 2019;36(2):247-252.
23. Oliveira MVP, Buarque DC. Refeeding syndrome in elderly individuals: evaluation of a series of five cases. *Geriatr Gerontol Aging*. 2017;11(1):18-24. [Crossref]
24. Saka B, Zirtil C, Erten SN, et al. Indications, effectiveness and safety of percutaneous endoscopic gastrostomy: A single center experience and literature review. *Asia Pac J Clin Nutr.* 2021;30(1):42-50.
25. 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(6):723-9. [Crossref]
26. Pitta MR, Campos FM, Monteiro AG, Cunha AGF, Porto JD, Gomes RR. Tutorial on diarrhea and enteral nutrition: A comprehensive step-by-step approach. *J Parenter Enteral Nutr.* 2019;43(8):1008-1019. [Crossref]

CLINICAL SCIENCE OF NUTRITION

Original Article

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Malnutrition Prevalence Increased During the COVID-19 Pandemic in Patients with Dementia: A Retrospective Study from the Geriatric Outpatient Clinic

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ABSTRACT

Objective: Individuals who are clinically vulnerable and older are more susceptible to severe consequences, either directly from the coronavirus disease 2019 (COVID-19) infection or indirectly from the rigorous social isolation policies. Increased frailty, reduced quality of life, high level of stress, and increased depressive symptoms were observed during the social isolation period. Patients with dementia are more vulnerable to the direct and indirect effects of COVID-19. In this study, we have explored the impact of the COVID-19 pandemic on nutrition in patients with dementia who were followed up in our outpatient clinic.

Methods: Patients with a diagnosis of dementia who were followed up in the geriatric outpatient clinic at our university hospital were included in the study. The risk of malnutrition was evaluated using the Mini-Nutritional Assessment-Short Form (MNA-SF). An MNA-SF score between 8 and 11 was defined as risk of malnutrition, and scores < 8 were accepted as malnutrition. A retrospective study was performed using the identified electronic records of 121 patients who were admitted to the hospital between March 11, 2020, and March 31, 2021.

Results: The mean age of the study population was 80.12 ± 7.12 years, and 60.3% of the patients were female. The MNA-SF scores decreased and malnutrition prevalence increased as the dementia worsened, and the difference before and during the pandemic was statistically significant ($P < .05$).

Conclusion: For patients living with dementia, COVID-19 restrictions, particularly those related to social isolation like social distancing and lockdowns, might not only have mental and cognitive implications but also disturb their already vulnerable nutritional status.

Keywords: Coronavirus disease 2019, dementia, malnutrition

INTRODUCTION

Since the first case of coronavirus disease 2019 (COVID-19) infection, globally there have been more than 400 million confirmed cases and 5.5 million deaths as of February 21, 2022.[1] COVID-19 has also had a major destructive impact on economic, food, and health systems. People who are clinically vulnerable and older are more susceptible to severe consequences, either directly from COVID-19 infection or indirectly from rigorous social isolation policies. Patients with dementia form a part of this vulnerable group.

Measures taken against the COVID-19 infection directly and indirectly impact the physical and psychological health of older people. Increased frailty, reduced quality of life, high level of stress, and increased depressive symptoms were observed during the social isolation period.[2] Another consequence was that changes in dietary choices and lifestyle characteristics because of the COVID-19 related quarantine, potentially resulted in malnourishment.[3] Mostly studies have concentrated on the effect of nutrition on COVID-19; however, there is a lack of evidence of how COVID-19 and COVID-19 related quarantine affects nutrition.[3]

Patients with dementia are more vulnerable to the direct and indirect effects of COVID-19. They are at high risk for COVID-19 infection as they cannot manage self-hygiene and maintain social distancing. Furthermore, once

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infected, older adults with dementia are more likely to experience severe COVID-19 related outcomes, including death. During the pandemic, patients with dementia also experienced cognitive decline, worsening of psychiatric symptoms, and severe behavioral disturbances.[4]

Therefore, in this study, we have explored the impact of the COVID-19 pandemic course on nutrition in patients with dementia who were followed up in our outpatient clinic.

METHODS

Study design

Patients with a diagnosis of dementia who were followed up in the geriatric outpatient clinic at our university hospital were included in the study. This was a retrospective study conducted using the identified electronic records of patients who were admitted to the hospital between March 11, 2020, and March 31, 2021. A total of 244 patients with dementia were admitted to the outpatient clinic during this period, and 121 patients were included in the study after excluding patients with incomplete data. The data about age, sex, education, marital status, type and stage of dementia, comorbidities, and number of medications were collected from the electronic records of the patient's files. Mild, moderate, and severe dementia groups were defined according to the patients' Clinical Dementia Rating (CDR) scale.[5]

Clinical Frailty Scale (CFS) was used to determine the frailty status.[6] CFS of the patient was defined according to the clinical judgement of the physician and ranged from 1 (very fit) to 9 (terminally ill). Patients living with frailty was determined as CFS ≥5. Incontinence was accepted as either urinary or fecal or both per the descriptions of the patients or caregivers. Polypharmacy was defined as using five or more medications.[7] Fall events were recorded if the patient had fallen unintentionally in the previous year. Difficulty in falling asleep, frequently awakening during the night, or awakening early in the morning were categorized as insomnia.

The risk of malnutrition was evaluated by the Mini-Nutritional Assessment-Short Form (MNA-SF).[8] An MNA-SF score between 8 and 11 was defined as risk of malnutrition, and scores <8 were accepted as malnutrition. The presence of depression was assessed by the 15-item Yesavage Geriatric Depression Scale (YGDS),[9] and scores ≥5 were evaluated as depression.

Main Points

- Patients with dementia are more vulnerable to adverse outcomes of a pandemic, including social isolation.
- Social distancing and lockdown might impact not only the mental status but also disturb the already vulnerable nutritional status in these patients.
- During the pandemic period, malnutrition rates increased in patients with dementia.

Ethical approval

Ethics committee approval was received for this study from the ethics committee of Hacettepe University Ethics Boards and Commissions Non-interventional Clinical Researches. (Date: January 18, 2022, Decision No:2022/02-29)

Statistical analysis

The data obtained in the study were analyzed statistically using IBM Statistical Package for Social Sciences version 24.0 software (IBM Co., Armonk, NY, USA). The data from the three groups according to stages of dementia were analyzed. Tests of normality were performed. Categorical variables were stated as number (n) and percentage (%), and continuous variables as median (IQR) or mean ± standard deviation (SD) values according to their distributions (normal or not). To evaluate relationships between categorical variables, the chi-squared test was used. For comparing the three groups, Bonferonni's correction was used and subgroup analysis performed. Analysis of variance was used to compare the normally distributed numerical parameters between the three independent groups when appropriate, and the Kruskal-Wallis test was used to compare the parameters which were not normally distributed. The Wilcoxon signed rank test was performed to compare the paired MNA-SF scores before and during the pandemic. A value of $P < .05$ (two-sided) was accepted as statistically significant.

RESULTS

A total of 121 patients diagnosed with dementia were enrolled in the study. The mean age of the study population was 80.12 ± 7.12 years, and 60.3% of the patients were female. Study participants were categorized according to their stages of dementia, 52.1% (63 patients) had mild dementia, 42.1% (51 patients) were diagnosed with moderate dementia, and 5.8% (7 patients) had severe dementia. There were no differences in age and sex between the groups ($P > .05$). Their demographical features were also similar ($P > .05$).

The patients were evaluated in terms of geriatric syndromes. No differences were observed between the groups regarding depression, falls, osteoporosis, incontinence, polypharmacy, and insomnia ($P > .05$). However,

Table 1. Characteristics and Demographic Features of The Study Population According to Stages of Dementia				
	Mild dementia N:63	**Moderate dementia N:51**	**Severe dementia N:7**	***P***
Age, mean ± SD	79.57 ± 6.75	80.86 ± 7.28	79.71 ± 9.58	.625
Age groups, n(%)				.205
65–74 years	13 (20.6)	11 (21.6)	3 (42.9)	
75–84 years	36 (57.1)	23 (45.1)	1 (14.3)	
>85 years	14 (22.2)	17 (33.3)	3 (42.9)	
Sex, female, n (%)	40 (63.5)	28 (54.9)	5 (71.4)	.535
Marital status, married, n (%)	30 (65.2)	14 (40.0)	3 (75.0)	.056
Education, <8 years, n (%)	25 (58.1)	20 (62.5)	2 (66.7)	.905
Geriatric Syndromes, n (%)				
Living w/ frailty	52 (82.5)	50 (98.0)	7 (100.0)	.015
Depression	20 (32.3)	18 (35.3)	2 (28.6)	.908
Incontinence	19 (30.2)	24 (47.1)	5 (71.4)	.039
Falls	12 (26.7)	6 (14.3)	3 (60.0)	.049
Osteoporosis	26 (54.2)	15 (34.1)	2 (28.6)	.151
Polypharmacy	42 (72.4)	38 (82.6)	4 (80.0)	.464
Insomnia	11 (23.9)	16 (37.2)	2 (28.6)	.284
Chronic Conditions, n (%)				
Hypertension	46 (73.0)	34 (66.7)	4 (57.1)	.588
Diabetes mellitus	18 (28.6)	18 (35.3)	2 (28.6)	.734
Coronary artery disease	16 (25.4)	17 (33.3)	1 (14.3)	.454
Hyperlipidemia	12 (19.4)	9 (17.6)	-	.442
Atrial fibrillation	8 (12.9)	13 (25.5)	-	.098
Hypothyroidism	7 (11.3)	1 (2.0)	-	.108
COPD	5 (8.1)	5 (9.8)	-	.675
Cerebrovascular disease	4 (6.5)	7 (13.7)	1 (14.3)	.407
Malignancy	8 (12.9)	8 (15.7)	1 (14.3)	.915
Rheumatologic disease	3 (4.8)	2 (3.9)	1 (14.3)	.497

COPD: Chronic Obstructive Pulmonary Disease
* After Bonferroni correction, the group from which the difference originated was specified.

the patients became more frail as the stage of dementia progressed, and the difference was statistically significant ($P < .05$). Furthermore, chronic conditions were not statistically different between groups ($P > .05$). The detailed results are shown in Table 1.

Malnutrition prevalence was also higher as the dementia worsened before and during the pandemic, and the difference was statistically significant ($P < .05$) (Table 2). However, the malnutrition ratio was 12.7% before the pandemic and rose to 23.8% during the pandemic in patients with mild dementia. In patients with moderate dementia, the malnutrition rates before and during the pandemic were detected as 15.7% and 49.0%, respectively. The number of malnourished patients with severe dementia had not changed; however, the rate of risk of malnutrition was in-

Table 2. Malnutrition Prevalence Before and During the Pandemic Course According the Stages of the Dementia

	Mild dementia N:63	Moderate dementia N:51	Severe dementia N:7	*P*
Malnutrition assessment before pandemic				.003
Normal, n (%)	28 (44.4)	11 (21.6)	1 (14.3)	
Malnutrition risk, n (%)	27 (42.9)	32 (62.7)	2 (28.6)	
Malnourished n (%)	8 (12.7)	8 (15.7)	4 (57.1)*	
MNA-SF scores, median (IQR)	11.0 (2.0)	11.0 (2.0)	7.0 (6.0)	.005
Malnutrition assessment during pandemic				.016
Normal, n (%)	13 (20.6)	3 (5.9)	-	
Malnutrition risk, n (%)	35 (55.6)	23 (45.1)	3 (42.9)	
Malnourished n (%)	15 (23.8)	25 (49.0)*	4 (57.1)*	
MNA decline, n (%)	41 (65.1)	39 (76.5)	4 (57.1)	.325
MNA-SF scores, median (IQR)	11.0 (3.0)	8.0 (5.0)	4.0 (7.0)	.003

*After Bonferroni correction, the group from which the difference originated was specified.
MNA-SF: mini-nutritional assessment short form; IQR: interquartile range

Table 3. Wilcoxon Signed-Rank Test Results of MNA-SF Scores of the Participants Before and During the Pandemic

	Median	(25^{th}–75^{th} percentile)	*P*
MNA-SF, before pandemic	11.0	9.0-12.0	< .001
MNA-SF, during pandemic	9.0	7.0-9.0	

MNA-SF: mini-nutritional assessment short

Table 4. Malnutrition Assessments According to MNA-SF Before and During the Covid-19 Pandemic Course.

	Before COVID-19	During COVID-19	*P*
Malnourishment	20 (16.5)	44 (36.4)	< .001
Malnutrition risk	40 (33.1)	61 (50.4)	
Normal	61 (50.4)	16 (13.2)	
Total	121 (100.0)	121 (100.0)	

MNA-SF: mini-nutritional assessment short form; COVID-19: coronavirus disease 2019

creased to 42.9% during the pandemic from 28.6% before the pandemic. More than half of the patients in all groups had a decline in their MNA-SF scores. The results can be seen in Table 2. The median MNA-SF score before the pandemic was 11.0 (9.0–12.0) decreased to 9.0 (7.0–9.0) during the pandemic, with the difference being significant ($P < .001$). The results are shown in Table 3. Malnutrition assessment according to MNA-SF scores before and during the COVID-19 pandemic is summarized in Table 4.

DISCUSSION

Patients with dementia are highly vulnerable to rigorous social isolation policies. The most important outcome of

our study was the observation of increased malnutrition risk rates and malnourishment during the pandemic period in all the three stages of dementia.

Patients with dementia are more vulnerable, neglected, and negatively discriminated and are not capable of caring for themselves. Multiple studies have shown that individuals with dementia are negatively affected by health decisions made in relation to COVID-19, and the long-term effects include neurological damage. It is known that the clinical condition of patients with dementia worsen owing to the enhancing effect of the pandemic, indirectly diminishing social support and decreasing interaction with the healthcare system.[10]

Malnutrition and dementia are two closely related geriatric syndromes, resulting in undesirable outcomes. Many different mechanisms may lead to malnutrition in patients with dementia. Changes in dietary habits and deficient nutrients and diet cause malnutrition in early stages of dementia. Dependency in preparing meals or shopping is another reason for malnutrition. In the later stages of dementia, patients may forget whether they have already eaten or may no longer know what they are supposed to do with the food. Furthermore, medications used for the treatment of dementia affect the appetite.[11] Malnutrition is strongly associated with cognitive decline, disease progression, institutionalization, mortality and decreased functional status, increased caregiver burden, and poor quality of life in patients with dementia.[12]

A study from Greece investigating the impact of COVID-19 on older individuals with mild cognitive impairment (MCI)/dementia has revealed an overall decline in mental and physical health in terms of communication, movement, and compliance with the new measures and also increased caregiver burden.[13] In that study, 46% of patients with MCI/dementia had "some" or "a lot" of changes in appetite. According to the authors, as the COVID-19 pandemic disrupted basic routines that support the mental and physical health of both older people with MCI/dementia and their caregivers, this disruption may have resulted in both physical and mental decline.[13] The reason for the increase in the rate of malnutrition in our study may be disruption of basic routines, decreased appetite, and increased caregiver burden.

In a study assessing the impact of the lockdown on nutritional status in older people living at home in France, a significant decrease in MNA scores, BMI, and weight was observed after the lockdown period.[14] Psycho-socio-environmental factors, psychiatric problems, mobility dependence, and acute infections had a major impact on malnutrition after confinement.[14] All these aforementioned factors were frequent in patients with dementia, though it may have led to increased malnutrition rates in our study population during pandemic course.

Our study has some limitations. First, as this was a retrospective study with a small number of participants, weight, BMI, anthropometric measurements, the amount and duration of weight loss, and also the reasons of malnutrition were undetermined. In the literature, studies and reviews have mostly focused on the direct relationship between malnutrition and COVID-19 infection; however, the indirect effect of this pandemic on the nutritional status in patients with dementia is pending. The impact of COVID-19 on patients with dementia has been mostly investigated from a psychosocial perspective. Considering all these findings, our study is important in terms of adding value to the literature.

CONCLUSION

For the patients living with dementia, the COVID-19 restrictions, particularly those related to social isolation like social distancing and lockdowns, might not only have mental and cognitive implications but also disturb their already vulnerable nutritional status.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Hacettepe University Ethics Boards and Commissions Non-interventional Clinical Researches. (Date: January 18, 2022, Decision No: 2022/02-29)

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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REFERENCES

1. World Health Organizations (WHO). Coronavirus (COVID-19) dashboard. Accessed February 22, 2022 https://covid19.who.int/
2. Cheung G, Rivera-Rodriguez C, Martinez-Ruiz A, et al. Impact of COVID-19 on the health and psychosocial status of vulnerable older adults: study protocol for an observational study. *BMC Public Health*. 2020;20(1):1814. [Crossref]
3. Antwi J, Appiah B, Oluwakuse B, Abu BAZ. The nutrition-COVID-19 interplay: a review. *Curr Nutr Rep*. 2021;10(4):364-74. [Crossref]
4. Numbers K, Brodaty H. The effects of the COVID-19 pandemic on people with dementia. *Nat Rev Neurol*. 2021;17(2):69-70. [Crossref]
5. Hughes CP, Berg L, Danziger W, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *Br J Psychiatry*. 1982;140(6):566-72. [Crossref]
6. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *Cmaj*. 2005;173(5):489-95. [Crossref]
7. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr*. 2017;17(1):230. [Crossref]
8. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition: The mini nutritional assessment. *Clin Geriatr Med*. 2002;18(4):737-57. [Crossref]
9. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res*. 1982;17(1):37-49. [Crossref]
10. Burns A, Lobo A, Olde Rikkert M, et al. COVID-19 and dementia: experience from six European countries. *Int J Geriatr Psychiatr*. 2021;36(6):943-9. [Crossref]
11. Volkert D, Chourdakis M, Faxen-Irving G, et al. ESPEN guidelines on nutrition in dementia. *Clin Nutr*. 2015;34(6):1052-73. [Crossref]
12. Soysal P, Dokuzlar O, Erken N, Dost Gunay FS, Isik AT. The relationship between dementia subtypes and nutritional parameters in older adults. *J Am Med Dir Assoc*. 2020;21(10):1430-5. [Crossref]
13. Tsapanou A, Papatriantafyllou JD, Yiannopoulou K, et al. The impact of COVID-19 pandemic on people with mild cognitive impairment/dementia and on their caregivers. *Int J Geriatr Psychiatr*. 2021;36(4):583-7. [Crossref]
14. Ghanem J, Colicchio B, Andres E, Geny B, Dieterlen A. Lockdown effect on elderly nutritional health. *J Clin Med*. 2021;10(21). [Crossref]

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Effect of the Enhanced Recovery After Surgery Protocol on Postoperative Cognitive Functions in Colorectal Surgery

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ABSTRACT

Objective: Enhanced Recovery After Surgery (ERAS®) protocols established for colorectal surgery and continuing to develop are multidisciplinary approaches combining several evidence-based interventions to reduce the patient's surgical stress response, to accelerate surgical recovery and to improve the outcome in all perioperative steps. However, it is not yet known how ERAS® protocols affect the cognitive functions in the early and late periods of patients.

Methods: Prospective observational study was performed with 51 cases. Mini Mental Test (MMT) was administered in the patients in the preoperative, postoperative early period (3rd hr,1st day) and postoperative late period (7th day, 30th day).

Results: Changes observed in MMT measurements during the period from the preoperative period to postoperative 30th day were determined to be statistically significant ($P < .01$). Decrease in postoperative 3rd hr and 24th hr measurements ($P < .01$), increase in the postoperative 24th hr, 7th day and 30th day measurements ($P < .01$), compared to the postoperative 3rd hr measurement; increase in the postoperative 7th day and 30th day measurements ($P < .01$), are statistically significant compared to the postoperative 24th hr measurement. When the differences between the preoperative and postoperative 30th day MMT measurements were considered; an improvement was observed with a rate of 76% (n=38). In the group observed improvement (Group I), ASA scores were lower ($P < .01$), and mobilization ($P < .01$), were earlier; lengths of in the intensive care unit stay ($P < .01$), were shorter.

Conclusion: Cognitive functions improve in the early period with ERAS® protocol and complication rate regresses significantly and it becomes cost efficient due to early discharge.

Keywords: cognitive dysfunction, Colorectal surgery, Enhanced Recovery after Surgery, ERAS protocol, POCD

INTRODUCTION

Enhanced recovery after surgery (ERAS) is an evidence-based perioperative protocol that was implemented for the first time in patients who had undergone colorectal surgery. Different surgical disciplines subsequently improved it, and specific guidelines were established for each surgical branch.[1,2] ERAS protocol provides various regulations for procedures, from the preoperative to the post-recovery period.[1] The data till date have revealed that ERAS protocol increases patients' comfort by providing adequate postoperative pain control, shortens the length of hospital stay, and reduces postoperative morbidity and healthcare costs.[3]

Postoperative cognitive dysfunction (POCD) is a complication that is diagnosed using neuropsychological tests. The International Postoperative Cognitive Dysfunction 1 (ISPOCD 1) study stated that the incidence of POCD was 25.8% one week after surgery and 9.9% three months after surgery.[4] The rate of POCD on the first seven days after general anesthesia in major non-cardiac surgery is 21.2%, especially in elderly patients but reduces to 14.3% three months after surgery.[5] Surgical methods targeting minimally invasive surgery such as ERAS protocol may reduce the likelihood of POCD thanks to minor tissue injury and less postoperative inflammatory response.[6] However, a possible reduction in the incidence and severity of the disease owing to ERAS protocol remains unclear. To our knowledge, there is not enough research to define the relation between ERAS protocol and POCD. Therefore, in this study, we aimed to determine the risk factors related to POCD in patients who underwent colorectal surgery managed by ERAS protocol.

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METHODS

Fifty-one patients who would undergo colorectal surgery and were scheduled for perioperative care and treatment within the frame of ERAS protocol with ethics committee approval (Date: January 17, 2017, Decision no: 2017/587) and written informed consent were included in this prospective observational study.

Study design

The cognitive functions of the patients who decided on an operation were evaluated using MMT (Mini-Mental Test, Appendix 1) during preoperative information and counseling. The same procedure was repeated during the early (postoperative 3rd hour, 1st day) and late (postoperative 7th day and 1 month) postoperative periods. Procedures performed were recorded according to the ERAS guidelines (1).

All the patients who underwent general anesthesia had an endotracheal intubation procedure, and preoperative medication was avoided. Vital signs such as heart rate (HR), electrocardiogram (ECG), non-invasive blood pressure (NIBP), pulse oxygen saturation (SpO_2), and end-tidal carbon dioxide ($PetCO_2$) were monitored during the surgery. Anesthesia was provided using intravenous injection of remifentanil (0.05–0.3 $\mu g^{-1}kg^{-1}min$), propofol 2% (2 $mg^{-1}kg^{-1}$), and rocuronium bromide (0.6–1 $mg^{-1}kg^{-1}$). Remifentanil (0.04–0.4 $\mu g^{-1}kg^{-1}min$) and propofol (1.5–2.5 $\mu g^{-1}kg^{-1}h$) were continuously infused for maintenance of anesthesia. In addition, intravenous injections of rocuronium bromide were provided intermittently. The effectiveness of anesthesia was adjusted during the procedure, and bispectral index (Aspect-100, BIS) was maintained between 40 and 50. The breathing parameters were adjusted, and the $etCO_2$ was maintained at 35–45 mmHg. Lung protective ventilation strategy was administered as PEEP at 4–6 cmH_20 and tidal volume at 5–7 mL kg^{-1} (low tidal volume) to reduce postoperative pulmonary complications. The nasogastric tube was removed before the anesthesia was completed. Intraoperative hypothermia was prevented, and normothermia was maintained with routinely used actively working suitable warming devices (Mistral-Air Warming, The 37 Company, The Netherlands). Euvolemia was attempted to be maintained with perioperative fluid management. In patients at risk with an excessive amount of blood loss (>7 mL kg^{-1}) and major open surgeries, advanced hemodynamic monitorization was ensured for easy follow-up of individual-specific fluid treatment and provision of optimal oxygen transport during the perioperative period.

MMT was performed at the preoperative informing and counseling and at 3rd postoperative hour and 1st and 7th postoperative days. MMT was repeated by inviting the patients one month after surgery. The groups were divided into two according to the preoperative and postoperative 30th day MMT measurements.

Group I: Cognitive Recovery + (n=38)

Group II: Cognitive Recovery − (n=12)

One patient who died had no MMT measurement, grouping was performed with 50 cases.

In addition, fluids administered in this period, first oral feeding time, glucose monitorization data, whether the patient needed analgesia or not, analgesic administered, time of first mobilization, length of stay in the hospital, length of stay in intensive care, possible postoperative complications, hyperglycemia/hypoglycemia, cardiac/respiratory complications, nausea and vomiting, and mortality were recorded.

Assessment of cognitive function

MMT is the most commonly used cognitive screening instrument. MMT was developed initially to differentiate depression from dementia, and it was suggested that it could be used as a quantitative criterion of the severity of cognitive impairment and change in due course.[7] MMT is a 30-point questionnaire comprising items with a total of 30 points (30 is the best) measuring the following; 10 points of time and space orientation, 6 points of memory including 3 points of record and 3 points of recall, 5 points of attention, 8 points of language, and 1 point of visual-spatial functions. MMT scores between 30 and 24, 23 and 18, and 17 and 0 are considered normal, mild, and severe cognitive impairment, respectively. If the MMT score is less than 23, it indicates cognitive impairment. A decrease of 2 or more in the total MMT score indicates cognitive disorder.[8]

Neuropsychological assessment was performed in a quiet room, where only the patient and the evaluator were present. Delirium was ruled out postoperatively. All the tests were conducted and scored in a standardized manner to minimize possible bias introduced by different evaluators. Project investigators trained in neuropsychological assessment completed all data scoring and interpretations.

Exclusion criteria

- Children under 18 years of age.
- Patients undergoing emergency surgery.
- Patients undergoing procedures related to other organs in addition to elective colorectal surgeries.
- Patients who cannot give informed consent because of mental disorders and other pathologies (Alzheimer's, Parkinson's disease, etc.).

Statistics

The primary outcome of the study was to evaluate the cognitive function data and possible risk factors of patients who underwent colorectal surgery managed with ERAS protocol.-

Statistical analysis

The Number Cruncher Statistical System (NCSS) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. During the evaluation of the study data, descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, and maximum) were used. The conformity of the quantitative data to a normal distribution was tested by using the Shapiro-Wilk test and graphical assessments. Friedman test was used for dependent variables without normal distribution, and Bonferroni-Dunn test was used to evaluate dual comparison of these variables. The Mann-Whitney U test was used for the comparisons of quantitative variables without normal distribution between two groups. The Pearson's chi-squared and Fisher-Freeman-Halton tests were used for comparisons of qualitative data. A $P < .05$ was considered statistically significant.

RESULTS

The study was performed with 51 patients who underwent colorectal surgery and implemented ERAS protocol at the University of Health Sciences, Okmeydanı Training and Research Hospital, Department of Anesthesiology and Reanimation. Of the patients, 30 (58.8%) were male (Table 1). The patients were divided into three age groups, and 66.7% of them (n=34) were between 18 and 65 years old. Most of the patients (n=30, 58.8%) had a normal body mass index (BMI). The number of overweight and obese patients was 15 (29.4%) and six (11.8%), respectively.

Table 1. Preoperative characteristics of patients.

		n (%)
Age (mean ± SD, years)	18-65	34 (66.7)
	66-75	12 (23.5)
	76-85	5 (9.8)
Gender	Male	30 (58.8)
	Female	21 (41.2)
BMI (mean ± SD) (kg/m^2)	Normal (18.5-24.9)	30 (58.8)
	Overweight (25-29.9)	15 (29.4)
	Obese (30-34.9)	6 (11.8)

BMI: Body Mass Index

The median American Society of Anesthesiologists (ASA) score was 2 (1–3) (Table 2). Most of them had an ASA score of 1 or 2. Only seven (13.7%) patients had an ASA score

Table 2. Distribution of clinical features.

		n (%)
ASA Classification	Min-Max (Median)	1-3 (2)
	Mean±SD	2±1
	I	23 (45.1)
	II	21 (41.2)
	III	7 (13.7)
Hematocrit (%)	Min-Max (Median)	29-43 (35)
	Mean±SD	35.33±3.47
Liver function tests	Normal	44 (86.3)
	Abnormal	7 (13.7)
Antiemetic use	Single	26 (51.0)
	Dual	21 (41.2)
	Three or more	4 (7.8)
Perioperative analgesia	IV infusion / PCA	39 (76.5)
	Intermittent epidural injection	5 (9.8)
	Regional block - TAP	7 (13.7)
First oral feeding time (hour)	Min-Max (Median)	4-24 (10)
	Mean±SD	11.00±5.84
First mobilization time (hour)	Min-Max (Median)	6-48 (12)
	Mean±SD	16.12±10.57
Hospital stay (day, mean ± SD)	Min-Max (Median)	4-17 (8)
	Mean±SD	9.14±3.13
ICU stay (day, mean ± SD)	Min-Max (Median)	0-10 (0)
	Mean±SD	0.78±1.64
Postoperative complication	No complication	27 (52.9)
	Cardiac	10 (19.6)
	Nausea	6 (11.8)
	Hyperglycemia	4 (7.8)
	Respiratory	3 (5.9)
	Exitus	1 (2.0)

ASA: American Society of Anesthesiologists, ICU: Intensive Care Unit, TAP: Transversus Abdominis Plane, PCA: Patient Controlled Analgesia, IV: Intravenous.

of 3. The median hematocrit (Htc) was 35 (29–43). Seven (13.7%) patients had impairment of liver function tests. Most of the patients used a single antiemetic therapy; however, 21 (41.2%) and four (7.8%) patients had dual and three or more antiemetic therapies, respectively. Perioperative analgesia was provided with patient-controlled intravenous infusion (IV) in 39 (76.5) patients, intermittent epidural injection in five (9.8%), and regional anesthetic techniques including transversus abdominis plane (TAP) block in seven (13.7%). The median first oral feeding time after surgery was 12 (4–24) hours. The first postoperative mobilization time ranged from six to 48 hours (median, 12 hours). The median hospital and intensive care unit (ICU) stay of the patients was eight (4–17) and zero (0–10) days, respectively. Most of the patients had no perioperative complications (n=27, 52.9%) (Table 2). Cardiac complications occurred in 10 (19.6%) patients, nausea in six (11.8%), hyperglycemia in four (7.8%), and respiratory complications in three (5.9%) patients. One (2.0%) patient died postoperatively.

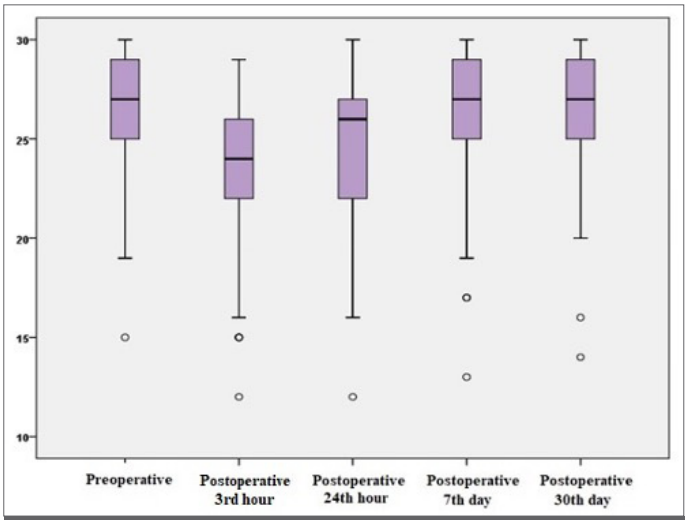

Figure 1. Distribution of MMT scores

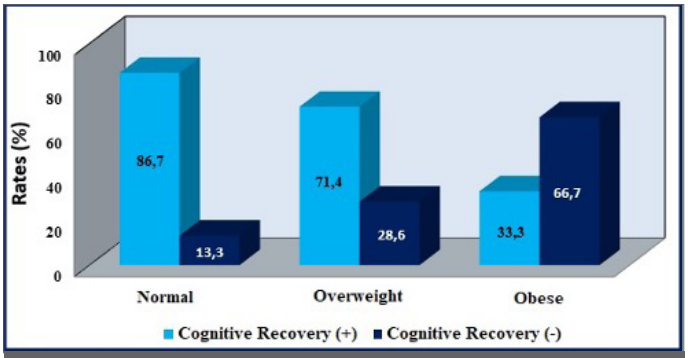

Figure 2. Distribution of cognitive recovery according to BMI rates

Fifty patients were assessed using MMT after the death of one patient (Figure 1). The MMT scores measured at different time periods from preoperative to 30th postoperative day revealed multiple kinds of statistical significance. According to differences in cognitive functions between the preoperative period and the 30th postoperative day, cognitive functions of 38 (76%) patients improved. Compared with those in the preoperative period, cognitive functions decreased in the 3rd and 24th postoperative hours (P = .001 and P = .001, respectively). However, compared with those in the 3rd preoperative hour, cognitive functions increased in the 24th postoperative hour and 7th and 30th postoperative days (P = .001, P = .001, and P = .001, respectively). Cognitive functions recovered significantly in the 7th and 30th postoperative days compared with those in the 24th postoperative hour (P = .004 and P = .001, respectively).

Although age and sex did not indicate any differences for the recovery of cognitive functions, patients with a nor-

Table 3. Evaluation of MMT scores.

	Preop.	Postop. 3rd hour	Postop. 24th hour	Postop. 7th day	Postop. 30th day	P
Mean±SD	26.37±3.12	23.48±3.91	24.74±3.85	25.88±3.76	26.20±3.64	.001* .666 † 1.000 ‡ .004 §
Min-Max (Median)	15-30 (27)	12-29 (24)	12-30 (26)	13-30 (27)	14-30 (27)	.001 ¶

MMT: Mini Mental Test; Preop.: preoperative; postop.: postoperative
* Comparison of preoperative and postoperative 3rd hour; preoperative and postoperative 24th hour; postoperative 3rd hour and postoperative 24th hour; postoperative 3rd hour and postoperative 7th day; postoperative 3rd hour and postoperative 30th day, postoperative 24th hour and postoperative 30th day, by using Bonferroni-Dunn Test.
† Comparison of preoperative and postoperative 7th day by using Bonferroni-Dunn Test.
‡ Comparison of preoperative and postoperative 30th day; postoperative 7th day and postoperative 30th day by using Bonferroni-Dunn Test.
§ Comparsion of postoperative 24th hour and postoperative 7th day by using Bonferroni-Dunn Test.
¶ Comparison of median MMT test results by using Friedman Test.

mal BMI had significantly higher rates of cognitive recovery than those who were overweight (26 [86.7%] vs. 10 [71.4%], *P* = .021) (Table 4). The rate of cognitive recovery in patients with normal weight was found to be higher than in those who were obese. Moreover, ASA scores revealed statistical significance between patients with and without cognitive recovery (Table 5). Patients with an ASA score I were significantly high in Group I (*P* = .043). The

Table 4. Evaluation of cognitive recovery according to patient characteristics.

		Group I (Recovery +) (n=38)	Group II (Recovery -) (n=12)	*P*
Age (years)	18-65	27 (81.8)	6 (18.2)	[c].311
	66-75	8 (66.7)	4 (33.3)	
	76-85	3 (60.0)	2 (40.0)	
Gender	Male	23 (79.3)	6 (20.7)	[d].520
	Female	15 (71.4)	6 (28.6)	
BMI (kg/m^2)	Normal (18.5-24.9)	26 (86.7)	4 (13.3)	[c].021*
	Overweight (25-29.9)	10 (71.4)	4 (28.6)	
	Obese (30 or 34.9)	2 (33.3)	4 (66.7)	

[c]FisherFreemanHalton Test
[d]PearsonChi-Square Test
**P* < .05
BMI: Body Mass Index

Table 5. Evaluation of cognitive recovery according to clinical features.

		Group I (Recovery +) (n=38)	Group II (Recovery -) (n=12)	[e]*P*
ASA score	Min-Max (Median)	1-3 (1.5)	1-3 (2)	.043*
	Mean±SD	1.58±0.64	2.08±0.79	
	I	19 (86.4)	3 (13.6)	
	II	16 (76.2)	5 (23.8)	
	III	3 (42.9)	4 (57.1)	
First oral feeding time (hour)	Min-Max (Median)	4-24 (8)	10-24 (18)	.001**
	Mean±SD	8.89±3.62	17.67±6.65	
First mobilization time (hour)	Min-Max (Median)	6-48 (12)	8-48 (24)	.009**
	Mean±SD	13.79±8.56	23.50±13.16	
Hospital stay (day)	Min-Max (Median)	4-17 (8)	6-14 (9.5)	.498
	Mean±SD	8.97±3.29	9.58±2.78	
ICU stay (day)	Min-Max (Median)	0-3 (0)	0-2 (2)	.002**
	Mean±SD	0.37±0.88	1.33±0.98	

[e]MannWhitney U Test
**P* < .05*
**P* < .01

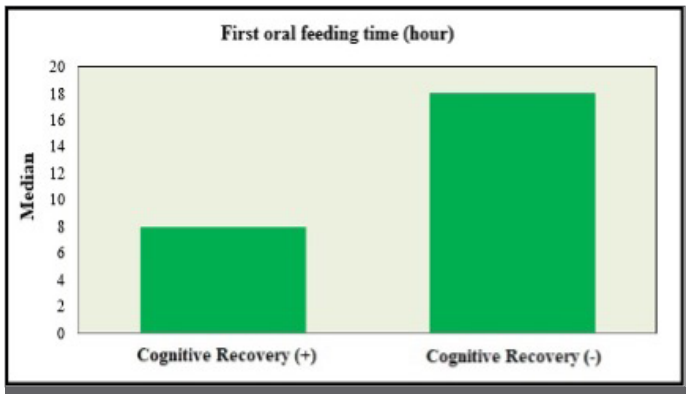

Figure 3. Distribution of first oral feeding times according to cognitive recovery

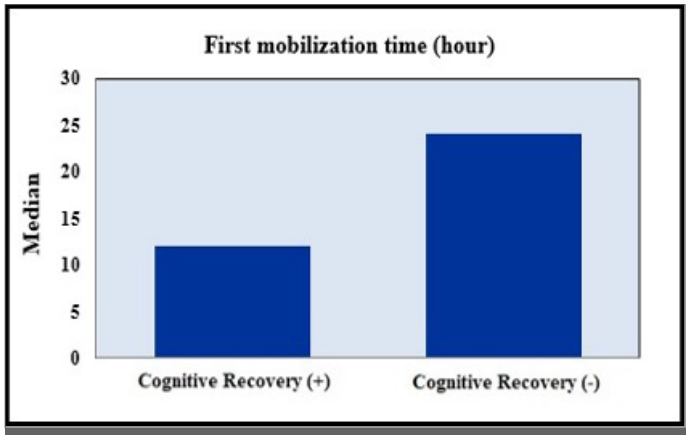

Figure 4. Distribution of first mobilization times according to cognitive recovery

first oral feeding was significantly earlier in the Group 1 than in Group 2 (median 8 [4–24] vs. 18 [10–24] hours, *P* = .001) (Figure 3). Patients in Group 1 had significantly earlier postoperative mobilization time (median 12, [6–48] vs. median 24 [8–48] hours, *P* = .001) (Figure 4). Hospital stays of the patients did not indicate any differences between the groups, but the length of ICU stay was significantly low in patients with cognitive recovery than the others (median, 0 [0–3] vs. median 2 [0–2] days, *P* = .002) (Table 5).

DISCUSSION

In this prospective observational study, we determined that preservation of cognitive function and minimization of complication development have occurred in parallel in patients who underwent colorectal surgery under the management of ERAS protocol.

In the study performed to detect the change in cognitive functions during early postoperative period of patients undergoing colorectal surgery and managed with ERAS protocol, it was determined that cognitive functions were preserved together with minimization of development of complications. Although neuropsychological tests are used for evaluation of cognitive functions, it is debatable whether there is a gold standard for this. In this study, we used MMT, the most commonly used test in international literature and in our country, to evaluate cognitive functions.

Colorectal surgery is the basis for the development of ERAS protocol. In this protocol, new evidence-based approaches are recommended instead of traditional approaches used in surgery and anesthesia. The primary purpose is to support organ functions to return to normal as soon as possible and enable patients to return to their daily routine quickly by minimizing the metabolic stress response to surgical trauma.[1] A multidisciplinary team consisting of a surgeon, an anesthesiologist, a nurse, a dietician, and a physiotherapist takes part in implementing the ERAS protocol beginning from patient optimization for surgical procedures to recovering at home. It has been shown that the ERAS protocol shortened the length of hospital stay by nearly 2–3 days, decreased complications by almost 50%, and provided cost saving of around USD 2,800 to 5,900 per patient.[9,10]

The diagnostic criteria of the cognitive dysfunction in the postoperative period have not been defined yet with a consensus as in other neurological complications such as delirium. POCD is a multifactorial condition that may affect patients in all age groups.[11] It has been reported that POCD was associated with the degeneration of the central nervous system, oxidative stress, inflammation, endocrinopathies, and immune dysfunction. There are some risk factors for developing POCD, including advanced age, coexisting comorbidity, prolonged surgery procedure, and lengthy intensive care unit stay.[12] The rate of POCD is 56% in patients discharged after coronary artery surgery and 23% three months after discharge. In addition, cognitive dysfunction is diagnosed preoperatively in patients with colorectal cancer 15% more frequently than healthy volunteers in the same age range. Its frequency was higher in women than men (52% vs. 40%). Processing speed, attention/working memory, and verbal learning were the most affected functions. These conditions indicate a dysfunction primarily in fronto-subcortical brain systems rather than being associated with inflammatory cytokines.[13] Age is the single risk factor generally accepted for prolonged or irreversible POCD. The high incidence of POCD in elderly individuals is not unusual and could be owing to possible interactions between anesthetic agents and amyloid beta-peptide, which is also associated with Alzheimer's disease.[14] The impairment of

cognitive functions occurs also in the postoperative period, especially in elderly patients. Plas et al.[15] in their study demonstrated that the rate of cognitive dysfunction in elderly patients undergoing colorectal surgery was 12% in the third postoperative month, and cognitive recovery was observed in only 53% of the patients. The incidence of cognitive impairment was 37% preoperatively in patients with a Mini-Mental State Examination (MMSE) score ≤26 and 18% in patients undergoing major surgery. In this study, the improvement of cognitive functions began at 24th postoperative hour compared to that in our study in the third postoperative hour owing to the implementation of ERAS protocol and reached the preoperative level on the 30th postoperative day in 76% of the patients. Tuman et al.[16] reported that there was a positive correlation between POCD and increased age in patients undergoing coronary artery bypass graft surgery. The researchers also showed POCD incidence with the rates of 0.9%, 3.6%, and 8.9% in patients aged <65, 65 to 74, and >75 years, respectively.

On the 7th postoperative day, POCD was detected in 26% of patients who underwent colorectal surgery. Zhang et al.[17] observed that age, ASA score, and diabetes mellitus were the risk factors for POCD. Radtke et al.[18] revealed that cognitive impairment occurred in patients with severe systemic diseases at a rate of 37.4% seven days after surgery, and the authors verified that increased morbidity was a risk factor related to the POCD. In our study, patients with lower ASA scores had better preserved cognitive functions than the patients with a higher ASA score, and age was not a risk factor for the POCD contrary to expected. In addition, advanced age, lower preoperative MMSE score, and major surgery were the risk factors for the POCD in the third postoperative month after surgery. Therefore, the risk factors defined above should be considered in the clinical decision-making progress, and patients with these risk factors should be closely followed up.

Studies targeting development of interventions for improving the quality of life should focus on the subpopulations at high risk.[15] In a previous study, including POCD patients (24.7% of 80 patients) who underwent colorectal surgery under general anesthesia, researchers determined that diabetes mellitus, length of the postoperative fasting time greater than three days, and a systemic inflammatory response syndrome score ≥ 3 two days after surgery were independent risk factors for early POCD.[12] According to ERAS protocol, oral feeding was started as soon as possible. The first oral feeding time ranged from four to 24 hours, and only 7.8% (n=4) of the patients had a complication of hyperglycemia. There was a high rate of POCD in the early postoperative period; however, cognitive functions improved over time in the late period. The main reason for the high rate of POCD in the early period might be the timing of the MMT. Similarly, in a previous study on weight loss and changes in cognitive functions in patients who underwent bariatric surgery, Spitznagel et al.[19] determined that cognitive impairment in the early period improved within 12 weeks after surgery. Furthermore, researchers revealed that cognitive functions were better preserved in patients with a lower BMI.

Early mobilization, one of the targets of the ERAS protocol, is also related to reduced rates of postoperative delirium in elderly patients.[20] In our study, mobilization time ranged between six and 48 hours, and it contributed positively to the improvement of cognitive functions. In our study, there was a correlation between early oral feeding and cognitive recovery. Although coexisting comorbidities can be optimized, prolonging hospital and ICU stay because of various postoperative complications may cause delirium-like cognitive impairment. Regional anesthesia or analgesia may reduce mortality in the early postoperative period, and the POCD rate may reduce in 80% of patients.[5,21,22] There was no correlation between the hospital stay and POCD, but cognitive functions were better preserved in patients with a short ICU stay. These consequences might be an argument for the efficiency of the ERAS protocol.

This study has some limitations, including the fact that it was performed in a single center with a limited number of patients. A large number of patients are necessary for a more accurate analysis; however, this is the first study on this topic. Therefore, the results should be reconfirmed with new randomized controlled studies.

CONCLUSION

We determined that cognitive functions were preserved within parallel of minimization of complication development in patients who had the ERAS protocol implemented. In addition, cognitive impairment was related to ASA score, BMI, and length of ICU stay. The complication rate regressed significantly in patients with the implementation of the ERAS protocol. POCD can be significantly reduced with persistent multidisciplinary implementation of the ERAS protocol.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Okmeydanı Training and Research Hospital local ethic committee. (Date: January 17, 2017, Decision no: 2017/587)

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - P.Ü., M.H.; Design: P.Ü., K.A., M.H.; Supervision – M.H.; Resources – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Materials – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Data Collection and/or Processing – P.Ü., K.A., Y.N.Ö., F.T., Ş.A., B.K.Ç.; Analysis and/or Interpretation – P.Ü., B.K.Ç., M.H.; Literature Search – P.Ü., M.H.; Writing Manuscript – P.Ü., M.H.; Critical Review - M.H.

Declaration of Interests: The authors have no conflicts of interest to declare.

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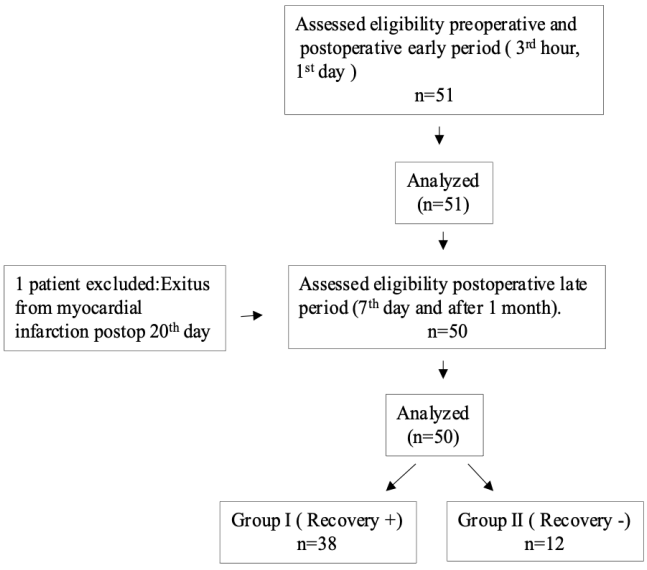
REFERENCES

1. Gustafsson UO, Scott MJ, Hubner M, et al. Guidelines for perioperative care in elective colorectal surgery: enhanced recovery after surgery (ERAS ®) society recommendations: 2018. *World J Surg*. 2019;43(3):659-695. [Crossref]
2. Nelson G, Bakkum-Gamez J, Kalogera E, et al. Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations-2019. *Int J Gynecol Cancer.* 2019;29(4):651-668. [Crossref]
3. Lemini R, Spaulding AC, Naessens JM, et al. ERAS protocol validation in a propensity-matched cohort of patients undergoing colorectal surgery. *Int J Colorectal Dis*. 2018;33(11):1543-1550. [Crossref]
4. Moller JT, Cluitmans P, Rasmussen LS, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. *Lancet* 1998;351(9106):857-861. [Crossref]
5. Rasmussen LS, Johnson T, Kuipers HM, et al. Does anaesthesia cause postoperative cognitive dysfunction? A randomised study of regional versus general anaesthesia in 438 elderly patients. *Acta Anaesthesiol Scand.* 2003;47(3):260-266. [Crossref]
6. Gameiro M, Eichler W, Schwandner O, et al. Patient mood and neuropsychological outcome after laparoscopic and conventional colectomy. *Surg Innov.* 2008;15(3):171-178. [Crossref]
7. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189-1898. [Crossref]
8. Tzabar Y, Asbury AJ, Millar K. Cognitive failures after general anaesthesia for day-case surgery. *Br J Anaesth*. 1996;76(2):194-197. [Crossref]
9. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152(3):292-298. [Crossref]
10. Varadhan KK, Neal KR, Dejong CHC, Fearon KCH, Ljungqvist O, Lobo DN. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr*. 2010;29(4):434-440. [Crossref]
11. Özlülerden P, İlhan S, Öztürk İ, Erbay H. Effect of intraoperative mean blood pressure on postoperative cognitive function in geriatric patients with hypertension. *Nobel Med*. 2015;11(1): 43-48
12. Zhang Y, Bao H-G, Lv Y-L, et al. Risk factors for early postoperative cognitive dysfunction after colorectal surgery. *BMC Anesthesiol*. 2019;19(1):6. [Crossref]
13. Knipp SC, Matatko N, Wilhelm H, et al. Cognitive outcomes three years after coronary artery bypass surgery: relation to diffusion-weighted magnetic resonance imaging. *Ann Thorac Surg*. 2008;85(3):872-879. [Crossref]
14. Hussain M, Berger M, Eckenhoff RG, Seitz DP. General anesthetic and the risk of dementia in elderly patients: current insights. *Clin Interv Aging*. 2014;9:1619-1628. [Crossref]
15. Plas M, Rotteveel E, Izaks GJ, et al. Cognitive decline after major oncological surgery in the elderly. *Eur J Cancer*. 2017;86:394-402. [Crossref]
16. Tuman KJ, McCarthy RJ, Najafi H, Ivankovich AD. Differential effects of advanced age on neurologic and cardiac risks of coronary artery operations. *J Thorac Cardiovasc Surg*. 1992;104(6):1510-1517. [Crossref]
17. Zhang Y, Qian Y, Si Y, Bao H, Zhou J. Differential expressions of serum cytokines in cognitive dysfunction patients after colorectal surgery. *Chinese J Cell Mol Immunol*. 2015;31(2):231-234.
18. Radtke FM, Franck M, Herbig TS, et al. Incidence and risk factors for cognitive dysfunction in patients with severe systemic disease. *J Int Med Res*. 2012;40(2):612-620. [Crossref]
19. Spitznagel MB, Alosco M, Strain G, et al. Cognitive function predicts 24-month weight loss success after bariatric surgery. *J Am Soc Bariatr Surg*. 2013;9(5):765-770. [Crossref]
20. Young J, Inouye SK. Delirium in older people. *BMJ*. 2007;334(7598):842-846. [Crossref]
21. Ely EW, Gautam S, Margolin R, et al. The impact of delirium in the intensive care unit on hospital length of stay. Intensive Care Med. 2001 Dec;27(12):1892-900. [Crossref]
22. Franco K, Litaker D, Locala J, Bronson D. The cost of delirium in the surgical patient. *Psychosomatics*. 2001;42(1):68-73. [Crossref]



APPENDIX 1. STANDARDIZED MINI MENTAL TEST

ORIENTATION (Total 10 points)

What is the year.....( )
What season is it?.....( )
What is the month? .....( )
What is today's date? .....( )
What is the day of the week today? .....( )
What country we are in?.....( )
What city we are in? .....( )
What locality we are in?.....( )
What building we are in?.....( )
What floor of the building are we in?.....( )

RECALL MEMORY (Total 3 points)

Now please listen carefully. I will say three words and you will repeat them after I have said them (Table, Flag, Cloth)(Allow time for a response, at least 20 seconds)
Score 1 point for each correct reply .....( )

ATTENTION and CALCULATE (Total 5 points)

I would like you to substract backward from 100 by 7. Continue until when I say you to stop. Score 1 point for each correct transaction on the account. (100, 93, 86, 79, 72, 65).....( )

VERBAL RECALL (Total 3 points)

Do you remember the words we repeated above? Say what you remember
Table, flag, cloth .....( )

LANGUAGE (Total 9 points)

a) What are the names of these objects you see? (watch, pencil) (2 points) (Allow time for a response, at least 20 seconds) .....()

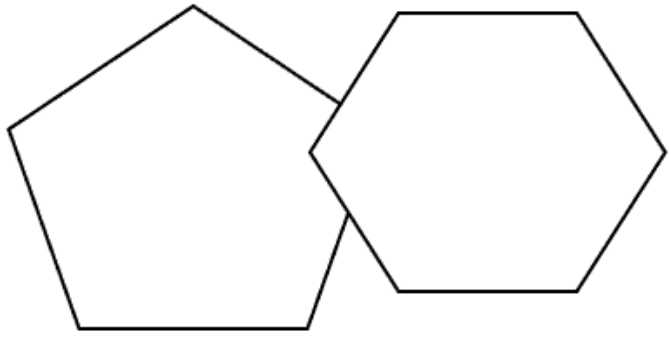
b) Now please listen to the sentence I will say carefully and repeat it after me. "No ifs, ands or buts".....( )

c) Now I'm going to ask you to perform a task, please listen to me carefully and do what I say. "Please take the paper on the table with your right/left hand, then fold it in half once with both your hand, and put it on the floor" (Total 3 points, time 30 seconds). Score 1 point for each correct action.....( )

d) Now I will give you a sentence. Please read it and do what is written in the paper. (1 point)"CLOSE YOUR EYES" .....( )

e) Now write the first sentence that comes to your mind on the piece of paper that I will give (1 point) .....( )

f) Please copy the design that I will show you (1 point)..( )



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Malnutrition and Nutritional Care in Patients with COVID-19

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ABSTRACT

Malnutrition causes serious morbidities and mortalities for both individuals and communities burdens healthcare systems. Its prevalence has become higher during the coronavirus disease 2019 (COVID-19) pandemic. COVID-19 may lead to weight loss, loss of muscle mass, malnutrition, sarcopenia, frailty, and obesity not only at the time of disease but also after disease. Nutrition risk should be assessed for all patients, and individualized nutritional care plan including one during post discharge should be generated. The fact that the risk of malnutrition and loss of muscle mass continue even several months after disease should be considered. Being aware of the increased risk of malnutrition and loss of muscle mass and their consequences during COVID-19 and in the following months would be appropriate.

Keywords: Covid-19, Diet and Foods, inflammation, malnutrition

INTRODUCTION

Coronavirus disease 2019 (COVID-19), a primarily respiratory disease caused by a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. It has brought unprecedented difficulties for healthcare systems globally thus far with inflammation, hypercatabolism, and increased energy expenditure observed during COVID-19 and predisposal to malnutrition and sarcopenia. Preexisting malnutrition and sarcopenia also worsen disease progression and related complications. Moreover, quarantine and social isolation measures may result in lack of physical activity, difficulties in accessing food, worsening in socioeconomic status, change in dietary habits, depression, anxiety, loneliness, sleep problems, deterioration in cognitive functions, and worsening of chronic diseases. All of these contribute to the development of malnutrition. Malnutrition is known to be associated with higher morbidity and mortality rates, longer length of stay in hospitals, infections, sarcopenia, frailty, delay in wound healing, and decreased life quality. Screening, diagnosing, assessing, treating, and monitoring malnutrition play a crucial role now more than ever. As the risk of malnutrition continues after the disease, following up nutritional status after COVID-19 is vital.

Clinical nutrition concepts and COVID-19

The definitions and terminology of clinical nutrition was defined by the European Society of Clinical Nutrition and Metabolism (ESPEN) guidelines in 2017.[1] According to these guidelines, clinical nutrition was classified as:

a) Malnutrition (undernutrition)
- Disease-related malnutrition (DRM) with inflammation
  - ▶ Chronic DRM with inflammation (cachexia)
  - ▶ Acute disease or injury related malnutrition
- DRM without inflammation (non-cachectic DRM)
- Malnutrition/undernutrition without disease (non-DRM): Hunger-related malnutrition and socioeconomic or psychologic related malnutrition

b) Sarcopenia
c) Frailty
d) Over-nutrition: Overweight, obesity, sarcopenic obesity, and central obesity
e) Micronutrient abnormalities: Deficiency, excess
f) Refeeding syndrome

Nutrition impact syndromes like nausea, vomiting, anorexia, diarrhea, loss of taste and smell, malnutrition, micronutrient deficiencies, sarcopenia, and obesity are common in COVID-19.[2]

Patients with COVID-19 are at high risk for malnutrition owing to heavy inflammation, hypercatabolism, and increased energy expenditure. Furthermore, advanced age, polymorbidities, and obesity increase the risk of malnutrition. Protracted hospitalization, immobility, and prolonged ventilation can cause malnutrition and sarcopenia or vice

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versa. Anorexia, dyspnea, dysosmia, dysgeusia, and digestive symptoms (diarrhea, vomiting, or abdominal pain) observed during the disease may block adequate food intake. Acute malnutrition induced by COVID-19 infection may reduce muscle mass and weaken the immune system that could contribute to the severity of COVID-19.

Malnutrition prevalence is estimated to be higher in patients with COVID-19. Most of the patients hospitalized with COVID-19 have reduced food intake, weight loss, and heavy inflammation. Risk of malnutrition and malnutrition were found to be 77% in hospitalized patients in a recent study.[3] Flippo et al.[4] revealed COVID-19 as being associated with significantly weight loss and risk of malnutrition independently of hospitalization in their prospective cohort study. Weight loss was related with systemic inflammation, impaired renal function and longer disease duration. The prevalence of the risk of malnutrition in patients with COVID-19 is reported as 37% in general medical inpatients, 53% in older inpatients, and 67% in those in the intensive care unit (ICU).[5] Malnourished patients were also 30% less likely to be discharged. High nutritional risk was significantly associated with the length of hospital stay.[6] In a systematic review of 14 articles with 4,187 participants, the pooled prevalence of malnutrition among hospitalized patients with COVID-19 was 49.11%. Patients with COVID-19 and malnutrition had a 10-fold higher mortality rate than patients with COVID-19 who were well-nourished.[7]

Currently, there are emerging studies about the importance of malnutrition and persistence of the loss of muscle mass after COVID-19 as a part of long COVID or post COVID-19 syndrome.[8-11] NutriCoviD30, a multicenter and longitudinal study, assessed hospitalized patients with COVID-19 and followed them for 30 days after hospital discharge. There was substantial weight loss, and only half of the patients regained their weight within one month of hospital discharge. Malnutrition affected 67% of hospitalized patients, and 41% of them had persistent malnutrition after one month from discharge.[12] Ramos et al. conducted an observational and prospective study assessing 936 inpatients with a mean age of 63.7 ± 15.3 years. All the patients admitted with COVID-19 for whom enteral or parenteral nutrition was indicated following an institutional protocol still presented with malnutrition at hospital discharge. The risk of malnutrition was present in only 1.7% of the patients, although the risk of sarcopenia persisted in 49.2% patients six months post discharge, highlighting the need for prolonged nutritional support and monitoring.[13]

Main Points

- Malnutrition and other nutrition-related conditions are common with COVID-19.
- Early screening and assessment of malnutrition, sarcopenia, frailty, obesity, and micronutrient abnormalities are the vital issues for patients with COVID-19
- Patients with COVID-19 should be monitored for malnutrition and other nutrition-related concepts for at least 3-6 months after COVID-19 disease.

Sarcopenia is defined as a progressive and generalized skeletal muscle disorder resulting in adverse outcomes, including falls, fractures, physical disability, and mortality. Sarcopenia is called primary sarcopenia when it is age-related. However, sarcopenia can emerge secondary to systemic diseases (especially inflammatory processes), physical inactivity, and malnutrition and is called secondary sarcopenia. Acute sarcopenia, associated with acute illness or injury, lasts less than six months, whereas chronic sarcopenia lasts more than six months.[14] Sarcopenia prevalence in patients with COVID-19 is higher than ever and also persists longer. In a prospective study, in patients with serious COVID-19 infection, sarcopenia can persist in about one-third of cases six months post discharge, when present at three months.[11,15]

Nutritional management of patients with COVID-19

ESPEN expert statements and practical guidance about nutritional management of individuals with SARS-CoV-2 infection was published recently.[16] This guideline mostly refers to previous guidelines about patients with polymorbidities in internal medicine, geriatrics, and ICUs.[17-19] Later, ESPEN reported the guideline about nutritional management of individuals with obesity and COVID-19.[20] The American Society for Parenteral and Enteral Nutrition (ASPEN) reported on "Nutrition therapy in critically ill patients with COVID-19" in September 2020.[21] The emergence of "long COVID" or "post COVID-19 syndrome" including post COVID-19 acute sarcopenia (9, 11) has led to reviews about the nutritional care in patients during the COVID-19 pandemic being published.[2,5,22]

Nutrition-impact syndromes, such as nausea, vomiting, anorexia, diarrhea, loss of taste and smell, malnutrition, micronutrient deficiencies, sarcopenia, and obesity are common in COVID-19 as mentioned above. As these increase morbidity and mortality rates, it is crucial to screen and assess malnutrition after a COVID-19 diagnosis. Individualized nutrition support and monitoring should be constituted,[2] and a checklist for screening and diagnosis of malnutrition and nutritional assessment in patients with COVID-19 should be made, which should be continued for at least three to six months after the disease.

Screening and diagnosis

Patients with risk factors such as older age, polymorbidity, and obesity are at risk for poor outcomes and mortality from COVID-19. Screening malnutrition with validated tools like the Malnutrition Universal Screening Tool and Nutrition Risk Screening 2002 (in hospitalized patients) is recommended by all the guidelines. The Mini-Nutritional Assessment criteria validated for geriatric patients, and the NUTRIC score criteria for ICU patients are also acceptable in clinical practice.[16] After screening, diagnostic assessment using GLIM criteria is recommended for patients who are at risk for malnutrition.[23] Malnutrition diagnosis requires at least one phenotypic and one etiologic criterion. Evaluation of reduced muscle mass using dual-energy absorptiometry (DXA), bioelectrical impedance analysis (BIA), computed tomography (CT), or magnetic resonance imaging (MRI) is recommended. Physical examination or standard anthropometric measures such as mid-arm muscle or calf circumference may be used when the other methods are unavailable, and handgrip strength can be considered a supportive measure. Severe inflammation in acute disease is likely to be associated with major infection, burns, trauma, or closed head injury. It is not generally associated with chronic disease conditions. Chronic or recurrent mild to moderate inflammation is likely to be associated with malignant disease, chronic obstructive pulmonary disease, congestive heart failure, chronic renal disease, or any disease with chronic or recurrent inflammation. Transient inflammation of a mild degree is not considered as an inflammation criterion. C-reactive protein may be used as a supportive value. Once malnutrition is diagnosed, severity grading should be performed as defined by the GLIM consensus.[23]

Sarcopenia can occur when systemic diseases (especially inflammatory processes), physical inactivity, and malnutrition are present. Screening and diagnosing sarcopenia during a pandemic is very important. EWGSOP2 recommends screening using a SARC-F questionnaire. SARC-F is a 5-item questionnaire that is self-reported by the patients. Strength, walking ability, rising from a chair, stair climbing, and fall events compose the questionnaire. EWGSOP2 recommends using grip strength and chair stand measures to assess muscle strength, and DXA, BIA, CT, and MRI are recommended to confirm sarcopenia by evaluating muscle quality and quantity. Finally, measuring physical performance (short physical performance battery, timed up and go, and 400-m walk tests) are recommended to assess the severity of sarcopenia.[14]

On discharge, the nutritional risk of patients should be reassessed, and individualized nutrition plans should be constituted, especially for high risk, frail, and sarcopenic patients and those with a history of ICU stay. Therefore, muscle mass should be assessed periodically. At this point, dysphagia should be identified in patients discharged from the ICU (post-extubation dysphagia). In addition, refeeding syndrome should be considered.[5]

Nutritional assessment[2]

- Dietary requirements versus intake; energy, protein, micronutrients, and fluid
- Social, physical, environmental; social (family support), physical (dentures, sight), age, and dependency (self-care, eating/drinking assistance)
- Clinical; disease (type, severity), comorbidities, nutrition impact symptoms, nutritional uptake (diarrhea, vomiting), and fever
- Body composition, muscle wasting, sarcopenia; weight loss, body mass index, muscle wasting (anthropometry, BIA, DXA, ultrasound, CT), muscle function (handgrip strength, leg muscle strength), physical function, and sarcopenia (SARC-F)
- Biochemistry; inflammation (albumin, prealbumin, CRP) and micronutrients (vitamin D, selenium)

Nutrition intervention

Multi-modal nutritional therapy should be performed on the course of disease. A combination of nutritional interventions like dietary counselling, food fortification, food texture modification, thickened fluids, oral nutritional supplements, and enteral or parenteral nutrition should be used based on the patient's needs. Specific micronutrients should be included, and other treatment modalities with physical activity should be planned.[10,24]

Nutritional requirements should include 25–30 kcal/kg/day energy and 1–2 g/kg body weight of protein. The nutritional requirements should be adjusted according to nutritional status, physical activity level, disease status, comorbidities, and tolerance.[5] Patients hospitalized with COVID-19 should be ensured their recommended daily allowance of vitamins and micronutrients with an oral diet or medical nutrition treatments. Vitamin C, D, B12, selenium, and iron are recommended to be replaced as their deficiency increase the risk of hospitalization and mortality owing to COVID-19. It is also recommended to maintain an adequate microbiome profile.[22] An active lifestyle is indispensable in nutritional management. Exercising every day for >30 minutes or every second day for >1 hour is recommended to maintain fitness, mental health, and muscle mass. Oral nutrition supplements (ONS) and enteral and parenteral nutrition should be administered whenever needed after assessment. When ONS is prescribed, it is recom-

mended to be continued for at least one month after discharge.[16]

Monitoring and review

Body weight, body mass index, food intake, compliance to dietary advice, ONS, blood tests, clinical condition, functional tests (such as sit to stand), self-reported activity, progress toward agreed goals, and ability to perform activities of daily living should be monitored. Under and overfeeding should be assessed. The patients should be reassessed weekly and high-risk patients every two to seven days during hospitalization for low to moderate nutrition risk. Patients dwelling in the community should be reassessed at one-week to three-month intervals.[5]

CONCLUSION

COVID-19 is associated with malnutrition, loss of muscle mass, obesity, micronutrient deficiencies, and increasing mortality and morbidity risks. Malnutrition screening and assessment should be performed, and individualized nutrition plans should be constituted, especially for high-risk and sarcopenic patients, and continued for several months post discharge.

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REFERENCES

1. Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr.* 2017;36(1):49-64. [Crossref]
2. van der Meij BS, Ligthart-Melis GC, de van der Schueren MAE. Malnutrition in patients with COVID-19: assessment and consequences. *Curr Opin Clin Nutr Metab Care.* 2021;24(6):543-554. [Crossref]
3. Pironi L, Sasdelli AS, Ravaioli F, et al. Malnutrition and nutritional therapy in patients with SARS-CoV-2 disease. *Clin Nutr.* 2021;40(3):1330-1337. [Crossref]
4. Di Filippo L, De Lorenzo R, D'Amico M, et al. COVID-19 is associated with clinically significant weight loss and risk of malnutrition, independent of hospitalisation: A post-hoc analysis of a prospective cohort study. *Clin Nutr.* 2021;40(4):2420-2426. [Crossref]
5. Latif J, Elizabeth Weekes C, Julian A, et al. Strategies to ensure continuity of nutritional care in patients with COVID-19 infection on discharge from hospital: A rapid review. *Clin Nutr ESPEN.* 2022;47:106-116. [Crossref]
6. Larrazabal RB, Jr., Chiu HHC, Palileo-Villanueva LAM. Outcomes of nutritionally at-risk Coronavirus Disease 2019 (COVID 19) patients admitted in a tertiary government hospital: A follow-up study of the MalnutriCoV study. *Clin Nutr ESPEN.* 2021;43:239-244. [Crossref]
7. Abate SM, Chekole YA, Estifanos MB, Abate KH, Kabthymer RH. Prevalence and outcomes of malnutrition among hospitalized COVID-19 patients: A systematic review and meta-analysis. *Clin Nutr ESPEN.* 2021;43:174-183. [Crossref]
8. Augustin M, Schommers P, Stecher M, Dewald F, Gieselmann L, Gruell H, et al. Post-COVID syndrome in non-hospitalised patients with COVID-19: a longitudinal prospective cohort study. *Lancet Reg Health Eur.* 2021;6:100-122. [Crossref]
9. Yong SJ. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. *Infect Dis.* 2021;53(10):737-754. [Crossref]
10. Barrea L, Grant WB, Frias-Toral E, et al. Dietary Recommendations for Post-COVID-19 Syndrome. *Nutrients.* 2022;14(6):1-15. [Crossref]
11. Piotrowicz K, Gąsowski J, Michel JP, Veronese N. Post-COVID-19 acute sarcopenia: physiopathology and management. *Aging Clin Exp Res.* 2021;33(10):2887-2898. [Crossref]
12. Vaillant MF, Agier L, Martineau C, et al. Food intake and weight loss of surviving inpatients in the course of COVID-19 infection: A longitudinal study of the multicenter NutriCoviD30 cohort. *Nutrition.* 2022;93:111433. [Crossref]
13. Ramos A, Joaquin C, Ros M, et al. Impact of COVID-19 on nutritional status during the first wave of the pandemic. *Clin Nutr.* 2021. [Crossref]
14. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing.* 2019;48(1):16-31. [Crossref]
15. Levy D, Giannini M, Oulehri W, et al. Long Term Follow-Up of Sarcopenia and Malnutrition after Hospitalization for COVID-19 in Conventional or Intensive Care Units. *Nutrients.* 2022;14(4). [Crossref]
16. Barazzoni R, Bischoff SC, Breda J, et al. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. *Clin Nutr.* 2020;39(6):1631-1638. [Crossref]
17. Gomes F, Schuetz P, Bounoure L, et al. ESPEN guidelines on nutritional support for polymorbid internal medicine patients. *Clin Nutr.* 2018;37(1):336-353. [Crossref]
18. Volkert D, Beck AM, Cederholm T, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. *Clin Nutr.* 2019;38(1):10-47. [Crossref]

19. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr.* 2019;38(1):48-79. [Crossref]
20. Barazzoni R, Bischoff SC, Busetto L, et al. Nutritional management of individuals with obesity and COVID-19: ESPEN expert statements and practical guidance. *Clin Nutr*. 2021. [Crossref]
21. Martindale R, Patel JJ, Taylor B, Arabi YM, Warren M, McClave SA. Nutrition therapy in critically ill patients with coronavirus disease 2019. *J Parenter Enteral Nutr.* 2020;44(7):1174-1184. [Crossref]
22. Clemente-Suárez VJ, Ramos-Campo DJ, Mielgo-Ayuso J, et al. Nutrition in the actual covid-19 pandemic. A narrative review. *Nutrients*. 2021;13(6). [Crossref]
23. Cederholm T, Jensen GL, Correia M, et al. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. *Clin Nutr.* 2019;38(1):1-9. [Crossref]
24. Cereda E, Clavé P, Collins PF, Holdoway A, Wischmeyer PE. Recovery focused nutritional therapy across the continuum of care: learning from COVID-19. *Nutrients*. 2021;13(9). [Crossref]