Original Communication

WILEY

Protein Intake at the First Day of Full-Oral Intake During Hospitalization Is Associated With Complications and Hospital Length of Stay

Dorian N. Dijxhoorn, MD, PhD[1],[*]; Vera E. IJmker-Hemink, MSc[2],[*] (iD);
Wietske Kievit, PhD[3]; Geert J. A. Wanten, MD, PhD[1]; and
Manon G. A. van den Berg, PhD[2]

Abstract

Background: Malnutrition at admission is associated with complication-related readmission and prolonged hospital stay. This underscores the importance of an adequate intake - more particular, protein intake - to prevent further deterioration and treat malnutrition during hospitalization. Our objective was to assess whether protein intake relative to requirements at the first day of full oral intake is associated with complications and hospital length of stay (LOS) in medical and surgical patients. *Methods:* This was a post hoc analysis of a prospective cohort study in patients on the wards of gastroenterology, orthopedics, urology, and gynecology. Protein intake was measured by subtracting the weight of each dish at the end of each mealtime from the weight at serving time. Complications and LOS were reported using patients' medical records. *Results:* In total, complications were observed in 92 of 637 (14.4%) patients, with a median LOS of 5 days (3.0–7.0). An absolute increase of 10% protein intake relative to requirements reduced the relative complication risk by 10% (odds ratio, 0.900; 95% CI, 0.83–0.97; $P < .05$). Also, LOS was shortened by 0.23 days for each increase of 10% in protein intake relative to requirements (95% CI, –0.3 to –0.2; $P < .05$). *Conclusion:* Protein intake relative to requirements at the first day of full-oral intake is associated with the risk of complications and hospital LOS. This analysis bolsters the evidence for the importance of any hospital meal service that increases protein intake. (*JPEN J Parenter Enteral Nutr.* 2021;45:1498–1503)

Clinical Relevancy Statement

Poor food intake and malnutrition are independent risk factors for complications and prolonged hospital stay. This underscores the importance of an adequate dietary intake, particularly protein intake, to prevent and treat malnutrition during hospitalization. The results of this study emphasize

---

From the [1]Department of Gastroenterology and Hepatology, Radboud University Medical Centre, Nijmegen, the Netherlands; and [2]Department of Gastroenterology and Hepatology—Dietetics and Intestinal Failure, Radboud University Medical Centre, Nijmegen, the Netherlands [3]Department for Health Evidence, Radboud Institute for Health Sciences, Radboud University Medical Centre, Nijmegen, the Netherlands.

*Dorian N. Dijxhoorn and Vera E. IJmker-Hemink contributed equally to this article.

Corresponding Author:
Vera E. IJmker-Hemink, MSc, Department of Gastroenterology and Hepatology—Dietetics and Intestinal Failure, Radboud University Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands.
Email: vera.ijmkerhemink@radboudumc.nl

the importance of adequate protein intake at the first day of full-oral intake during hospitalization.

Introduction

Adequate nutrition intake is a prerequisite to maintain or improve the nutrition status and to support crucial body functions during illness.[1,2] Many patients (up to 38%) in Dutch hospitals are already malnourished at hospital admission, and this number further increases during their hospital stay.[3] Poor food intake and malnutrition are independent risk factors for complication-related readmissions, prolonged hospital stay, and, hence, increased healthcare costs.[4–7]

These risk factors underscore the importance of an adequate dietary intake to prevent and treat malnutrition during hospitalization. Particularly, protein intake is important because protein requirements are higher for hospitalized patients to stimulate muscle-protein synthesis, prevent loss of muscle mass, and enhance recovery.[2,8] Various nutrition therapies are available in hospitals to improve protein intake such as dietary counseling, use of oral nutritional supplements (ONS), or tube feeding. In addition, there is increasing attention for optimization of hospital meal services as part of nutrition interventions. Recently, we showed evidence that implementation of a novel hospital meal service, coined FoodforCare (FfC), improves protein and energy intake relative to the requirements by serving protein-rich meals 6 times a day combined with proactive advice by nutrition assistants when compared with the traditional 3-meals-per-day service.[9]

Scientifically sound evidence on the direct association between an increased, or even adequate, protein intake and clinical outcomes is limited. One study showed that the length of stay (LOS) for hospitalized patients eating ≤25% of the offered food was significantly higher than those eating ≥50% (13 vs 11 days) [4]. Another cohort study, comparing enhanced recovery after surgery (ERAS) with conventional care, reported that the consumption of ≥60% of protein requirements during the first 3 days of hospitalization was associated with a shorter LOS of 4.4 days in surgical patients.[10] Unfortunately, in this respect, literature on the effect of adequate protein intake on complications is lacking. Given the importance of lowering the risk of complications and hospital LOS, there is an urgent need to provide evidence for this association in a mixed hospital population with surgical and medical patients. Therefore, the objective of the present study was to reanalyze the data from our previous prospective cohort study to assess whether protein intake relative to requirements at the first day of full-oral intake is associated with the occurrence of complications and hospital LOS in medical and surgical patients.[9]

Materials and Methods

Study Design

This is a post hoc analysis of a prospective cohort study, performed at our academic center in Nijmegen, the Netherlands, which compared a traditional meal service (TMS) (July 2015–May 2016) with FfC (January 2016–December 2016).[9] However, in this post hoc analysis, we were interested in the association between protein intake relative to requirements and clinical outcomes regardless of the type of meal service. The Medical Ethics Committee of the Radboud University Medical Center (UMC) decided that a formal approval was not required (2015-1805) (clinicaltrials.gov: NCT03195283). All patients gave informed consent before participation.

Study Population

Patients at the departments of gastroenterology, orthopedics, urology, and gynecology were recruited at their day of admission. Inclusion criteria were being ≥18 years of age and having oral intake for at least 1 full day. Patients who were receiving tube- or parenteral feeding, who had a language barrier, or who were unable to adequately answer our questions were excluded.

Hospital Meal Services

TMS consisted of 3 meals, 2 small snacks, and drinks with each round served by nutrition assistants. Breakfast and lunch include cold dishes such as slices of bread with several bread spreads or yogurt. Dinner consisted of predefined choices for meat, potatoes/rice/pasta, and vegetables. The amount of protein and energy (kcal) of the meals ranged from 0 to 26 g and 0 to 575 kcal, respectively. FfC consisted of 6 meals served by nutrition assistants. Breakfast included yogurt, oatmeal, or slices of protein-rich bread with several bread spreads. Dependent on the time of day, in-between meals consisted of protein-rich smoothies, fruit salads, cheese, wraps, and sausages. Lunch consisted of salads, sandwiches, and hot soups, and dinner consisted of warm meals served in a small pan. Amount of protein and energy of the meals ranged from 0 to 29 g and 0 to 621 kcal, respectively.

Primary Outcome

The primary outcome of this analysis was the occurrence of complications during hospital stay. A complication was defined in line with the Dutch Association of Medical Specialists (FMS) as an unintended and undesirable event or condition, during or following medical specialist intervention, that is so harmful to the health of the patient that change in medical treatment is necessary or that there is irreversible damage. Complications were obtained from

patients' medical records during hospital stay and coded as infectious, decubitus, surgical (noninfectious), and other complications (eg, cardiopulmonary).

Secondary Outcomes

As a secondary outcome, we assessed hospital LOS. LOS refers to the amount of calender days (day of admission till day of discharge) that patients spend in the hospital, reported in patients' medical records. In addition, baseline data on age, gender, Malnutrition Universal Screening Tool (MUST) ≥ 2, department, admission indication (elective vs emergency), oncologic disease, surgery, infection at admission, and comorbidities were collected from the medical records.

Protein Intake Relative to Requirements

Nutrition intake was evaluated at the first day of full-oral intake: the first day during admission that patients did not have any restrictions (eg, owing to surgery) to eat for a full day.

Intake was measured in detail on a calibrated scale by the researcher or research assistants by subtracting the weight of each dish and drink at the end of each mealtime from the weight at serving time. The nutrition value per dish and drink at serving time was based on the recipe of the meals served by the central kitchen of Radboud UMC and FfC derived from the Dutch Food Composition Database. Individualized adequate protein intake was calculated by using 1.2 grams of protein per kilogram of body weight (g/kg BW) per day as minimum requirement for all patients.[2,9] Protein requirements were corrected for patients with a body mass index (BMI) <18.5 kg/m^2 by correcting the body weight corresponding to a BMI = 20 and for patients with a BMI >30 kg/m^2 by correcting the body weight corresponding to a BMI = 27.5.[11] With the amount of protein consumed and the protein requirement of each patient, we calculated the percentage of protein requirements that was achieved. Energy requirement (kcal) was calculated using the Harris and Benedict formula and multiplied by 1.3 for illness and physical activity.[9]

Statistical Analysis

Baseline characteristics were described by mean $\pm$ SD or median and interquartile range in case of continuous data, depending on whether the data were normally distributed frequencies and percentages that were described in case of dichotomous data. The occurrence of a complication was defined as a dichotomous variable (yes/no) and LOS in days as a continuous variable. Protein intake relative to requirements was defined as a continuous variable. We chose to describe this variable in steps of 10% for a distinct

interpretation of the results. Table 5 shows examples per variable for a proper interpretation.

We performed an etiological analysis to answer our research questions. Logistic regression was used to assess the association of protein intake relative to requirements with the occurrence of complications. Because the LOS distribution was skewed, generalized linear models with an identity link function and γ-distribution were applied to assess the association of protein intake relative to requirements with LOS.

The following variables were tested for potential confounding by using linear regression: meal service, age, gender, MUST ≥ 2, department, admission indication (elective vs emergency), oncologic disease, surgery, infection at admission, and comorbidities. Variables with an assumed association with the primary and secondary outcome and a proven association with protein intake relative to requirements (in our data) were included in the regression model. For all statistical tests, a two-tailed P-value $<.05$ was considered to be statistically significant. All data were analyzed with the software package SPSS (version 22, SPSS Inc, Chicago, IL).

Results

Patient Characteristics

Patient selection and demographics. A total of 2603 patients were assessed for eligibility; 707 patients were included in the study, of which, 637 were eligible for analysis. Table 1 shows baseline characteristics of the 637 patients included in the analysis. The mean age of the patients was 59.3 $\pm$ 16.6 years and 46.9% was male. The median number of days between admission and the first day of full-oral intake was 1 (1–2) day. A flowchart and details of differences in patient characteristics are provided in a previous publication.[9]

Outcomes

Mean protein intake relative to requirements was 68.7% $\pm$ 31.8% and mean energy intake relative to requirements was 79.1% $\pm$ 33.1% at the first day of full-oral intake.

Complications. Table 2 shows that complications were observed in 92 of 637 patients (14.4%). Protein intake relative to requirements at the first day of full-oral intake was significantly associated with the risk of complications after adjusting for confounding factors. When the percentage of protein intake to requirements increased by 10%, the risk of a complication relatively decreased with 10%. Age, MUST ≥ 2, and department were associated with protein intake relative to requirements and have an assumed association with complications. Therefore, these confounders were included in the adjusted model. Table 3 shows the crude odds ratio

Table 1. Baseline Characteristics of Included Patients.

Baseline characteristics	N = 637
Gender, n (%) Male	299 (46.9)
Age, years, mean ± SD	59.3 ± 16.6
Meal service, n (%)	
Traditional meal service	326 (51.2)
FoodforCare	311 (48.8)
BMI, kg/m^2, mean ± SD	26.5 ± 5.2
MUST ≥ 2, n (%)	78 (12.3)
PG-SGA stadium C, n (%)	75 (12.8)
PG-SGA activities, n (%)	
No limitations	227 (35.6)
Fairly normal activities	150 (23.5)
In bed or chair less than half the day	87 (13.5)
Most of the day in bed/chair or bedridden	121 (19.0)
Admission, n (%)	
Emergency	259 (40.7)
Elective	378 (59.3)
First day of full-oral intake, days after admission, median (IQR)	1 (1–2)
Oncological disease, n (%)	150 (23.5)
Surgical procedure, n (%)	61.7 (393)
(Suspected) Infection, n (%)	121 (19.0)
Department, n (%)	
Gastroenterology and hepatology	198 (31.1)
Orthopedics	216 (33.9)
Urology	148 (23.2)
Gynecology	75 (11.8)
Primary diagnosis, n (%)	
Gastrointestinal	134 (21.0)
Hepatic	58 (9.1)
Urogenital	144 (22.6)
Genital	78 (12.2)
Musculoskeletal	216 (33.9)
Respiratory	2 (0.3)
Internal medicine	3 (0.5)
Dermatological	4 (0.6)
Comorbidity, n (%)	
Diabetes mellitus	72 (11.3)
Cerebrovascular	25 (3.9)
Cardiovascular	107 (16.8)
Other	213 (33.4)

BMI, body mass index; IQR, interquartile range; MUST, Malnutrition Universal Screening Tool; MUST ≥ 2, high risk of malnutrition; PG-SGA, Patient-Generated Subjective Global Assessment; Stadium C, patient is severely malnourished.

(OR) from the univariate model and the adjusted OR from the adjusted model.

Hospital LOS. Overall, patients were admitted for a median LOS of 5 days (3.0–7.0). Figure 1 shows the univariate association between protein intake relative to requirements at the first day of full-oral intake and LOS. After adjusting for age, MUST ≥ 2, and department as confounding factors,

Table 2. Number of Total Patients With >1 Complication and Number of Complications per Different Type of Complications.

Variables	N = 637	Examples
Total patients with ≥1 complication, n (%)	92 (14.4)	
Total infectious complications, n (%)	26 (4.1)	Urinary tract infection
Decubitus, n (%)	2 (0.3)	
Surgical (noninfectious), n (%)	27 (4.2)	Wound leakage
Other, n (%)	45 (7.1)	Pneumonia

Table 3. Univariate and Multivariate Logistic Regression Analysis to Assess the Association of Protein Intake Relative to Requirements With Complications.

Logistic regression model	β	SE	Wald	Odds ratio (95% CI)	P-value[b]
Univariate model (N = 637)	–0.071	0.037	3.738	0.931 (0.87–1.00)	.053
Multivariate model[a] (N = 637)	–0.105	0.040	6.981	0.900 (0.83–0.97)	.008

SE, standard error.
[a] Adjusted for age, MUST ≥ 2, department.
[b] *P* < .05 is considered statistically significant.

the association between protein intake relative to requirements and LOS remained. Each increase of 10% in protein intake relative to requirements was associated with a shorter LOS of 0.23 days (Table 4).

Discussion

This study shows that in our cohort of medical and surgical patients, an increase in protein intake relative to requirements at the first day of full-oral intake is associated with complications and hospital LOS. More specifically, an increase of 10% in protein intake relative to requirements reduced the risk for complications and LOS with 10% and 0.23 days, respectively.

Previous research about the association between protein intake and clinical outcomes has mainly been performed in patients after surgery. Thus, these studies differ greatly from our study, which makes it difficult to compare. Our finding is in line with a study reporting about the association between protein intake and complications. A retrospective study from Australia (n = 95) reported that patients with gastrointestinal cancer who achieved adequate intake 7 days after surgery were more likely to experience at least 1 complication compared with patients achieving adequate intake
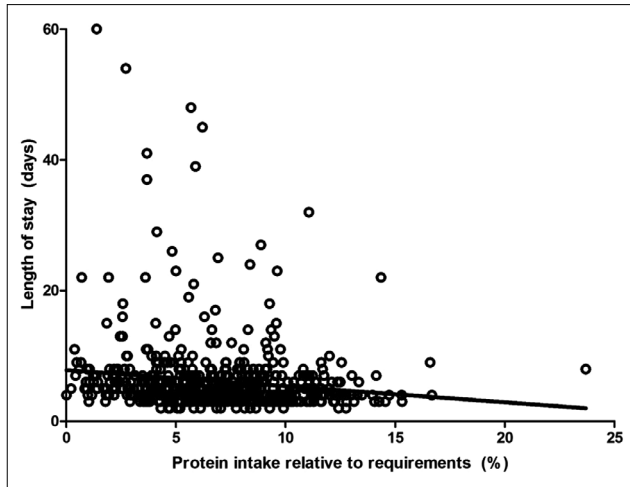
Figure 1. The negative univariate association between protein intake relative to requirements and length of stay analyzed by a linear regression model.

Table 4. Univariate and Multivariate Generalized Linear Models to Assess the Association of Protein Intake Relative to Requirements With Hospital LOS.

	SE	Wald χ	LOS (95% CI)	P-value[b]
Univariate model (N = 637)	0.032	33.147	−0.185 (−0.25 to −0.12)	.000
Multivariate model[a] (N = 636)	0.035	42.106	−0.225 (−0.32 to −0.18)	.000

CI, confidence interval; LOS, length of stay; SE, standard error.
[a] Adjusted for age, MUST ≥ 2, and department.
[b] $P < .05$ is considered statistically significant.

Table 5. Examples of the Interpretation of the Results per Variable.

Result per variable	Interpretation
An absolute increase of 10% in protein intake relative to requirements	Mean protein intake relative to requirements increases from 50% to 60%
The risk of a complication relatively decreases with 20%	Complication risk decreases from 30% to 24% (30 − [30 × 0.2])
LOS decreases with 1 day	LOS decreases from 3 days to 2 days

LOS, length of stay.

within the first 7 days.[12] Nutrition intake was measured in a retrospective manner, which is inferior to our prospective accurate measurements. Furthermore, the patient population was homogeneous, the number of complications was higher (35%), and the definition was different (all kinds of complications) than in our analysis (9.1%). A recent prospective study (n = 115) showed that an intake of ≥60% of protein requirements in the first 3 days after colorectal surgery was associated with a shorter LOS of 4.4 days.[10] This is a greater difference than our results (4.4 vs 0.25), which can be explained by the mean LOS of around 8 days compared with the median LOS of 5 days in our study. Another important difference is that this study assessed the ERAS protocol in which oral nutritional supplements (ONS) was offered in addition to a regular diet compared with our study, which was focused on a regular diet.[10] These studies emphasize the importance of adequate intake within the first days after surgery.

Our study marks the relevance of adequate protein intake at the first day of full-oral intake for a broader group of hospitalized patients because it shows beneficial effects on LOS in surgical and medical patients. Optimal nutrition support resulting in an increased protein intake is, therefore, of crucial importance during the hospital stay. In this respect, implementation of an optimal hospital meal service is a powerful strategy. In our clinical study, we showed that the FfC meal service significantly improved protein intake relative to requirements at the first day of full-oral intake with 20% when compared with the TMS,[9] which may suggest extra benefits for patients receiving this meal service regarding complications and LOS. However, a larger sample size is probably needed to confirm these extra benefits. In addition, adequate nutrition support might also prevent patients from becoming at risk for malnutrition, which might save malnutrition-related costs.[13]

This is the first study that analyzed the association between protein intake relative to requirements at the first day of full-oral intake and clinical outcomes in such a substantial cohort with patients from medical and surgical departments. Confounding factors that could influence this association, such as age or malnutrition, were taken into account. We thoroughly examined such factors in the statistical analysis and adjusted for them when necessary to ultimately conclude that protein intake does play a role in reducing the risk of complications and LOS in this population.

We made no distinction between different types of complications in our analysis. Multiple factors play a role in the development of a complication, and there is no standardized method on which the inclusion of complications in such an analysis should be based. Furthermore, because complications were observed in only 92 of 637 patients (14.4%), a considerably larger sample size would be required to obtain more information on the association at different levels of complications. Also, our population could be healthier compared with the general hospital population

by excluding patients receiving tube or parenteral feeding, resulting in a relatively low complication rate.

Conclusions and Recommendations

We provide evidence that an increase in protein intake relative to requirements at the first day of full-oral intake is associated with a decrease in the risk of complications and hospital LOS. Therefore, we recommend that hospitals focus on the provision of an adequate protein intake for all patients and on strategies to improve intake by means of optimization of their meal services. This strategy might prove to be a highway toward improved clinical outcomes.

Statement of Authorship

D. N. Dijxhoorn, G. J. A. Wanten, and M. G. A. van der Berg contributed to the conception and design of the research; D. N. Dijxhoorn conducted the research; D. N. Dijxhoorn and V. E. IJmker-Hemink contributed equally to the analysis and interpretation of the data. W. Kievit advised about the statistical analysis and interpretation of the results. D. N. Dijxhoorn and V. E. IJmker-Hemink drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

References

1. Davies ML, Chapple LS, Chapman MJ, Moran JL, Peake SL. Protein delivery and clinical outcomes in the critically ill: a systematic review and meta-analysis. *Crit Care Resusc*. 2017;19(2):117-127.
2. Deutz NE, Bauer JM, Barazzoni R, et al. Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. *Clin Nutr*. 2014;33(6):929-936.
3. Kruizenga H, van Keeken S, Weijs P, et al. Undernutrition screening survey in 564,063 patients: patients with a positive undernutrition screening score stay in hospital 1.4 d longer. *Am J Clin Nutr*. 2016;103(4):1026-1032.
4. Agarwal E, Ferguson M, Banks M, et al. Malnutrition and poor food intake are associated with prolonged hospital stay, frequent readmissions, and greater in-hospital mortality: results from the Nutrition Care Day Survey 2010. *Clin Nutr*. 2013;32(5):737-745.
5. Correia MI, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. *Clin Nutr*. 2003;22(3):235-239.
6. Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. *Clin Nutr*. 2008;27(1):5-15.
7. Kruizenga H, van Keeken S, Weijs P, et al. Undernutrition screening survey in 564,063 patients: patients with a positive undernutrition screening score stay in hospital 1.4 d longer. *Am J Clin Nutr*. 2016;103(4):1026-1032.
8. Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr*. 2017;36(1):49-64.
9. Dijxhoorn DN, van den Berg MGA, Kievit W, Korzilius J, Drenth JPH, Wanten GJA. A novel in-hospital meal service improves protein and energy intake. *Clin Nutr*. 2018;37(6):2238-2245.
10. Yeung SE, Hilkewich L, Gillis C, Heine JA, Fenton TR. Protein intakes are associated with reduced length of stay: a comparison between enhanced recovery after surgery (ERAS) and conventional care after elective colorectal surgery. *Am J Clin Nutr*. 2017;106(1):44-51.
11. Weijs PJ, Sauerwein HP, Kondrup J. Protein recommendations in the ICU: g protein/kg body weight - which body weight for underweight and obese patients? *Clin Nutr*. 2012;31(5):774-775.
12. Garth AK, Newsome CM, Simmance N, Crowe TC. Nutritional status, nutrition practices and post-operative complications in patients with gastrointestinal cancer. *J Hum Nutr Diet*. 2010;23(4):393-401.
13. Freijer K, Tan SS, Koopmanschap MA, Meijers JM, Halfens RJ, Nuijten MJ. The economic costs of disease related malnutrition. *Clin Nutr*. 2013;32(1):136-141.