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Impact of Nutritional Intervention on Length of Hospital Stay and Mortality among Hospitalized Patients with Malnutrition: A Clinical Randomized Controlled Trial

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ABSTRACT

Objective: The objective of this study was to evaluate the impact of a nutritional intervention on hospital stay and mortality among hospitalized patients with malnutrition.

Methods: Hospitalized patients with a diagnosis of malnutrition were enrolled and randomly allocated to either an intervention or control group. Participants in the intervention group received an individualized nutrition plan according to energy and protein (1.0–1.5 g/kg) intake requirements as well as dietary advice based on face-to-face interviews with patients and their caregivers or family members. Individuals in the control group received standard nutritional management according to the Hospital Nutrition Department. Nutritional status and disease severity were assessed using nutritional risk screening. Length of hospital stay was defined by the number of days of hospitalization from hospital admission to medical discharge. Reference to another service or death were criteria for study withdrawal. To evaluate mortality, individuals were followed up for 6 months after hospital discharge. Hospital stay and mortality were the intention-to-treat analysis.

Results: A total of 55 patients with an average age of 57.1 ± 20.7 years were included into intervention ($n = 28$) and control ($n = 27$) groups, respectively. At basal condition, nutritional status, measured by nutritional risk screening score, was similar between the study groups (4.1 ± 0.8 vs 4.2 ± 1.2, $p = 0.6$). The average hospital stay was lower in the intervention group compared to the control group (6.4 ± 3.0 vs 8.4 ± 4.0 days, $p = 0.03$). Finally, the mortality rate at 6 months of follow-up was similar in both groups (hazard ratio [HR] = 0.85; 95% confidence interval [CI], 0.17–4.21).

Conclusions: Results of this study suggest that, in hospitalized patients with malnutrition, nutritional intervention and dietary advice decrease hospital stay but not mortality.

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Nutritional intervention; malnutrition; hospital stay; mortality; hospitalized patients

Introduction

Malnutrition is a state of nutritional deficiency that modifies body composition (mainly fat and muscle tissues), disturbs gastrointestinal function (changes in digestion, absorption, and immunity), alters the musculoskeletal system (predominantly chest muscle dysfunction) and even impairs the process of wound healing [1–3].

The negative impact of malnutrition in hospitalized patients is well known; in 1936, Studley [4] described the positive relationship between undernutrition and postoperative mortality in patients with duodenal ulcer. Later, Buzby et al. [5] reported a high incidence of complications in malnourished surgical patients, and Von Meyenfeldt and Meijerink [6] reported an increased length of postoperative hospital stay among patients with nutritional depletion. However, even taking into account the historical background, usually the early recognition of malnutrition is not performed at hospital admission [7,8].

Furthermore, several factors can exert an adverse influence on nutritional status in hospitalized patients such as prolonged fasting, inappropriate nutritional support, increased catabolic state due to ongoing disease, comorbidities, nosocomial infections, and metabolic or physical disorders, which that lead to a reduction in energy reserves [9].

Otherwise, undernutrition is a common characteristic of hospitalized patients, ranging from 30% at hospital admission to up to 50% through during the hospital stay [7,8,10]. In Latin America, it a prevalence of 50.2 and 11.2% for malnutrition and severe malnutrition among hospitalized patients, respectively, has been reported [11]. The early recognition of undernutrition and nutritional support during a hospital stay may reduce the length of stay, complications, mortality, and hospital costs [12].

Several studies have reported few benefits of nutrition support therapy on clinical outcomes compared to standard care [13]. In this context, a recent systematic review and meta-analysis of randomized clinical trials focused in malnourished medical inpatients found no significant effects of nutritional support regarding to mortality, hospital-acquired infections, functional outcome, or length of hospital stay compared intervention and control groups [14]. Nonetheless, the results are

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controversial to date; though some studies have reported reduced length of stay and decreased mortality after nutritional intervention [12], others no found significant differences in these outcomes [15]. These inconsistencies may be attributed to the short interval of treatment or by the inclusion of patients without undernutrition; hence, this issue requires clarification. Thus, the objective of our study was to evaluate the impact of nutritional intervention on hospital stay and mortality among hospitalized patients with malnutrition.

Materials and methods

Protocol approval by the Ethical Committee of the Escuela de Medicina, Tecnológico de Monterrey (S/N) was received to conduct a randomized controlled trial. Eligible participants were individuals with malnutrition admitted to the Department of Internal Medicine of the Hospital Metropolitano "Dr. Bernardo Sepulveda" in Monterrey, N.L., a city in northern México.

Men and women 20 years of age or older who agreed to participate signed an informed consent and underwent a complete medical history and evaluation of nutritional status. Patients with expected hospital stay of less than 48 hours, consciousness disturbances, psychiatric disease, pregnancy or breastfeeding, chronic kidney disease, parenteral or enteral nutrition requirements, mechanical ventilation, liver disease, cerebrovascular disease, alcohol intake or malignancy, and inability to follow nutritional recommendations were excluded.

Within 24 hours after admission, the enrolled patients were randomly allocated (using a list of random numbers generated by computer) to an intervention or control group. During the total length of hospital stay in the Internal Medicine Department, participants in both groups received daily nutritional care and dietary advice. Reference to another service or death were criteria for study withdrawal.

Participants in the intervention group received an individualized nutrition plan according to energy (estimated by Mifflin's predictive equation) [16] and protein (1.0–1.5 g/kg) requirements [17] as well as dietary advice based on face-to-face interviews with patients and their caregivers or family members [18]. The advice consisted of (1) motivation to adhere to a diet, (2) estimation of daily dietary intake, and (3) counseling regarding nutritional information of food supply.

Individuals in the control group received standard nutritional management established by the Hospital Department of Nutritional Support, which consisted of an intake of 20–30 kcal/kg per day.

Nutritional evaluation for all patients and advice for intervention patients was performed by a clinical dietitian; use of nutritional supplements was avoided in both groups. Adherence to dietary intake was assessed by 24-hour recording.

After hospital discharge, patients were followed up for 6 months to evaluate mortality; for this purpose, data on mortality were collected through telephone survey at 2, 4, and 6 months.

Definitions

Nutritional status and disease severity were assessed using nutritional risk screening (NRS) [19]; patients with total score ≥ 3 were classified as malnourished.

Length of hospital stay was defined by the total days of hospitalization, from hospital admission to medical discharge, reference to another service, or death.

Depression was diagnosed using the Patient Health Questionnaire [20] and the Geriatric Depression Scale [21] in subjects under 65 and older than 65, respectively; a score equal or greater than 5 established a diagnosis of depression.

The primary outcome treatment was a reduction in length of hospital stay. Sample size was calculated based on an expected reduction in length of hospital stay of 2.0 ± 0.5 days in the intervention group compared with the control group, a statistical power of 80%, and alpha value 0.05. The estimated sample size was 25 subjects per group.

Statistical analysis

The results are expressed by central and dispersion measures. Differences between the groups were estimated using 2-tailed unpaired Student's t test for normally distributed numerical variables (Mann-Whitney U test for nonparametric distribution) and χ^2 test for qualitative variables. A multivariate linear regression analysis adjusted by age, gender, NRS score, and diet adherence was performed to evaluate the association between nutrition intervention (independent variable) and length of hospital stay (dependent variable).

Kaplan-Meier curves were used to estimate survival during 6 months of follow-up after hospitalization; differences between the groups were estimated using Cox regression analysis.

Statistical significance was considered by $p < 0.05$ or by 95% confidence interval (CI). All data were processed and analyzed using SPSS 22.0 for Windows (SPSS, Chicago, IL).

Results

A total of 216 patients were screened; 161 (74.5%) were excluded from the study because they did not fulfill the inclusion criteria or met exclusion criteria. Thus, 55 hospitalized patients with an average age of 57.1 ± 20.7 years were enrolled and randomized into the intervention ($n = 28$) and control ($n = 27$) groups. Seven patients did not complete the full follow-up study: 2 from the intervention group (one due to death during the hospital stay [chronic obstructive pulmonary disease] and one for withdrawal of consent) and 4 from the control group (4 due to death during the hospital stay [2 due to chronic obstructive pulmonary disease, 2 due to congestive heart failure, and one due to pneumonia]). The 48 patients who completed the follow-up period were included in the analysis; see Fig. 1.

The percentage of adherence to diet during hospital stay was significantly higher in the intervention group (90.1 ± 18.1% vs 77.7 ± 16.9%, $p = 0.01$).

Diagnosis at hospital admission for individuals in both groups is shown in Table 1, highlighting that 16 (61.5%) and 13 (59.0%) of the patients in the intervention and control groups were hospitalized due to chronic disease.

The clinical and biochemical characteristics of the patients are summarized in Table 2. At baseline, no significant statistical differences were found in anthropometric variables. In addition, frequency of depression (21.4% vs 40.7%, $p = 0.2$) and

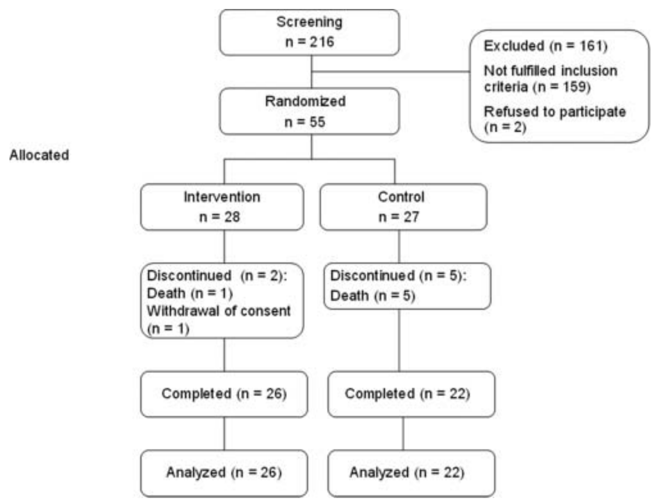

Figure 1. Flow diagram of the study.

NRS score (4.1 ± 0.8 vs 4.2 ± 1.2, $p = 0.6$) were similar in the intervention and control groups. Patients in the intervention group showed higher hemoglobin and lower urea levels compared to the control group. Other biochemical variables were similarly distributed in both groups; see Table 2.

At the end of hospitalization, anthropometric measurements showed no statistically significant differences between intervention and control groups; hemoglobin levels remained higher in patients in the intervention group compared to the control group; other biochemical variables were not significantly different (see Table 2).

Length of hospital stay was significantly lower in the intervention group compared to the control group (see Table 2). In addition, the linear regression analysis adjusted by age, gender, NRS score, and diet adherence revealed that nutritional intervention is negatively associated with length of hospital stay (odds ratio = −2.04; 95% CI, −3.86 to −0.21).

Finally, the mortality rate at 6 months was similar in both groups (HR = 0.85; 95% CI, 0.17–4.21), without statistical significance; see Fig. 2.

Table 1. Diagnosis at Hospital Admission of Patients Who Completed 6 Months of Follow-Up, $N = 48$.

	Intervention $n = 26$	Control $n = 22$
Chronic obstructive pulmonary disease	8	2
Acute metabolic complications of diabetes	6	2
Congestive heart failure	2	3
Urosepsis	1	2
Acute pancreatitis	1	1
Nonischemic central nervous disease	2	—
Pulmonary tuberculosis	1	1
Asthmatic crisis	1	—
Epilepsy	1	—
Ischemic cardiac disease	1	1
Fever of unknown origin	1	1
Pneumonia	1	2
Gastrointestinal bleeding	—	3
Hypertensive crisis	—	2
Connective tissue disease	—	1
Septic shock	—	1

Discussion

Findings of this study suggest that nutritional intervention and dietary advice, involving patients and their caregivers, reduced hospital stay but not mortality among hospitalized patients with malnutrition.

Our results are in accordance with previous reports showing that nutrition intervention and dietary advice in malnourished patients reduce complications and length of hospital stay [9,15,22]. Hence, screening of patients' nutrition status at hospital admission or the start of medical care as well as the early intervention and routine monitoring of nutritional status during hospital stay and required adjustments in nutrition care plans are recommended [23]. Furthermore, nutrition education of patients and their caregivers should be provided before hospital discharge in order to maintain an appropriate nutrition care plan in the outpatient setting [24].

In addition, in our study, both groups exhibited similar mortality rates at 6 months of follow-up; Bally et al. [14], who conducted a systematic review and meta-analysis to assess the effects of nutritional support on outcomes of medical inpatients with malnutrition or at risk for malnutrition, reported no differences between the intervention and control groups with respect to mortality (9.8% vs 10.3%; odds ratio = 0.96; 95% CI, 0.72–1.27).

It has been suggested that very low albumin levels predict the risk of long-term mortality better than other measures in non-critically ill patients [25]; relatedly, among participants in both groups in our study, at basal conditions, the mean of serum albumin levels was lower than 3.5 g/dL; at discharge from this hospital there were no significant changes, probably related to the short hospital stay.

In addition, our findings are consistent with a previous study by Holyday et al. [15], who, based in a randomized controlled trial, reported that there were no significant differences in mortality during hospital stay between individuals who received dietetic intervention compared to the control group.

Given that some variables could exert a confounding effect in our study, in order to minimize selection and analysis bias related to the expected heterogeneity of patient comorbidities, we used the validated NRS score [19], which allows assessment of nutritional status and disease severity. In this context, no significant differences regarding NRS score between the intervention and control groups were found (4.07 ± 0.84 vs 4.09 ± 1.34, $p = 0.96$). Although chronic clinical conditions such as chronic obstructive pulmonary disease and acute metabolic complications of diabetes were significantly higher in the intervention groups than in control group, the length of hospital stay was lower in individuals who received an individualized nutrition plan than in those who received the hospital standard nutritional management. Additionally, anthropometric variables and biochemical parameters such as albumin, total protein, glucose concentration, creatinine, and triglyceride levels showed no significant differences between study groups at basal condition; these findings support the efficacy of individualized nutritional intervention.

Furthermore, because depression is a condition that can promote loss of appetite [26], we use the Patient Health Questionnaire and Geriatric Depression Scale to diagnosis

Table 2. Clinical and Biochemical Characteristics of Participants.

	Basal			Final		
	Intervention $n = 28$	Control $n = 27$	p Value	Intervention $n = 26$	Control $n = 22$	p Value
Women, n (%)	14 (50.0)	19 (70.0)	0.20	12 (46.0)	16 (72.0)	0.11
Age (years)	54.7 ± 22.7	59.6 ± 18.3	0.38	53.2 ± 23.1	58.45 ± 18.1	0.39
Body mass index (kg/m^2)	24.7 ± 7.7	27.3 ± 8.8	0.25	24.6 ± 7.4	26.1 ± 7.0	0.47
Systolic blood pressure (mmHg)	124.1 ± 18.3	121.9 ± 23.5	0.70	115.3 ± 12.0	116.5 ± 9.8	0.69
Diastolic blood pressure (mmHg)	73.2 ± 16.0	70.8 ± 11.7	0.51	72.1 ± 9.0	74.0 ± 7.9	0.45
Waist circumference (cm)	97.2 ± 21.0	98.6 ± 21.6	0.81	96.3 ± 20.6	97.6 ± 14.5	0.79
Calf circumference (cm)	29.9 ± 4.7	31.0 ± 7.3	0.48	29.73 ± 4.2	31.9 ± 6.7	0.16
Arm circumference (cm)	25.9 ± 4.8	27.1 ± 6.5	0.46	25.9 ± 5.3	28.1 ± 5.5	0.16
Albumin (g/dL)	3.1 ± 0.9	2.7 ± 0.7	0.14	3.0 ± 0.8	2.6 ± 0.6	0.08
Total protein (g/dL)	5.6 ± 0.9	5.9 ± 0.9	0.30	5.8 ± 0.7	5.7 ± 0.8	0.67
Hemoglobin (g/dL)	12.3 ± 2.7	10.2 ± 2.3	0.003	11.9 ± 2.6	9.6 ± 1.9	0.002
Lymphocytes (×10^9/L)	1.3 ± 0.7	1.4 ± 0.9	0.66	1.7 ± 0.7	1.5 ± 0.7	0.55
Glucose (mg/dL)	174.7 ± 140.4	135.0 ± 80.2	0.79	138.3 ± 63.7	155.8 ± 68.5	0.24
Creatinine (mg/dL)	0.9 ± 0.66	1.4 ± 1.1	0.22	0.9 ± 0.7	1.4 ± 1.3	0.08
Urea (mg/dL)	47.3 ± 33.5	71.5 ± 48.3	0.03	43.4 ± 37.6	59.7 ± 44.2	0.17
Total cholesterol (mg/dL)	176.4 ± 100.4	134.4 ± 47.1	0.05	164.3 ± 58.5	134.4 ± 43.5	0.05
Triglycerides (mg/dL)	300.2 ± 942.4	125.7 ± 54.1	0.96	162.3 ± 111.8	149.2 ± 70.1	0.92
Hospital stay (days)	—	—		6.4 ± 3.0	8.4 ± 4.0	0.03
Depression, n (%)	6 (21.4)	11 (40.7)	0.20	—	—	

depression in individuals under or older than 65 years, respectively; nonetheless, the frequency of depression was not statistically significant between the study groups. Thus, the presence of depression exerts a minimal influence on our results.

Serum albumin is considered a biomarker of long-term malnutrition because it has a half-life of 14–20 days. In both groups, at baseline condition, the mean serum albumin was lower than 3.5 g/dL, the cutoff point for malnutrition [27,28]. The absence of significant changes in serum albumin levels is most likely related to the short hospital stay.

In addition, patients in the control group showed the lowest hemoglobin concentrations and highest urea and creatinine levels, which could be because some subjects were admitted for gastrointestinal bleeding, a condition that results in azotemia due to degradation of blood in the gastrointestinal tract [29].

Total cholesterol is an indicator of protein–calorie malnourishment particularly associated with decreased levels of albumin; however, it has been suggested that using total cholesterol as an indicator of malnutrition should be used with caution and requires further evaluation [30]. We did not find significant differences in total cholesterol concentrations between the groups in this study.

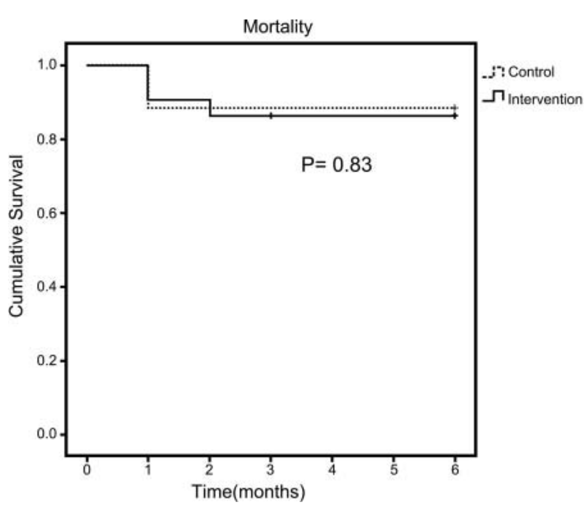

Figure 2. Kaplan-Meier curves that estimate survival during 6 months of follow-up after hospitalization in the groups that received nutritional support during and after hospitalization and individuals who received the usual nutritional support from the Hospital Nutrition Department.

Several limitations of our study deserve mention. Although there were 5 deaths during the hospital stay in the control group, the decrease in the sample size was not greater than 20%, which allowed us to maintain an appropriate statistical power. Second, given the strict inclusion–exclusion criteria, our results cannot be extrapolated to all hospitalized patients. Third, sample size was estimated based on a reduction in length of hospital stay; hence, it is possible that sample size did not have the appropriate power to measure differences in mortality. Fourth, nutrition intervention was only provided during the hospital stay but no further dietary counseling was given post-discharge, which may influence mortality. Fifth, although individuals in the intervention group showed greater adherence to diet, the total percentage of energy intake was not available. Finally, although assignment of individuals to groups in this study was not revealed to other personnel, it was not possible to blind the patients and dietitian to group allocation.

Conclusion

The results of this study suggest that, among hospitalized patients with malnutrition, nutrition intervention and dietary counseling decrease length of hospital stay but not mortality. Further studies in this field are required, testing larger populations and with longer follow-up of the nutritional intervention. In addition, screening of hospitalized patients to identify malnourishment is strongly recommended.

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