Clin Nutr Res. 2021 Jan;10(1):1-13
https://doi.org/10.7762/cnr.2021.10.1.1
pISSN 2287-3732·eISSN 2287-3740

CLINICAL NUTRITION RESEARCH

Original Article

Effect of the Timing of Nutritional Support Team Intervention on Nutritional Status on Patients Receiving Enteral Nutrition

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Received: Oct 20, 2020
Revised: Jan 9, 2021
Accepted: Jan 11, 2021

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Conflict of Interest
The authors declare that they have no competing interests.

ABSTRACT

Many hospitalized patients usually have a high risk of malnutrition, which delays the therapy process and can lead to severe complications. Despite of the potential benefits, the effects of timely intervention by nutrition support team (NST) on the nutritional status of admitted patients are not well established. This study aimed to compare the nutritional status between patients with early and delayed NST supports and to assess the effect of the timing of NST support initiation on the nutritional status of enteral nutrition patients. In a simple comparison between the two groups, the early NST intervention group had shorter hospital stays and fewer tube feeding periods than the delayed NST intervention group. The increase in the amount of energy intake from first to last NST intervention was 182.3 kcal in patients in the early NST intervention group, higher than that in patients in the delayed intervention group ($p = 0.042$). The extent of reduction in serum albumin and hemoglobin levels between the initial and last NST intervention tended to be lower in the early NST intervention group than in the delayed NST intervention group. The mean odds ratio for the patients who were severely malnourished in the early NST intervention group was 0.142 (95% confidence interval, 0.045–0.450) after adjusting for hospital stay and age. The results of this study indicate that early NST intervention can improve patients' overall nutritional status.

Keywords: Nutritional support; Support team; Malnutrition; Enteral nutrition

INTRODUCTION

Patients who are subjected to tube feeding or admitted to the intensive care unit usually have a high risk of malnutrition [1,2]. Without proper nutritional care, malnutrition leads to severe complications as well as other consequences including financial cost, increased length of stay (LOS), high risk of infection, and increased mortality [3,4]. Nutrition support (NS) is a form of the auxiliary care provided to patients to help them secure suitable energy and nutrients required to maintain body mass, prevent cellular injury, and facilitate metabolic responses to stress or treatment [1,2]. Among the available routes, enteral nutrition (EN) can be used to provide nutrients in an easily assimilated form and enable the gastrointestinal (GI) tract to be involved in the absorption process [5]. Many studies have shown that early decision to start EN with appropriate amounts of macro- and micronutrients can improve clinical outcomes in admitted patients [2,6]. A preemptive strategy to provide early NS may favorably impact patient outcomes such as disease severity, number of complications, and LOS [2]. On the other hand, artificial factors, including late initiation of EN, unsuitable delivery, improper prescription, failure to define GI dysfunction, and inappropriate infusion rate may lead to insufficient nutrition supply [7,8].

A nutrition support team (NST) is a multi-professional team composed of physicians, nurses, pharmacists, and dietitians, whose main task is to ensure and promote proper nutrition among admitted patients [9,10]. In South Korea, NST consultation was initiated in 1996 by a small group of health professionals who were interested in NS and officially acknowledged by the national health insurance system in 2014 [11]. Through interdisciplinary communication and performance, physicians and other health professionals in their local hospitals can improve the quality of NS, thereby avoiding malnutrition and reducing the medical expenses of patients [9,10]. Previous studies have demonstrated the efficacy of the NST approach on the nutritional status and clinical outcomes of hospital inpatients [10,12]. In a study involving malnourished inpatients in Switzerland, more than 75% of the patients in the NST intervention group versus 54% of them in the control group reached their energy and protein requirements and circumvented adverse clinical outcomes and death [12]. A multicenter, cluster-randomized clinical trial with patients from seven control hospitals and seven hospitals that adopted NST intervention showed a trend of decreased mortality in patients from the NST-favoring hospitals [13]. Despite of the potential benefits, the effects of timely NS on the nutritional status of admitted patients are not well established. According to the Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition guidelines, nutritional risk in a patient can be identified through nutritional screening, and EN should be initiated as early as possible in high-risk patients [2]. In a study of patients with gastrointestinal disease in the intensive care unit in South Korea, a longer transition period to EN was recognized as an independent risk factor of increased mortality [14]. Guidelines also recommend initiating EN within the first 24–48 hours of admission if patients cannot receive oral feeding and if there are no clear reasons to delay EN [2,15,16]. In a case of patients who received surgery, initiating EN within 72 hours after surgery could safely satisfy nutritional needs without complications [17,18]. Many studies have shown that NST performance and proper and timely management of inpatients significantly improve the patients' nutritional status and clinical outcomes [19,20] and also result in cost savings for hospitals [21]. Based on these findings, NST intervention for admitted patients would be expected to enhance the nutritional status of the patients. Despite of the several benefits of NST in enhancing patient outcomes as specified in the handbooks on NST preparation, the timing of NST initiation for admitted patients has not been well established, and NST's role in nutrition care has been found to vary in the hospitals in South Korea.

Hence, this study aimed to compare the nutritional status between patients with early and delayed NST supports and to assess the effect of the initiation timing of NST intervention on the nutritional status of hospitalized patients who received EN.

MATERIALS AND METHODS

Study subjects

Electronic medical records of 627 adult patients aged 19 years and older who were on EN for more than 3 days under NST consultation in both intensive care unit (ICU) and general unit at

Daegu Fatima Hospital between January 2017 and August 2018 were retrospectively reviewed. Subjects whose diet was switched to oral feeding during the tube feeding period (n = 199) were excluded. Subjects who died during the study period (n = 87), received the first NST intervention before January 2017 (n = 11), were discharged after August 30, 2018 (n = 4), and had missing biochemical parameters (n = 9) and those whose families were not supportive of tube feeding (n = 5) were excluded. In the case of subjects who were re-admitted to a hospital, the first NST intervention data were included and the second NST intervention data were excluded (n = 32). Finally, this study analyzed data from 280 subjects, consisting of 153 men and 127 women. The protocols of this study were approved by the Institutional Review Board of Daegu Fatima Hospital (IRB No. DEF18ORIO036-SRI).

NST intervention and the study group

The hospital had an NST consisting of nurses, dietitians, pharmacists, and physicians for admitted patients. When physicians consult with NST, the physician in charge or NST doctor and other NST health professionals review the patient's record and prescribe the required amount of nutrients and the time frame of EN. Besides the NST intervention, the patient's tube feeding status, including the amount and type of nutrients used in tube feeding, were recorded. Because patients who underwent surgery were included in this study, reference point of early NST was set at within 72 hours of admission based on the definition of early NS in previous studies [17,18]. In this study, patients were divided into two groups: early NST intervention group consisting of patients who underwent NST consultation within 3 days of admission and delayed NST intervention group consisting of patients who underwent NST consultation after 4 days or more after admission. The energy intake ratio (total delivered energy to total required energy), the duration of tube feeding, changes in biochemical indicators related to patient nutritional status, days of hospital stay, and prevalence of malnutrition were evaluated and compared between the two groups.

Collection of baseline data

The following baseline data were obtained: sex, age, admission department, type of discharge, type of enteral feeding formula, duration of tube feeding and ventilator care, and length of hospital stay. Total hospital stay was calculated as the change between admission and discharge dates and reported as the quartile of average days of hospital stay: less than 19 days, 19–31 days, 32–61 days, and ≥ 61 days. The tube feeding period was calculated as the duration from the start to the end of tube feeding.

Anthropometric data such as height, body weight, percent of ideal body weight (PIBW), and body mass index (BMI) were collected from the medical records. Data of the following biochemical variables were reported: albumin (Alb), total lymphocyte count (TLC), hemoglobin (Hb), C-reactive protein (CRP), blood urea nitrogen (BUN), serum creatinine (Cr), alanine aminotransferase (ALT), and aspartate aminotransferase (AST); the accuracy of measurement was routinely monitored and reported by health professionals in Daegu Fatima Hospital.

Calculation of energy and protein intake

For the analysis of patients' nutrient intake, the percentages of energy supply and daily required energy [22] were calculated using the following equations:

$$\text{(1) The Percent of Energy Supply (\%)} = \frac{\text{Energy Supply}}{\text{Required Energy}}$$

(2) Daily Required Energy (kcal) = Basal Energy Expenditure × Activity Factor × Injury Factor [22]

https://doi.org/10.7762/cnr.2021.10.1.1

The patients' daily required energy was calculated using the Harris-Benedict equation [22] which utilizes the data of basal energy expenditure, activity factor, and injury factor.

Nutritional risk screening

The nutritional status of all patients in this study was examined within 24 hours of NST initiation. Malnutrition in patients at the start and end of NST was assessed based on the International Classification of diseases, Ninth Revision, Clinical Modification (ICD-9-CM) that categorizes the degree of malnutrition by the patient's PIBW and Alb values [23,24] into the following types: moderate, mild, severe, protein, energy, and protein-energy malnutrition.

Statistical analysis

In this study, SPSS version 25.0 (SPSS Inc., Armonk, NY, USA) was used for all statistical analyses. Continuous variables including anthropometric measurements, biochemical parameters, and total LOS were reported as means and standard deviations. Categorical variables were reported as frequencies and percentages. Because we did not have enough information about the normal distribution of the study participants, a nonparametric test was performed to compare the differences in mean values or the distribution between the early NST and the delayed NST intervention groups. Comparisons were made using the Wilcoxon rank-sum test for quantitative variables and χ^2 test for qualitative variables. Multivariable logistic regression analyses were performed to investigate the risk of malnutrition in patients. Odds ratios and the corresponding 95% confidence intervals were estimated by setting the delayed intervention group as the reference. The significance of the data was set at $p < 0.05$.

RESULTS

General characteristics of study patients

The general characteristics of the study patients are described in **Table 1**. There was no difference in the sex and age distribution between the early NST and delayed NST intervention groups. Further, 30.1% and 31.8% of the patients received Harmonilan, commercial nutrition formulas in the early and delayed NST intervention groups, respectively ($p = 0.795$). The number of NST interventions, discharge pattern, and proportion of NST doctors who made the NST referral for patients were not different between the two groups. Patients in both early and delayed NST intervention groups were admitted mostly in neurosurgery, pulmonology and infectious disease departments. The proportion of patients per each admitted department in the early and delayed NST groups were 51.2% and 45.2% for neurosurgery department, 22.9% and 30.9% for pulmonology department, and 8.3% and 12.2% for infectious disease department, respectively. Most patients in both groups received EN through the nasogastric tube. Considering the time of hospital admission or first NST intervention, the number of patients with malnutrition tended to be higher in the early NST group than in the delayed NST group while the number of patients with moderate or protein malnutrition was lower in the early NST group than in the latter.

Anthropometric measurements and hospital stay at admission

At the time of hospital admission, the patients in the early NST intervention group tended to be older on average ($p = 0.063$) and had fewer tube feeding periods ($p < 0.001$) than the patients in the delayed NST intervention group (**Table 2**). Overall, the early NST intervention group had a significantly shorter hospital stay than the delayed NST group ($p < 0.001$). The

https://doi.org/10.7762/cnr.2021.10.1.1

Table 1. General characteristics of all patients according to time of NST referral

Variables	Early NST intervention (n = 123)	Delayed NTS intervention (n = 157)	p value
Sex			0.717*
Male	69 (56.1)	84 (53.5)	
Female	54 (43.9)	73 (46.5)	
Harmonilan use‡			0.795
Yes	37 (30.1)	50 (31.8)	
No	86 (69.9)	107 (68.2)	
Age (yr)			0.196†
20–29	0 (0.0)	2 (1.3)	
30–39	0 (0.0)	2 (1.3)	
40–49	7 (5.7)	8 (5.1)	
50–59	13 (10.6)	25 (15.9)	
60–69	24 (19.5)	30 (19.1)	
70–79	38 (30.9)	56 (35.7)	
≥ 80	41 (33.3)	34 (21.7)	
No. of NST care			0.469
Once	62 (50.4)	87 (55.4)	
Twice or more	61 (49.6)	70 (44.6)	
Person of making a NST referral			0.067
NST doctor	43 (35.0)	73 (46.5)	
Physician in charge	80 (65.0)	84 (53.5)	
Discharge pattern			0.581
Transfer to local clinic	94 (76.4)	123 (78.3)	
Home	23 (18.7)	30 (19.1)	
The others§	6 (4.9)	4 (2.5)	
Admission category			0.003
Infectious disease	15 (12.2)	13 (8.3)	
Rheumatology	1 (0.8)	3 (1.9)	
Gastroenterology	2 (1.6)	17 (10.8)	
Cardiology	0 (0.0)	4 (2.5)	
Neurology	0 (0.0)	4 (2.5)	
Neurosurgery	63 (51.2)	71 (45.2)	
Nephrology	2 (1.6)	1 (0.6)	
Surgery	0 (0.0)	2 (1.3)	
Rehabilitation medicine	2 (1.6)	2 (1.3)	
Hemato-oncology	0 (0.0)	1 (0.6)	
Pulmonology	38 (30.9)	36 (22.9)	
Thoracic surgery	0 (0.0)	3 (1.9)	
Nutritional status at first NST referral			0.000
No malnutrition	46 (37.4)	31 (19.7)	
Mild malnutrition	34 (27.6)	33 (21.0)	
Moderate malnutrition	18 (14.6)	26 (16.6)	
Protein malnutrition	20 (16.3)	67 (42.7)	
Energy malnutrition	0 (0.0)	0 (0.0)	
Severe protein energy malnutrition	5 (4.1)	0 (0.0)	
EN feeding route of access			0.204
Nasogastric tube	123 (100.0)	153 (97.5)	
Nasojejunal tube	0 (0.0)	1 (0.6)	
Percutaneous endoscopic gastrostomy	0 (0.0)	3 (1.6)	

Categorical values are presented as numbers of frequency with percent ratio.
NST, nutrition support team; EN, enteral nutrition.
*The χ^2 test is used to verify whether the observed frequency is significantly different from the expected frequency; †Fisher's exact test for categorical variables when the numbers of frequency per each cell are less than 5; ‡Harmonilan use "no" indicate using regular nutrition formula that dietitian team manually prepare; §Sanatorium, nursing center, welfare foundation, silver town.

mean BMIs of patients in the early and delayed NST intervention groups were 21.7 ± 3.9 and 22.7 ± 4.2, respectively, showing a significant difference. Body weight and PIBW were not significantly different between the groups (**Table 2**).

https://doi.org/10.7762/cnr.2021.10.1.1

Table 2. Anthropometric measurements and hospital stay for all patients at admission

Variables	Early NST intervention (n = 123)	Delayed NTS intervention (n = 157)	p value
Average age (yr)	72.4 ± 12.2	69.2 ± 13.6	0.063*
Anthropometric measurement			
Height (cm)	161.6 ± 8.9	162.3 ± 10.1	0.406
Weight (kg)	57.1 ± 13.0	59.9 ± 12.4	0.089
PIBW (%)†	101.1 ± 17.8	105.2 ± 19.8	0.094
BMI (kg/m²)	21.7 ± 3.9	22.7 ± 4.2	0.049
Length of hospital stay (day)	29.7 ± 24.4	55.9 ± 42.1	< 0.0001
Average length of hospital stay (day)			0.015
≤ 18	42 (34.1)	30 (19.1)	
19–31	30 (24.4)	38 (24.2)	
32–61	29 (23.6)	42 (26.8)	
≥ 62	22 (17.9)	47 (29.9)	
Treatment period			
Length of tube feeding (day)	25.8 ± 24.5	34.6 ± 38.1	0.041

Data are presented as mean ± standard deviation.
NST, nutrition support team; PIBW, percent of ideal body weight; BMI, body mass index.
*The Wilcoxon rank-sum test, a nonparametric statistical test, was used to compare the difference of mean values between 2 groups; †PIBW = Real Weight ÷ Standard Weight.

Change in nutrient intake and biochemical parameters of patients according to time of NST referral

Table 3 shows the nutrition intake and biochemical parameters of patients according to the time of NST referral during hospital stay. The energy intake of patients in the early and delayed NST intervention groups was 1,491.1 ± 352.9 kcal and 1,459.0 ± 323.3 kcal, respectively, and the difference was not significant. However, the percentage of energy supply of patients in the early NST intervention group was 90.2% ± 20.2%, which was significantly higher than that in the delayed NST group, i.e., 85.1% ± 16.6%. The mean values of the biochemical parameters and distribution of nutritional status were not significantly different between the groups. Additionally, ratios of patients who met 100% of energy requirement at the time of discharge in early and delayed NST groups were 40.7% (n = 50) and 24.2% (n = 38), respectively, and those numbers in early NST group was significantly higher than those in delayed NST group (**Supplementary Table 1**).

The changes in energy intake and biochemical parameters during hospital stay according to the time of NST referral were analyzed. The mean increase in the amount of patient's energy intake and energy supply ratio from the first to last NST interventions was 182.3 and 112.6 kcal in the early and delayed NST intervention groups, respectively. The degree of change in energy intake in the early NST intervention group was significantly higher than that in the delayed intervention group ($p = 0.040$). The values of all biochemical parameters decreased after NST intervention in both groups. Of these biochemical parameters, the extent of reduction in Alb and Hb levels between the initial and last NST interventions tended to be lower in the early NST intervention group than in the delayed NST intervention group.

Estimation of risk of moderate malnutrition during NST intervention in patients

At discharge, the proportion of patients without malnutrition tended to decrease in both early and delayed NST groups. However, the prevalence rate of each type of malnutrition between early and delayed NST was not significantly different (**Table 4**).

Since EN alone cannot satisfy a patients' metabolic or physical needs [25], patients tend to be malnourished at the end of tube feeding. Only simple comparison of prevalence of all type of

Table 3. Change in indicators of nutritional status of all patients during hospital stay according to time of NST referral

Nutrient intake and biochemical indicators	Early NST intervention (n = 123)	Delayed NTS intervention (n = 157)	p value
At first NST care			
Energy intake (kcal)	1,308.8 ± 272.5	1,346.4 ± 228.6	0.331*
Protein intake (g)	55.4 ± 15.1	58.6 ± 14.5	0.101
Alb (g/dL)	3.6 ± 0.9	3.6 ± 0.8	0.487
AST (U/L)	45.9 ± 121.0	47.4 ± 87.0	0.790
ALT (U/L)	33.5 ± 79.3	27.6 ± 37.3	0.356
BUN (mg/dL)	22.7 ± 24.5	20.3 ± 16.1	0.464
Cr (mg/dL)	1.2 ± 1.9	1.1 ± 1.2	0.790
Hb (g/dL)	11.9 ± 2.2	11.9 ± 2.3	0.648
TLC (cells/mm^3)	1,592.8 ± 1,059.9	1,873.2 ± 1,235.2	0.063
CRP (mg/dL)	5.5 ± 8.0	4.8 ± 7.4	0.735
At discharge			
Energy intake (kcal)	1,491.1 ± 352.9	1,459.0 ± 323.3	0.522*
Percent of energy supply (%)†	90.2 ± 20.2	85.1 ± 16.6	0.011
Alb (g/dL)	3.3 ± 0.7	3.2 ± 0.7	0.272
AST (U/L)	23.8 ± 10.7	31.6 ± 47.5	0.517
ALT (U/L)	21.3 ± 14.0	25.6 ± 41.7	0.755
BUN (U/L)	17.6 ± 16.4	14.9 ± 9.6	0.278
Cr (mg/dL)	0.9 ± 1.2	0.7 ± 0.5	0.441
Hb (g/dL)	11.0 ± 1.6	10.7 ± 1.6	0.097
TLC (mm^3)	1,502.3 ± 705.4	1,632.8 ± 684.3	0.060
CRP(mg/dL)	2.3 ± 3.6	2.5 ± 4.2	0.910
Amount of change during hospital stay			
Energy intake (kcal)†	182.3 ± 310.1	112.6 ± 282.5	0.040
Alb (g/dL)	−0.3 ± 0.9	−0.5 ± 0.8	0.066
AST (U/L)	−22.1 ± 121.5	−15.8 ± 97.4	0.596
ALT (U/L)	−12.2 ± 80.9	−1.9 ± 52.8	0.724
BUN (U/L)	−5.1 ± 19.1	−5.4 ± 15.3	0.774
Cr (mg/dL)	−0.3 ± 1.0	−0.3 ± 0.9	0.360
Hb (g/dL)	−0.8 ± 1.9	−1.2 ± 2.3	0.066
TLC (mm^3)	−90.5 ± 1,139.6	−240.5 ± 1,214.7	0.176
CRP (mg/dL)	−3.2 ± 8.6	−2.3 ± 8.1	0.460

Data are presented as mean ± standard deviation.
NST, nutrition support team; Alb, albumin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; Hb, hemoglobin; TLC, total lymphocyte count; CRP, C-reactive protein.
*The Wilcoxon rank-sum test, a nonparametric statistical test, was used to compare the difference of mean values between 2 groups; †Energy Received (kcal/day): Amount of energy supplied upon discharge − Energy supply during first nutrition management by NST.

Table 4. Distribution of nutritional status of all patients at discharge according to time of NST referral

ICD-9-CM based nutrition screening tool	Early NST intervention (n = 123)	Delayed NTS intervention (n = 157)	p value
No malnutrition	37 (30.1)	41 (26.1)	0.170*
Mild malnutrition	41 (33.3)	47 (29.9)	
Moderate malnutrition	18 (14.6)	17 (10.8)	
Protein malnutrition	24 (19.5)	50 (31.8)	
Energy malnutrition	0 (0.0)	1 (0.6)	
Severe protein energy malnutrition	3 (2.4)	1 (0.6)	

Categorical values are presented as numbers of frequency with percent ratio.
NST, nutrition support team.
*Fisher's exact test for categorical variables when the frequency per each cell are less than 5.

malnutrition could not reflect the effect of timing of NST. Hence, we further examined the risk of moderate malnutrition during NST intervention by re-categorizing the patients' malnutrition status. The prevalence rates of moderate or severe type of malnutrition (protein, energy, and severe protein-energy malnutrition) in the early and delayed NST intervention groups were 43.9% and 56.1%, respectively (**Table 5**). The odds ratio of malnutrition in the early NST intervention group was 0.142 (95% CI, 0.045–0.450), after adjusting for hospital stay, age, and gender.

https://doi.org/10.7762/cnr.2021.10.1.1

Table 5. Risk of moderate malnutrition or severe type of malnutrition during NST intervention in all patients

Variables	Values	OR	95% CI	p value
Delayed NST intervention	157 (56.1)	1	-	-
Early NST intervention	123 (43.9)	0.142*	0.045–0.450	0.001

Categorical values are presented as numbers of frequency with percent ratio.
NST, nutrition support team; OR, odds ratio; CI, confidence interval.
*Logistic regression analysis was performed with adjusting age and hospital stay and gender.

DISCUSSION

Many studies have shown that NST enhances proper and timely provision of nutrition support to patients and significantly improves their nutritional status and clinical outcomes [19,20]. Based on previous findings, this study further investigated whether early NST initiation positively affects patients' outcomes and nutritional status.

In this study, clinical outcomes during hospital stay improved in patients who received early NST intervention as compared to patients who received delayed NST intervention. Particularly, the early NST intervention group had significantly shorter hospital stays and treatment periods than the delayed NST group. Although no report has indicated the effect of the timing of NST intervention on clinical outcome, receiving nutrition support in proper time frame has shown several benefits in the healing process [6,26,27]. A systematic review [27] that evaluated ten randomized controlled trials (RCTs) including 1,424 patients with severe acute pancreatitis showed that as compared with late EN or parenteral nutrition (PN), early EN (starting within 48 hours after admission) significantly reduced the rates of mortality, multi-organ failure, surgical interventions, systemic infections, local septic complications, and gastrointestinal symptoms. The result was similar to that of a study conducted in a hospital in South Korea; the LOS in the early EN group (EN was initiated within 48 hours after admission) was 23.3 days and that in the delayed EN group (EN was initiated after 48 hours of admission) was 36.7 days [6]. These results show that early EN may have improved the nutritional status of the patients. A proper amount of nutrition supply that meets individual needs can improve nutritional consequences and, consequently, enhance the efficacy of treatments and lead to a decrease in the LOS [6,26].

The clinical outcomes of patients receiving NS are also related to the patient's nutritional status and biochemical metabolism [28,29]. This study showed that body weight, PIBW, energy and protein intakes, and biochemical parameters measured at the time of admission were not significantly different between the two groups. In addition, the mean values of the biochemical parameters and distribution of nutritional status of the study patients at the time of discharge were also not significantly different between the groups, indicating that there was no carry-over effect of the patient's initial nutritional status on the outcome at discharge. However, the change in energy supply amount before and after the NST interventions, the post-hoc indicator of nutrition intake through EN in the early NST group was significantly higher than that in the delayed NST group (182.3 vs. 112.6 kcal). In addition, the ratio of energy supply to the required energy in the early NST intervention group was significantly higher than that in the delayed NST intervention group. Although the recommended energy intake (≥ 75% of required energy) is prescribed by several authorities such as ASPEN, the specific amount of energy support is still unclear [30] and a delicate balance between over- and under-feeding seems to be necessary. Nevertheless, it is relatively agreed that supplying too much energy or energy deficient is associated with disease aggravation and delayed treatment [29,31]. For example, ICU patients who receive < 25% or > 25% of their

https://doi.org/10.7762/cnr.2021.10.1.1

recommended energy intake (kcal) are usually at risk of acquiring infections, increased mortality [31], increased duration of medication or antibiotic use, complications, and adverse outcomes [29]. Sufficient supply of energy through EN helps increase the total lymphocyte count that is related to improved immune response [32]. In a multicenter randomized study involving malnourished inpatients in Switzerland, 79% of the patients in the NST intervention group reached their energy and protein requirements (76% within 3 days), while only 54% of the patients in the control group reached their energy requirements. In the same study, the functional status of patients and clinical outcomes including mortality rate had significantly improved in the NST intervention group [12].

Previous studies also showed that increased energy intake in EN patients was associated with improvements in biochemical parameters [33-35]. In addition, early fulfillment of the energy requirements led to positive outcomes. In a study on the effect of NST intervention on Korean patients, the NST-mediated group met 75% of their energy requirement earlier than the non-NST group (3 vs. 9 days after the admission). In the same study, reduction in the Alb level of the NST-mediated group (0.24 g/dL) was lower than that in the non-NST-mediated group (0.5 g/dL) during hospitalization [35]. In this study, the values of all biochemical parameters decreased after NST intervention in both the early and delayed NST intervention groups. In particular, the extent of reduction in serum Alb and Hb levels between the initial and last NST interventions tended to be lower in the early NST intervention group than in the delayed NST intervention group. Although biochemical markers are usually not changed by EN and tend to be affected by the patients' disease status or other confounding factors [36], serum Alb is a relatively sensitive marker for assessing dietary intake and protein deficiency [34,37] and low serum Alb level is associated with anemia and low Hb levels in EN patients [38].

Since EN alone cannot provide sufficient amount of nutrition to meet patients' metabolic or physical need in the long term [25,38], patients tend to be malnourished at the end of tube feeding, as evidenced by the energy deficit [25] and decrease in biochemical parameters such as Alb and Hb levels [38]. The higher energy supply and smaller reduction in Alb and Hb levels in the early NST group than in the delayed NST group indicated that early NST prevented tube feeding-induced nutrition deficit; this may be the reason why both groups had more patients with severe malnutrition at the end of the NST intervention than at the beginning. However, the rates of moderate malnutrition and severe types of malnutrition were higher in the early NST intervention group than in the delayed NST intervention group, and the risk of malnutrition in the early NST intervention group was less than one quarter of that in the delayed NST intervention group, regardless of adjustments in the multivariate analysis. Taken together, the results of this study indicate that early NST initiation attenuated malnutrition in patients on EN and also led to increased energy supply and improvements in the levels of biochemical markers of nutritional status.

Our study has some limitations. The data were retrospectively obtained, so the causal effect of NST on nutritional status could not be identified and the confounding factors were not properly controlled for. For example, sample size was relatively small and the patients, included in the analysis, had diverse diseases, which may have affected their nutritional status. Several confounding factors could have mediated the difference observed in early NST and delayed NST groups. EN-fed patients usually experience critical illness, and specific responses to acute illness or injury are related to specific nutritional needs and affect the nutritional status of the patients [28,39]. For instance, ICU patients with a high BMI could have diabetes more frequently than patients with a low BMI. Uncontrolled blood glucose or glucose variability is associated with an increased risk of low nutritional status and high mortality [28]. In addition, when the age of patients is taken into account when designing nutritional strategies in the ICU, younger patients experience an increased delay in nutrition support [39]. However, none of these factors independently affected the decreased odds ratio of malnutrition in the early NST group as per the results of the multivariate analysis (data was not shown). Studies suggest that protein intake could be another critical factor for optimal nutrition support [2,30]. In this study, protein supply was recorded only at NST initiation and we could not measure muscle-related parameters such as triceps skinfold thickness (TSF). It is possible that protein intake or ratio of protein supply affected the changes in the patients' biochemical parameters or nutritional status including skeletal muscle contents and study might have missed those changes. Nevertheless, we found that the early NST group had a better protein status than the delayed group given the attenuated decrease in serum Alb levels. In addition, energy deficiency in patients on EN is related to underfeeding due to co-morbidities such as stomach residue, diarrhea, and vomiting [2]. These co-symptoms or the route of EN should be identified from the medical records of patients and assessment of the patient's condition should be considered in future studies; prospective studies with improved designs to determine the effect of early NST in a homogeneous patient pool are needed.

To the best of our knowledge, this is the first study to examine the effect of the timing of NST intervention on patients on EN. Shorter hospital stays and treatment period, higher fulfillment of energy requirement, and better nutritional status were observed in the early NST intervention group than in the delayed intervention group. According to a systemic review and the 2008 survey by ASPEN [40,41], there is a gradual decrease in the adoption of NST intervention in hospitals, possibly because many hospitals and healthcare organization are trying to find ways to reduce their expenses. Since 2014, NST consultation has been subjected to a medical charge reimbursement program under the national health insurance system in South Korea [11]. Although quantitative and qualitative progress has been made in the field of NST, given the lack of recognition of the need for NST interventions and the complexities in the NST handbook, it has not been adopted in many Korean hospitals, especially those located in local districts [6,11]. The impact of the timing of NST intervention on admitted patients with EN outlined in this study may contribute to improved NST guidelines and shed light on the role and importance of NST interventions.

CONCLUSION

In this study, clinical outcomes related to nutritional status during hospital stay were improved in patients in the early NST group compared to those in patients in the delayed NST group. The energy supply was higher and the extent of reduction in serum Alb and Hb was smaller in early NST group than in delayed NST group. The results were concurrent with lower rates of moderate or severe type of malnutrition in early NST group than in the delayed NST group. The results of this study indicate that early NST attenuated nutrition deficit in patients with EN and may improve patients' overall nutritional status. The results obtained here need to be further examined in a study with a large cohort of homogenous patient pool to find those that are relevant to NST guideline improvement.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

Ratio of patients who met energy requirement at discharge according to time of NST referral

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