Original Communication

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Clinical Impact of Prescribed Doses of Nutrients for Patients Exclusively Receiving Parenteral Nutrition in Japanese Hospitals: A Retrospective Cohort Study

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Abstract

Background: In patients receiving parenteral nutrition (PN), the association between nutrition achievement in accordance with nutrition guidelines and outcomes remains unclear. Our purpose was to assess the association between nutrition achievement and clinical outcomes, including in-hospital mortality, activity of daily living (ADL), and readmission. *Methods:* In this retrospective cohort study, data were extracted from an inpatient medical-claims database at 380 acute care hospitals. This study included patients who underwent central venous catheter insertion between January 2009 and December 2018. Patients were classified into 3 groups: (1) target-not-achieved; (2) target-partially-achieved; and (3) target-achieved. The target doses of energy, amino acids, and lipid were defined as ≥ 20 kcal/kg/day, ≥ 1.0 g/kg/day, and ≥ 2.5 g/day, respectively. To examine the effect of nutrition achievement on outcomes, a multivariable logistic regression analysis was performed. *Results:* A total of 54,687 patients were included; of these, 21,383 patients were in the target-not-achieved group, 29,610 patients were in the target-partially-achieved group, and 3694 patients were in the target-achieved group. The adjusted odds ratio (OR) (95% CI) for in-hospital mortality was 0.69 (0.66–0.72) in the target-partially-achieved group and 0.47 (0.43–0.52) in the target-achieved group with reference to the target-not-achieved group. The adjusted ORs for deteriorated ADL was 0.93 (0.85–1.01) in the target-partially-achieved group and 0.77 (0.65–0.92) in the target-achieved group with reference to the target-not-achieved group. Readmission was not associated with nutrition achievement. *Conclusion:* In-hospital mortality was lower and deteriorated ADL was suppressed in patients whose PN management was in accordance with the nutrition guidelines. (*JPEN J Parenter Enteral Nutr.* 2021;45:1514–1522)

Clinical Relevancy Statement

Malnutrition is common among patients receiving parenteral nutrition (PN). International guidelines recommend PN for patients who are unable to oral or enteral nutrition for prolonged periods. Because little has been known on the impact of nutrition achievement on clinical outcomes in patients receiving PN, this study assessed the association between nutrition achievement in prescribed mean daily doses of energy, amino acids, and lipid between days 4 and 10 after central venous catheter insertion and clinical outcomes among inpatients receiving PN, using a large inpatient medical-claims database. The risks for in-hospital mortality and deteriorated activity for daily living were lower among patients who achieved the target level of all nutrients, compared with those who partially achieved or did not achieve it. PN management in accordance with nutrition guidelines may be a key factor in achieving better clinical outcomes for inpatients receiving PN.

Introduction

Malnutrition is prevalent in hospitalized patients, with a range of 20%–50%.[1] Malnutrition increases the risk of complications,[2–4] prolonged hospital stay,[2–7] readmission,[2,3,6] and mortality[2–4,6,7] in hospitalized patients. Given these poor prognoses, malnutrition is a major public health problem.

The international guidelines recommend parenteral nutrition (PN) for patients when there is intolerance to oral nutrition or enteral nutrition, when they are inadequate, or when enteral nutrition is contraindicated[8–10]; PN should be considered in cases being unable to receive oral or enteral nutrition for prolonged periods. The guidelines in Japan, Europe, and the United States recommend approximately 20–30 kcal/kg/day of energy, 0.8–1.2 g/kg/day of protein,[8,11,12] and 15%–30% of nonprotein energy for lipid,[11] for adult patients receiving PN. However, malnutrition has been reported to be common in patients receiving PN.[13] Our previous study[14] and other studies[15–18] showed that the majority of patients receiving PN did not receive adequate nutrition intake.

A randomized controlled trial showed that an individualized nutrition support prescription to reach energy and protein goals improved clinical outcomes among medical inpatients at high risk of malnutrition.[19] Another observational study showed that critically ill patients who achieved both energy and protein targets had lower mortality than those who reached neither target.[20] However, the impact of nutrition achievement on clinical outcomes has not been assessed in patients receiving PN. Therefore, the objective of this study was to assess the association between nutrition achievement and clinical outcomes, including in-hospital mortality, activity of daily living (ADL), and readmission in hospitalized patients receiving PN, using a Japanese medical-claims database.

Methods

Data Source

Data for this retrospective cohort study were extracted from an inpatient-claims database provided by Medical Data Vision Co, Ltd (MDV, Tokyo, Japan). The database includes deidentified patient-level information, including age, sex, discharge status, and medical claims, including main diagnoses, preexisting comorbidities, and postadmission complications (recorded according to the *International Classification of Diseases, Tenth Revision* [ICD-10] codes), date-stamped procedures, and date-stamped medications. Type of admission (elective and emergency) is also recorded. As of August 2019, the database contained both outpatient and inpatient data of approximately 27 million patients treated at 380 acute care hospitals, which covered approximately 22% of all Japanese acute care hospitals where

diagnosis procedure combination/per diem payment system (a case-mix inpatient classification system for acute care hospitals in Japan) is used.

Patients

This study included hospitalized patients who underwent central venous catheter (CVC) insertion between January 2009 and December 2018 and who were aged ≥18 years on the day of CVC insertion (day 1). The following patients were excluded from the study: patients whose data on body weight were missing or <10 kg; those who were discharged, had oral dietary intake, or had enteral nutrition on or before day 10; or those whose mean energy prescription was <5 kcal/kg/day or >60 kcal/kg/day, mean amino acid prescription was <0.1 g/kg/day or >3 g/kg/day, or mean lipid prescription was >3 g/kg/day between days 4 and 10. These exclusion criteria were determined to eliminate data of pediatric patients, data entry errors, clinically unlikely data, and data of patients who had a CVC insertion but were not receiving PN (eg, for anticancer drug administration purposes and for water and electrolyte administration at the end of life) from a clinical perspective.

Exposure

Prescription records of energy, amino acids, and lipid were identified, and mean daily doses of energy, amino acids, and lipid prescribed between days 4 and 10 were calculated based on the prescription records under the assumption that nutrient doses reach 100% of the requirement on day 4 after a gradual increment from day 1. The target daily doses of energy, amino acids, and lipid were defined as ≥20 kcal/kg, ≥1.0 g/kg, and ≥2.5 g, respectively. The target doses of energy and amino acids were defined according to the nutrition guidelines for geriatric patients,[8,9] and that of lipid was defined in reference to the Japanese nutrition guidelines, determined from the perspectives for the prevention of essential fatty acid deficiency.[8] It should be noted that the lipid emulsions approved in Japan are only soybean oil–based, approximately 60% of which consist of linoleic and α-linolenic acids. Patients were classified into the following 3 groups according to their nutrition target achievement on the basis of their prescription records: (1) target-not-achieved group, including patients who did not meet any of the target doses of energy, amino acids, and lipid; (2) target-partially-achieved group, including those who met 1 or 2 of the target doses of energy, amino acids, and lipid; and (3) target-achieved group, including those who met all the target dose of energy, amino acids, and lipid.

For the calculation of energy and lipid intake, propofol (for general anesthetic and sedative agents, containing lipid emulsion as solvent) and other solutions used for medicine preparation (ie, carbohydrate solutions and carbohydrate-electrolyte solutions) were included in addition to PN products.

In this study, we did not focus on intentional hypocaloric feedings in obese patients, because obesity (body mass index [BMI] > 30 among Japanese) was not prevalent (1.9%, 1,053 of 54,687) and underfeeding was notable in our previous study.[14]

Outcomes

The primary end point was in-hospital mortality. The secondary end points were deteriorated ADL and 30-day readmission after discharge. Deteriorated ADL was defined as a Barthel Index score[21] lower at discharge than at admission.

Other Variables

The following data were extracted for patient characteristics at admission: age, sex, height, body weight, treatment year, number of beds at hospitalized institutions (hospital beds), main disease, comorbidities, ADL (Barthel Index),[21] level of consciousness (Japan Coma Scale [JCS]),[22] and type of admission (elective or emergency). Data on type of medical treatments, including surgery, blood transfusion, intensive care unit admission, respirator use, and blood purification therapy, received between the day of admission and day 3 were also extracted.

Age categories were 18–59 years, 60–69 years, 70–79 years, 80–89 years, and ≥90 years. BMI was calculated based on height and body weight data, and categories were <16.0 kg/m², ≥16.0 to <18.5 kg/m², ≥18.5 to <25.0 kg/m², ≥25.0 to <30.0 kg/m², and ≥30.0 kg/m² based on the World Health Organization classification. Number of bed categories were <200, ≥200 to <500, and ≥500. The main disease was identified by the following ICD-10 codes: digestive system malignancy (C15-C26), hematological malignancy (C81-C96), other malignancies (C00-C14, C30-C80, C97), sepsis (A40-A41), coagulopathy (D65-D69), cerebrovascular diseases (I60-I69), cardiovascular diseases (I00-59, I70-I99), respiratory diseases (J00-J99), digestive system diseases (K00-K93), kidney and urinary tract diseases (N00-N99), and others. Preexisting comorbidities were summarized by the Charlson Comorbidity Index, using algorithms developed by Quan,[23] and categorized as 0, 1–2, and ≥3. The Barthel Index categories were 0, 5–60, 65–95, and 100. For the level of consciousness, the JCS indicates the following values: 0, alert; 1-digit code, not fully alert but awake without any stimuli; 2-digit code, arousable with stimulation; 3-digit code, unarousable.[22]

Ethical Statements

Ethical approval was obtained from the clinical ethics committee of Jichi Medical University (No. Clinical 19–044). This study was registered at the University Hospital Medical Information Network Center (UMIN 000038054).

Because deidentified data were used in this study, obtaining consent was not required. This study was conducted in accordance with the Declaration of Helsinki and the Ethical Guidelines for Medical and Health Research Involving Human Subjects.

Statistical Analysis

Patient characteristics were descriptively summarized. For the changes in daily dose of nutrients over time, median daily doses of energy, amino acids, and lipid prescribed between days 1 and 10 were calculated. The median duration of PN from CVC insertion to discharge was calculated in days. The clinical outcomes were descriptively summarized and compared among the 3 groups using the χ^2 test.

To examine the effect of nutrition target achievement on clinical outcomes, multivariable logistic regression analysis adjusting for patient characteristics (factors included in Table 1) as confounding factors was performed, and odds ratios (ORs) and the corresponding 95% CIs were estimated. The survival time between day 1 and death in the hospital, according to the nutrition target achievement groups, was estimated using the Kaplan-Meier survival curve, and comparison among the nutrition target achievement groups was made using the log-rank test. The hazard ratio (HR) for in-hospital mortality in the target-partially-achieved group and target-achieved group against the target-not-achieved group was calculated, adjusting for patient characteristics (factors included in Table 1), using a Cox proportional hazard model. Data for discharge alive and continued hospitalization ≥90 days after day 1 were censored.

Additionally, given that sufficient energy and protein intakes improved clinical outcomes as reported earlier,[19,20] ORs and the corresponding 95% CIs for in-hospital mortality were calculated among patients who reached the target dose of both energy and amino acid in reference to those who did not reach the target of either nutrient when patient characteristics and the achievement status of lipid dose were adjusted.

All statistical analyses were performed using SAS release 9.4 (SAS Institute, Inc, Cary, NC, USA). All statistical tests were 2-sided with a significance level of $P < 0.05$.

Results

Patients

The patient-selection flowchart is shown in Figure 1. A total of 381,420 hospitalized patients underwent CVC insertion during the study period. After excluding patients who met any of the exclusion criteria, 54,687 were included in this study. Of these, 21,383 patients were in the target-not-achieved group (39.1%), 29,610 patients were in the target-partially-achieved group (54.1%), and 3694 patients were in the target-achieved group (6.8%).

Table 1. Patient Characteristics in Hospitalized Patients With Parenteral Nutrition at Admission and Medical Treatments Between the Day of Admission and Day 3[*] According to Nutrition Target Achievement.

Characteristics	Target-not-achieved group[†] (n = 21,383)		Target-partially-achieved group[†] (n = 29,610)		Target-achieved group[†] (n = 3694)	
	n	(%)	n	(%)	n	(%)
Age (years)						
18–59	2148	(10.0)	4015	(13.6)	735	(19.9)
60–69	3201	(15.0)	5391	(18.2)	784	(21.2)
70–79	5718	(26.7)	8168	(27.6)	1003	(27.2)
80–89	7486	(35.0)	9166	(31.0)	938	(25.4)
≥90	2830	(13.2)	2870	(9.7)	234	(6.3)
Sex						
Male	13,212	(61.8)	17,787	(60.1)	1988	(53.8)
Female	8171	(38.2)	11,823	(39.9)	1706	(46.2)
BMI (kg/m^2)						
<16.0	1548	(7.2)	4027	(13.6)	832	(22.5)
≥16.0 to <18.5	3335	(15.6)	6288	(21.2)	1107	(30.0)
≥18.5 to <25.0	12,016	(56.2)	15,505	(52.4)	1596	(43.2)
≥25.0 to <30.0	3124	(14.6)	2604	(8.8)	76	(2.1)
≥30.0	662	(3.1)	391	(1.3)	0	(0.0)
Unknown	698	(3.3)	795	(2.7)	83	(2.2)
Treatment year						
2009	5	(0.0)	8	(0.0)	0	(0.0)
2010	434	(2.0)	762	(2.6)	121	(3.3)
2011	893	(4.2)	1542	(5.2)	214	(5.8)
2012	1213	(5.7)	1876	(6.3)	223	(6.0)
2013	1849	(8.6)	2802	(9.5)	358	(9.7)
2014	2742	(12.8)	3864	(13.0)	494	(13.4)
2015	3138	(14.7)	4458	(15.1)	564	(15.3)
2016	3558	(16.6)	4794	(16.2)	617	(16.7)
2017	3952	(18.5)	4932	(16.7)	591	(16.0)
2018	3599	(16.8)	4572	(15.4)	512	(13.9)
Number of hospital beds						
<200	1830	(8.6)	2207	(7.5)	179	(4.8)
≥200 to <500	13,597	(63.6)	17,877	(60.4)	2014	(54.5)
≥500	5956	(27.9)	9526	(32.2)	1501	(40.6)
Main disease						
Digestive system malignancy	5058	(23.7)	9235	(31.2)	1468	(39.7)
Hematological malignancy	489	(2.3)	472	(1.6)	31	(0.8)
Other malignancies	1406	(6.6)	1514	(5.1)	145	(3.9)
Sepsis	671	(3.1)	822	(2.8)	57	(1.5)
Coagulopathy	376	(1.8)	445	(1.5)	37	(1.0)
Cerebrovascular diseases	1920	(9.0)	1418	(4.8)	91	(2.5)
Cardiovascular diseases	1295	(6.1)	1407	(4.8)	60	(1.6)
Respiratory diseases	4111	(19.2)	4789	(16.2)	427	(11.6)
Digestive system diseases	3508	(16.4)	6253	(21.1)	1047	(28.3)
Kidney and urinary tract diseases	492	(2.3)	652	(2.2)	41	(1.1)
Others	2057	(9.6)	2603	(8.8)	290	(7.9)
Charlson Comorbidity Index score						
0	7256	(33.9)	9896	(33.4)	1311	(35.5)
1–2	9208	(43.1)	13,674	(46.2)	1741	(47.1)
≥3	4919	(23.0)	6040	(20.4)	642	(17.4)
Barthel Index score						
100	5398	(25.2)	10,806	(36.5)	1738	(47.0)
65–95	1338	(6.3)	2160	(7.3)	348	(9.4)
5–60	3561	(16.7)	4312	(14.6)	435	(11.8)
0	8289	(38.8)	8731	(29.5)	757	(20.5)
Unknown	2797	(13.1)	3601	(12.2)	416	(11.3)
Japan Coma Scale score						
0	13,217	(61.8)	21,349	(72.1)	3025	(81.9)
1–3	3835	(17.9)	4103	(13.9)	374	(10.1)
10–30	1760	(8.2)	1831	(6.2)	124	(3.4)
100–300	1566	(7.3)	1361	(4.6)	93	(2.5)
Unknown	1005	(4.7)	966	(3.3)	78	(2.1)

(continued)

Table 1. (continued)

Characteristics	Target-not-achieved group[†] (n = 21,383)		Target-partially-achieved group[*][†] (n = 29,610)		Target-achieved group[†] (n = 3694)	
	n	(%)	n	(%)	n	(%)
Type of admission						
Elective	9012	(42.1)	14,457	(48.8)	2114	(57.2)
Emergency	12,344	(57.7)	15,120	(51.1)	1580	(42.8)
Unknown	27	(0.1)	33	(0.1)	0	(0.0)
Type of medical treatments						
Surgery	7815	(36.5)	12,189	(41.2)	1454	(39.4)
Blood transfusion[‡]	5589	(26.1)	8391	(28.3)	976	(26.4)
Intensive care unit admission	3845	(18.0)	5647	(19.1)	588	(15.9)
Respirator use	3264	(15.3)	4494	(15.2)	353	(9.6)
Blood purification therapy	607	(2.8)	1092	(3.7)	74	(2.0)

Percentages may not add up to 100%, because of rounding.

BMI, body mass index.

[*]Day 1 was regarded as the day of central venous catheter insertion.

[†]The target daily doses of energy, amino acids, and lipid were defined as ≥ 20 kcal/kg, ≥ 1.0 g/kg, and ≥ 2.5 g, respectively. The target-not-achieved group included patients who did not meet any of the target dose of the nutrients. The target-partially-achieved group included those who met 1 or 2 of the target dose of the nutrients. The target-achieved group included those who met all the target dose of the nutrients.

[‡]Performed by day 3 from the hospitalization day. Blood transfusion was considered as performed in patients if any red blood cells, platelets, or fresh-frozen plasma was transfused.

Baseline Characteristics

Patient characteristics of each group are shown in Table 1. The proportion of patients aged ≥ 80 years was 48.2% in the target-not-achieved group, 40.6% in the target-partially-achieved group, and 31.7% in the target-achieved group. The proportion of patients with BMI <18.5 kg/m^2 was the highest in the target-achieved group (52.5%) and the lowest in the target-not-achieved group (22.8%). The 3 most common main diseases in the target-not-achieved group, target-partially-achieved group, and target-achieved group were digestive system malignancy (23.7%, 31.2%, and 39.7%, respectively), digestive system disease (16.4%, 21.1%, and 28.3%, respectively), and respiratory diseases (19.2%, 16.2%, and 11.6%, respectively). More patients required full assistance in their daily activity (Barthel Index score of 0) and had moderate to severe disturbance of consciousness (JCS ≥ 1) in the target-not-achieved group (38.8% and 33.5%, respectively) than in the target-partially-achieved (29.5% and 24.6%, respectively) and target-achieved groups (20.5% and 16.0%, respectively).

Changes in the Daily Dose of Nutrients and PN Duration

In the target-achieved group, the median daily dose of all the nutrients reached the target level on day 2 or day 3. Conversely, in both the target-not-achieved group and target-partially-achieved group, the median daily dose of all nutrients did not reach the target level, except for energy in

the target-partially-achieved group, which was reached on day 3 (Figure 2).

The median (interquartile range) duration of PN from CVC insertion to discharge was 24 days (15–41), 26 days (17–44), and 31 days (21–49) in the target-not-achieved, target-partially-achieved, and target-achieved groups, respectively.

Clinical Outcomes

In-hospital mortality was 34.5% in the target-not-achieved group, 25.5% in the target-partially-achieved group, and 17.2% in the target-achieved group, with a statistical significance among the 3 groups ($P < 0.001$) (Table 2). Deteriorated ADL and readmission were 10.4% and 4.8% in the target-not-achieved group, 10.3% and 5.1% in target-partially-achieved group, and 8.4% and 4.8% in the target-achieved group, respectively, with a statistical significance between the 3 groups only for deteriorated ADL ($P < 0.001$ for deteriorated ADL and $P = 0.36$ for readmission).

Nutrition Target Achievement Affecting Clinical Outcomes

The adjusted OR (95% CI) for in-hospital mortality was 0.69 (0.66–0.72) in the target-partially-achieved group and 0.47 (0.43–0.52) in the target-achieved group with reference to the target-not-achieved group (Table 3), and it was 0.76 (0.69–0.83) in the target-achieved group with reference to the target-partially-achieved group. The adjusted OR for deteriorated ADL was 0.93 (0.85–1.01) in the target-partially-
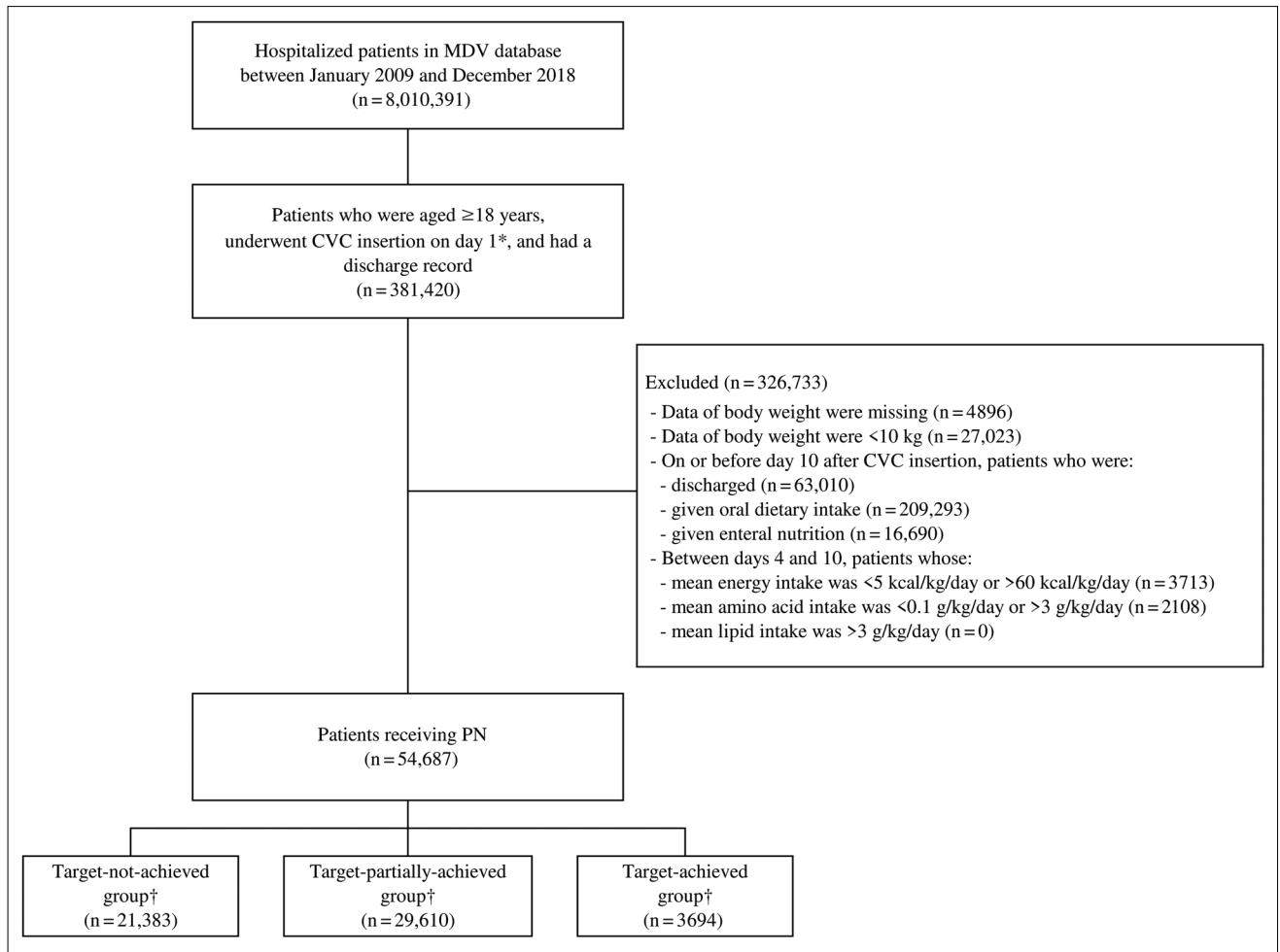
Figure 1. Patient-selection flowchart.*Day 1 was regarded as the day of CVC insertion.†The target daily doses of energy, amino acid, and lipid were defined as ≥20 kcal/kg, ≥1.0 g/kg, and ≥2.5 g, respectively. The target-not-achieved group included patients who did not meet any of the target dose of the nutrients. The target-partially-achieved group included those who met 1 or 2 of the target doses of the nutrients. The target-achieved group included those who met all the target dose of the nutrients. CVC, central venous catheter; MDV, Medical Data Vision; PN, parenteral nutrition.

achieved group and 0.77 (0.65–0.92) in the target-achieved group with reference to the target-not-achieved group. The adjusted ORs for all clinical outcomes were the lowest in the target-achieved group with reference to the target-not-achieved group. The Kaplan-Meier curves for in-hospital mortality according to the nutrition target achievement are shown in Figure S1. The in-hospital mortality rate was the highest in the target-not-achieved group and was the lowest in the target-achieved group, with a significant difference between the 3 groups (log-rank test, $P < 0.001$). The HR (95% CI) for in-hospital mortality was 0.72 (0.69–0.74, $P < 0.001$) in the target-partially-achieved group and 0.51 (0.46–0.56, $P < 0.001$) in the target-achieved group with reference to the target-not-achieved group.

In addition, the adjusted OR (95% CI) for in-hospital mortality among patients who reached the target dose of

both energy and amino acids was 0.63 (0.60–0.68) with reference to those who did not reach the target of either nutrient.

Discussion

This was the first study assessing clinical outcomes in hospitalized patients exclusively receiving PN according to their nutrition achievement in PN prescription at an early stage. The risk for in-hospital mortality was lower in patients whose prescribed PN dose partially or fully satisfied the target PN doses in accordance with the nutrition guidelines, compared with those who did not satisfy the target doses. The risk for deteriorated ADL was lower in patients whose prescribed PN dose fully satisfied the target doses compared

Table 2. Clinical Outcomes of Hospitalized Patients With Parenteral Nutrition According to Nutrition Target Achievement.

Clinical outcomes	Target-not-achieved group (n = 21,383)		Target-partially-achieved group (n = 29,610)		Target-achievedgroup (n = 3694)		P-value*
	n	(%)	n	(%)	n	(%)	
In-hospital mortality	7369	(34.5)	7549	(25.5)	637	(17.2)	<0.001
Deteriorated ADL	1464	(10.4)	2279	(10.3)	256	(8.4)	<0.001
Readmission	675	(4.8)	1131	(5.1)	146	(4.8)	0.36

ADL, activity of daily living.
*χ^2 Tests.

Table 3. Multivariate Logistic Regression* of Clinical Outcomes in Hospitalized Patients With Parenteral Nutrition According to Nutrition Target Achievement.

Clinical outcomes	Target-partially-achieved[†]		Target-achieved[†]		Target-achieved[‡]	
	Adjusted OR	(95% CI)	Adjusted OR	(95% CI)	Adjusted OR	(95% CI)
In-hospital mortality	0.69	(0.66–0.72)	0.47	(0.43–0.52)	0.76	(0.69–0.83)
Deteriorated ADL	0.93	(0.85–1.01)	0.77	(0.65–0.92)	0.83	(0.72–0.97)
Readmission	0.98	(0.89–1.09)	0.87	(0.71–1.07)	0.87	(0.73–1.05)

ADL, activity of daily living; OR, odds ratio.
*The following factors were included in the model as confounders: age, sex, body mass index, treatment year, number of hospital beds, main disease, Charlson Comorbidity Index, Barthel Index, Japan Coma Scale, type of admission, presence of surgery, blood transfusion, intensive care unit admission, artificial respirator use, and blood purification therapy
[†] The reference group was the target-not-achieved group.
[‡] The reference group was the target-partially-achieved group.

with those whose prescription doses partially or did not satisfy the target doses.

Our results were consistent with previous studies. A randomized controlled trial showed that individualized nutrition support to achieve energy and protein goals for hospitalized patients at nutrition risk improved clinical outcomes, compared with standard hospital food.[19] Positive clinical outcomes, such as suppressed muscle wasting,[24] decreased nosocomial infections,[25] and lowered in-hospital mortality,[26] were also reported among critically ill patients when nutrient doses were monitored and adjusted to maintain nutrition targets. In addition, increased protein and energy intakes were associated with lower mortality in nutritionally high-risk patients.[27] Although the nutrition risk was not assessable, patients at nutrition risk were presumably included in the present study given that patients had received PN alone for longer than 10 days and that those who were aged ≥70 years and whose BMI was <18.5 kg/m^2 accounted for 70.2% and 31.3% of the study population, respectively. Therefore, patients with adequate PN management to reach their nutrition targets showed better prognosis in this study. However, it should be noted that the identification of patients at risk of refeeding syndrome is important, and

so is the slow initiation of feeding according to the risk.[28] Further awareness of nutrition management may lead to better prognoses in patients receiving PN.

Previous studies have shown that insufficient energy intake did not affect clinical outcomes[29–31] and early achievement of energy goal increased complications[32] in critically ill patients. However, the association between protein administration and clinical outcomes was not investigated in these previous studies. Although the present study was not limited to critically ill patients, the risk for in-hospital mortality was lower among patients who reached the target doses of both energy and amino acids compared with those who did not reach the target of either nutrient. In fact, other studies reported that higher intake of protein was associated with lower mortality in critically ill patients[33,34] or patients who achieved both energy and protein targets were associated with lower mortality than those who reached neither target.[20] Taking into account our results and results of these previous studies, even though the target patients were not parallel, it is indicated that adequate administration of energy, amino acids, and lipid, or at least energy and amino acids, may improve clinical outcomes in patients receiving PN.
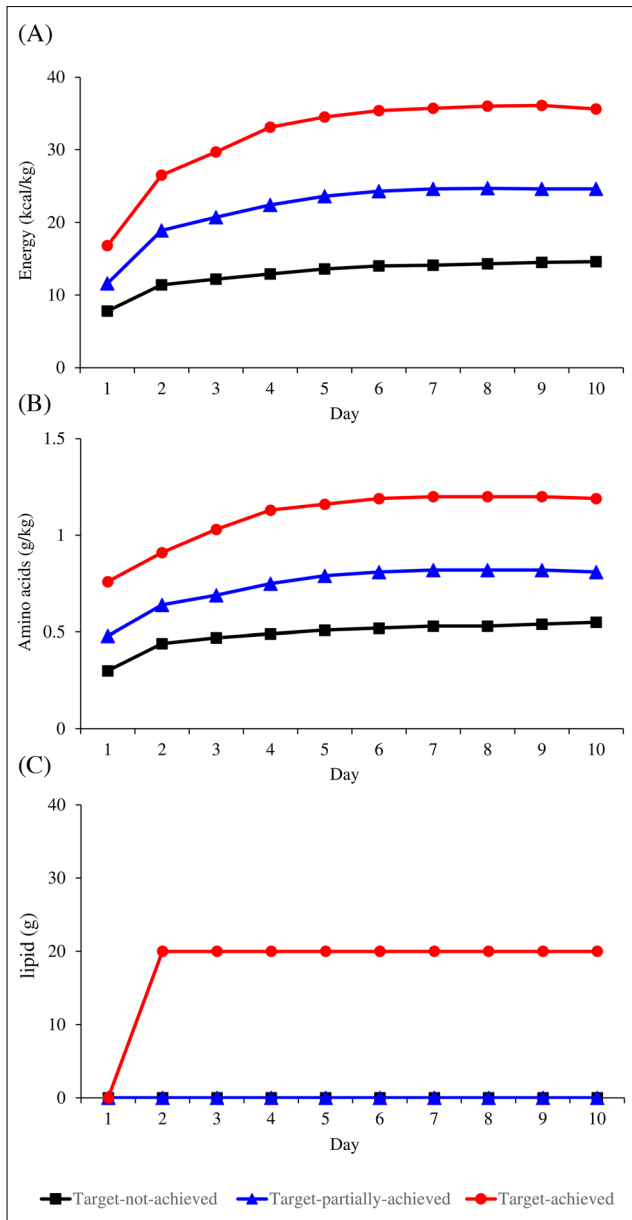
Figure 2. Change in median daily doses of (A) energy, (B) amino acids, and (C) lipid in hospitalized patients with PN according to nutrition target achievement between days 1[*] and 10.[*]Day 1 was regarded as the day of central venous catheter insertion. PN, parenteral nutrition.

There were some limitations in this study. First, our results may not be applicable to patients receiving PN outside acute care hospitals in Japan because the data used in this study only included patients who were admitted to acute care hospitals in Japan. In addition, BMI of the overall patients receiving PN was lower (mean, 20.5 kg/m^2) than that of previous reports from Western countries.[15–18] Our results may also not be generalizable to the Western population. Second, readmission may be underestimated.

As the database is hospital-based, readmissions to other hospitals cannot be identified. Third, the actual volume of nutrients administered to patients may be overestimated, as well as the target achievement. The prescribed volume of nutrients was considered as intake of nutrients; however, the volume of disposed waste solution cannot be identified in the database. Fourth, the amount of nutrients required for the patient may be inaccurate. The energy and amino acid doses were calculated based on the body weight at admission. Some researchers recommend indirect calorimetry to determine energy dose[35,36] and the patients' physical capabilities and activities to determine the amino acid dose.[37] Fifth, although the present study extracted all the potential factors affecting clinical outcomes from the database for inclusion in the study, clinical information (such as severities of diseases and results of laboratory tests) was unavailable. Regardless of the possible adjustments including severity, there may, however, be residual confounders. It should also be noted that the causal relationship between nutrition achievement and clinical outcomes could not be assessed in this study because of the observational nature of the study. Our results should be interpreted with caution given these limitations.

In conclusion, in-hospital mortality was lower and deteriorated ADL was suppressed in patients whose PN management was conducted in accordance with the nutrition guidelines. Further awareness toward nutrition management is suggested for better prognosis in patients receiving PN.

Statement of Authorship

Y. Sasabuchi conceptualized and designed the study, interpreted the data, and drafted and critically revised the article. S. Ono conceptualized and designed the study, interpreted the data, and critically revised the article. A. Kuroda conceptualized and designed the study, interpreted the data, and critically revised the article. S. Kamoshita conceptualized and designed the study, interpreted the data, and drafted and critically revised the article. T. Tsuda conceptualized and designed the study, interpreted the data, and critically revised the article. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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