—Regular Articles—

Development of Clinical Application for a Nutritional Prescription Support System for Total Parenteral/Enteral Nutrition

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One of the important roles of pharmacists as members of a nutrition support team is nutritional prescription support. We developed a nutritional prescription support system (NPSS) that facilitates prescription support and analysis and evaluated its usefulness in nutritional therapy. An NPSS for prescription support and the management of patient information was created. With this NPSS, the nutritional status was assessed, and, on the basis of the results, such variables as the total energy expenditure were calculated. This system allows prescription support for parenteral nutrition (PN) therapy, enteral nutrition (EN) therapy, and the transition period between them. This system was used for 2 representative patients and evaluated. In a malnourished patient receiving oral warfarin, EN solutions were compared by means of the NPSS, and an appropriate EN solution was selected. In addition, the prothrombin time-international normalized ratio was monitored, and favorable results were obtained regarding the adjustment of the warfarin dose and nutritional management. In a patient with aspiration pneumonia, continuous nutritional management to EN from PN therapy was straightforwardly performed with the NPSS. This NPSS allows rapid, comprehensive nutritional management during the transition period to EN from PN therapy, despite these therapies being considered separately in conventional nutritional management. The NPSS is useful for simplifying prescription support and facilitating information sharing among members of a nutrition support team.

Key words——nutrition support team; parenteral nutrition; enteral nutrition; prescription formulation; dietary reference intakes; system

INTRODUCTION

Nutrition support teams (NSTs) in Japan have traditionally used management systems developed by individual institutions, and few systems for nutritional assessment can be used cooperatively by persons in different specialities. We developed a nutritional prescription support system (NPSS) as a database management system that allows members of an NST to assess a patient's nutritional status. This system enables other medical staff, such as pharmacists, nutritionists, and nurses, to perform prescription support for parenteral nutrition (PN) therapy, enteral nutrition (EN) therapy, and the transition between them, a task that has traditionally been performed by physicians. In this study, the characteristics of the NPSS are described and its usefulness for nutritional therapy in 2 patients is reported.

METHODS

The software program FileMaker Pro 8.5 Advanced (FileMaker, Inc., Santa Clara, CA, USA) was used to create an NPSS to manage information regarding patients' nutritional status and prescriptions (Fig. 1). First, three assessments of the patient's nutritional status were performed: 1) a subjective global assessment (SGA),[1,2] an assessment of the physical status, and 3) an objective data assess-

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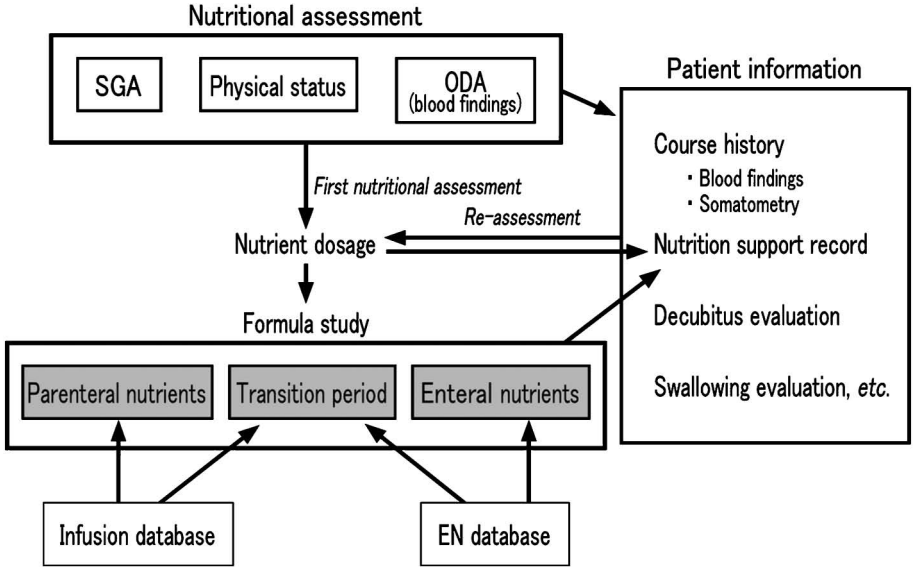

Fig. 1. Flow Chart of the NPSS
The gray boxes in the figure indicate areas for supporting the prescription formulation depending on the patient's condition.

ment (ODA), such as assessment of the results of hematologic examinations. On the basis of the assessment results, total energy expenditure (TEE) and the requirements for glucose (carbohydrates), amino acids (protein), fat, water, and NaCl were determined within the nutritional intake calculation window. On the basis of the these results, one of three types of prescription was selected: 1) a prescription for total PN (TPN) when PN therapy alone was administered, 2) a prescription for EN when EN alone was administered, or 3) a prescription for the transition period to EN from PN therapy.

The EN prescription system was more difficult to construct than the TPN prescription system. Commercially available EN solutions include elemental diets and semidigested nutrient solutions intended as medicines and semidigested nutrient solutions intended as food. In Japan, there are no strict standards for EN solutions intended as food, as there are for solutions intended as medicines; nutritional labeling by manufacturers is not standardized; and product inserts included with some EN solutions do not list components. In addition, because natural materials are used in EN solutions, unlike infusion solutions, many nutrients must be considered. Sex- and age-related differences are also considered in recommended dietary allowances, adequate intakes, tolerable upper intake levels, and estimated average requirements provided by the dietary reference intakes in Japanese (2005 edition)[2] for each nutrient in the nutrient solution.

This NPSS was applied to 2 patients. The nutritional component levels required in the prescribed solutions were gradually adjusted. The publication of this case was discussed and approved by the Ethical Committee, Hibino Hospital.

Background of Patients

Patient 1 A 69-year-old man with heart disease was receiving oral warfarin potassium (warfarin). He had difficulty with oral ingestion because of multiple cerebral infarctions and had undergone an artificial gastric fistula.

The patient was admitted due to cellulitis of the right lower leg. Before admission, he had received the EN solution Ensure Liquid (ESL; Abbott Japan Co., Ltd., Osaka, Japan; 1000 kcal/1000 ml/day). A sacral decubitus was observed for 5 days after admission. Because the patient was receiving warfarin, the NST evaluated EN solutions, with consideration of vitamin K, to improve the patient's nutritional status.

Patient 2 An 85-year-old woman was admitted because of suspected aspiration pneumonia. Due to fasting, an NST consultation was requested at admission.

RESULTS AND DISCUSSION

TPN Prescription For TPN prescriptions, the requirements regarding TEE and nutrients should be calculated, and appropriate nutrients selected. This NPSS enables TPN nutrients to be rapidly prescribed.

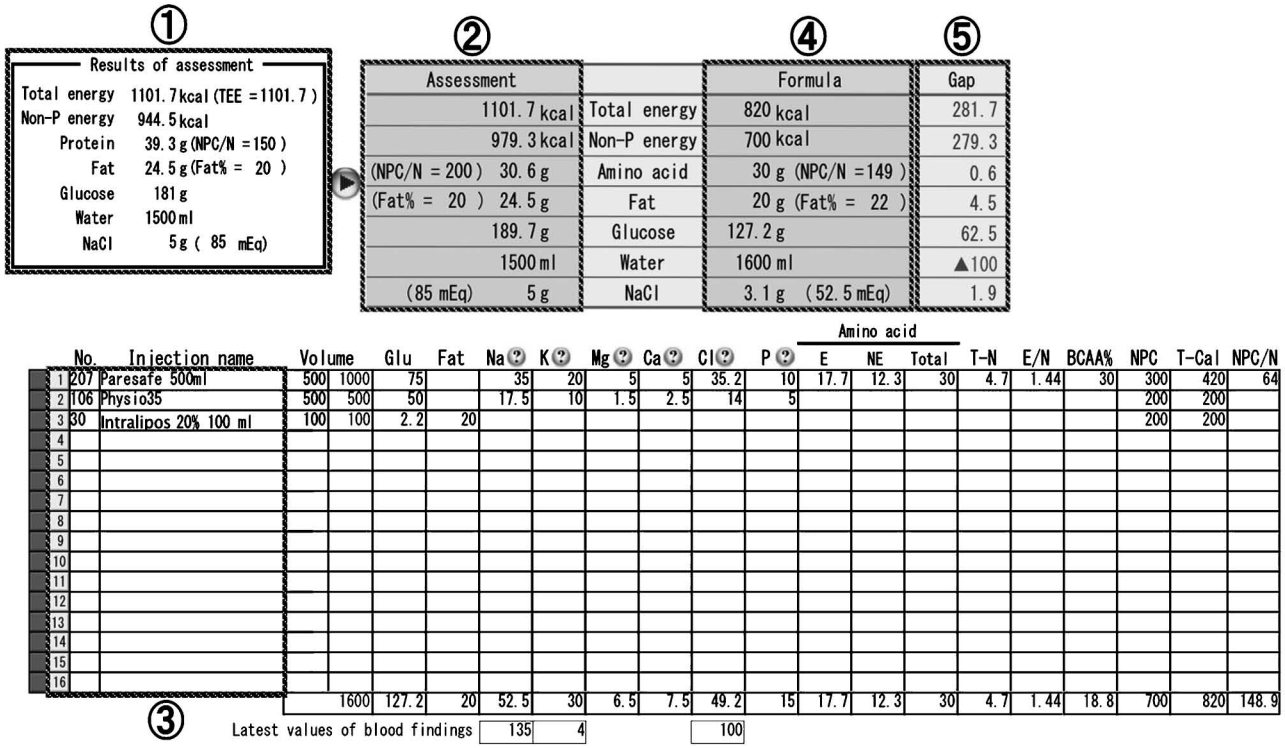

Fig. 2. Support System for Prescribing PN Solutions

The calculated TEE and nutrients needed are indicated in ''Results of Assessment'' (window ①) and ''Assessment'' (window ②). Window ① is linked to the patient's information, but window ② is not linked and can be modified. The type of transfusion needed is selected in window ③. The total nutrients contained in the selected transfusion in window ③ are indicated in ''Formulation'' (window ④). The difference between the vales in windows ② and ④ is shown in the ''Gap'' (window ⑤).

The windows for TPN prescriptions are shown in Fig. 2. Calculated nutritional intake values are displayed as target values in both the ''Results of Assessment'' window (window ①) and the ''Assessment'' window (window ②). Our infusion master includes a function for each component of the nutrient solution and facilitates the selection of an appropriate infusion solution for the target values of glucose, crystallized amino acids, and fat shown in window ③. When the infusion solution is selected, the values of the nutrients are automatically displayed in the ''Formulation'' window (window ④) as values in the formula. In addition, the difference between the target value and the value in the formula is displayed in the ''Gap'' window (window ⑤), and an infusion solution is selected to minimize this difference. Finally, differences in the water and NaCl values are adjusted with the injection of water and the use of sodium chloride ampules. Optimal TPN prescriptions can be rapidly determined with this system.

EN Prescription The windows for EN prescriptions are shown in Fig. 3. Values calculated in the window for nutritional intake are displayed as target values in both the ''Results of Assessment'' window (window ①) and ''Assessment'' window (window ②). An EN solution is selected from the EN solution master shown in window ③. The EN solution master has a function for each nutrient in EN solutions and a function to compare nutrient values at the same dose or calorie content. These functions facilitate the selection of EN solutions. When an EN solution is selected, the TEE and values of nutrients are automatically displayed in the ''Formulation'' window (window ④), and the difference between the values in windows ④ and ② is displayed in window ⑤. The volume of the EN solution is adjusted to minimize this difference, and the sufficiency rates of the total caloric value and the three major nutrients are readily assessed. Finally, the appropriateness of the selected EN solution is assessed by comparison with the values of the dietary reference intakes shown in window ⑥.

Prescription during the Transition to EN from PN Therapy The windows for prescriptions during the transition period are shown in Fig. 4. The list table (window ①) is changed to EN from PN, and an infusion or EN solution is selected from the infusion

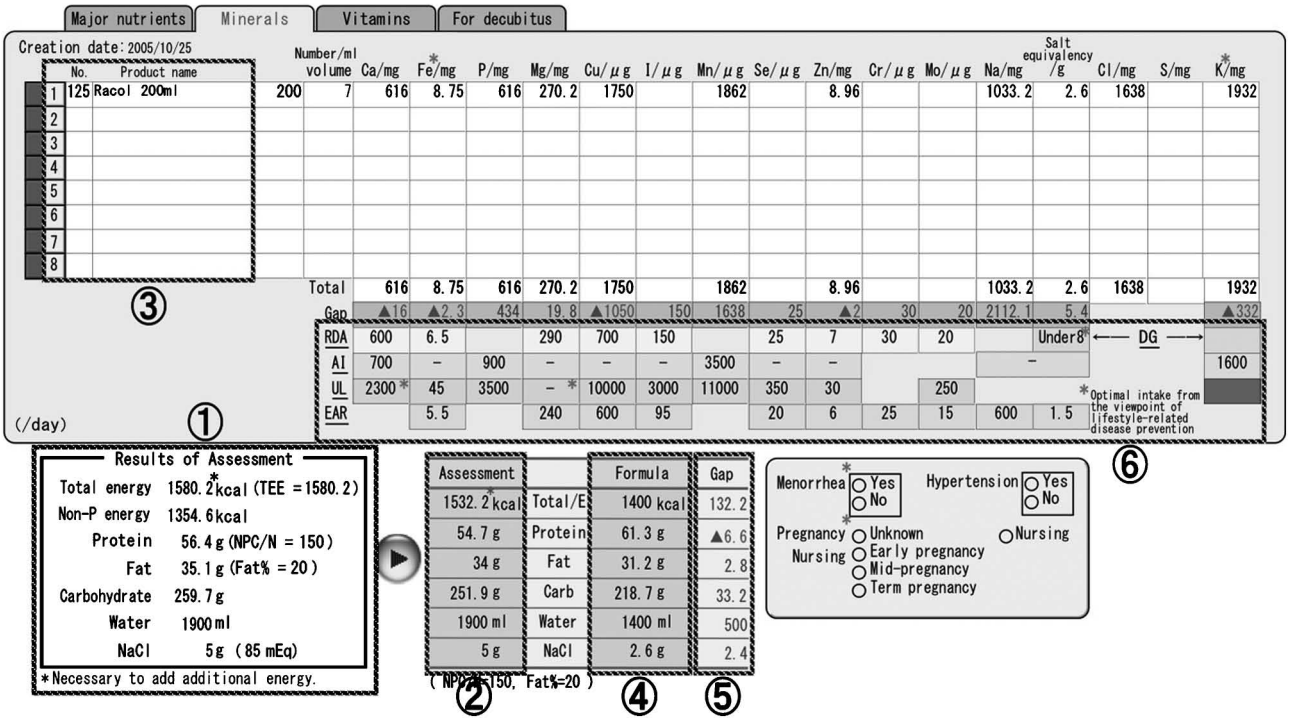

Fig. 3. Support System for Prescribing EN Solutions

The calculated TEE and nutrients needed are shown in ''Results of Assessment'' (window ①) and ''Assessment'' (window ②). Window ① is linked to the patient's information, but window ② is not linked and can be modified. The type of EN solution is selected in window ③. The total nutrients needed in the selected EN in window ③ are indicated in ''Formulation'' (window ④). The difference between values in windows ② and ④ is shown in the ''Gap'' window (window ⑤). The specified values in the Dietary Reference Intakes in Japanese (2005 edition) are shown in window ⑥. RDA, recommended dietary allowance; AI, adequate intake; UL, tolerable upper intake level; EAR, estimated average requirement; Carb, carbohydrates.

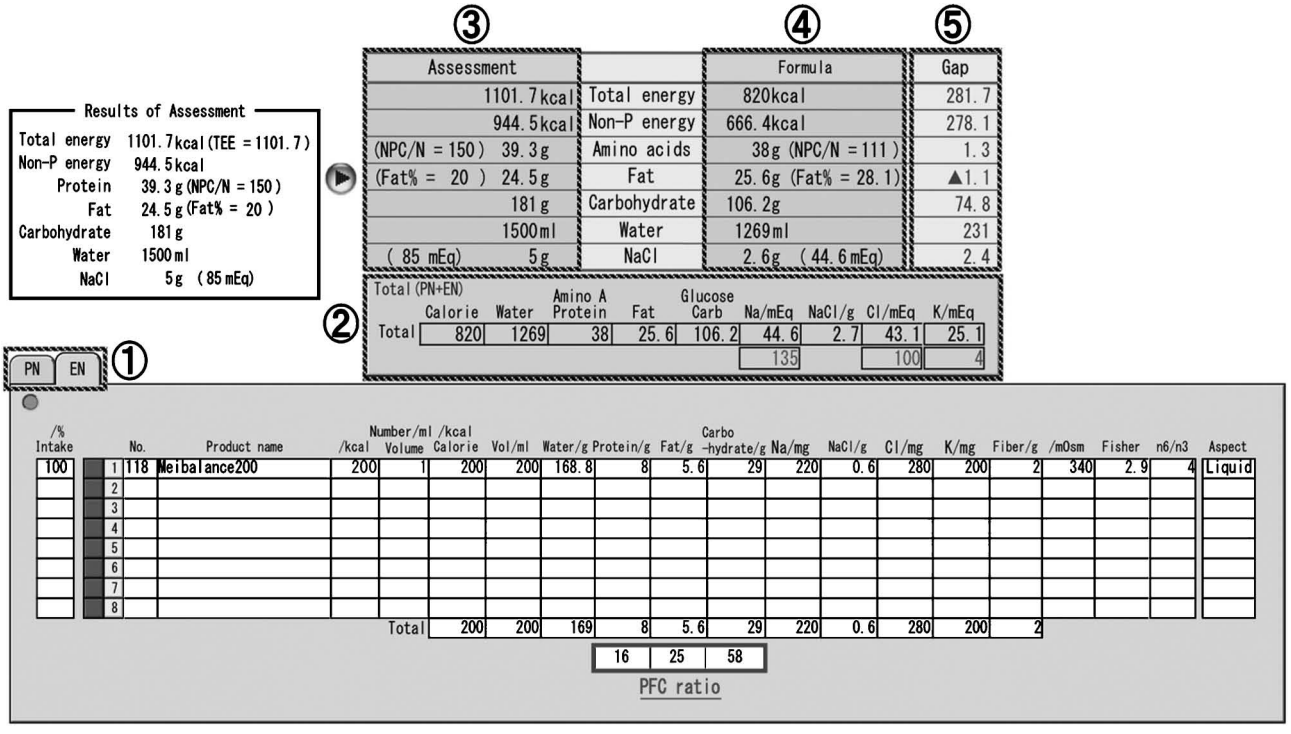

Fig. 4. Support System for Prescribing Both PN and EN Solutions

Window ①, The tab is changed from PN to EN, and an infusion solution or EN solution is selected from the infusion or EN solution master. Window ②, the total nutrients needed for the transfusions or EN solution selected in either the PN or EN list table are calculated. The calculated total nutrients needed and the TEE are shown in the ''Assessment'' window (window ③), which can be modified. The selected total nutrients needed for the transfusions or EN solution are shown in the ''Formulation'' window (window ④). The difference between windows ③ and ④ is indicated in the ''Gap'' window (window ⑤).

or EN solution master. When the solution type has been selected, the values of nutrients contained are shown in window ②. Target values are displayed in the ''Assessment'' window (window ③), as in the PN prescription, the nutrient values of the infusion solution selected from the PN table or of the EN solution selected from the EN table are shown in the ''Formulation'' window (window ④), and the difference between the values in the ''Assessment'' window (window ③) and the ''Formulation'' window (window ④) is shown in the ''Gap'' window (window ⑤). An infusion or EN solution should be selected to minimize this difference.

Nutritional Intervention in Patients

Patient 1 The appropriateness of the EN solution used before admission was evaluated by the NPSS, and recommendations on nutritional therapy were made to the primary-care physician. First, SGA, ODA, and somatometry were performed. The data obtained were input into the NPSS, which automatically evaluated the nutritional status and calculated basal energy expenditure (BEE), TEE, and nutrient requirements. The results of nutritional assessment are shown in Table 1.

Body weight is an important element for calculating TEE. The NPSS uses six types of body weight value: 1) body weight at initial consultation, 2) target body weight, 3) ideal body weight, 4) usual body weight, 5) latest body weight, and 6) manually measured body weight. The TEE can be instantly calculated for each type of weight. In addition, the difference in TEE between any two of the six types of weight can be calculated. The activity and stress factors should be determined in case studies by the NST. In patient 1, the calculated TEE, 1350.7 kcal/day, had not been achieved before admission. Therefore the ap-

Table 1. Nutritional Assessment Using the NST

Patient 1

• Physical status			
Height	165 cm	Weight	50.9 kg
Tricep skinfold thickness	5 mm	Arm circumference	20.5 cm
% Tricep skinfold thickness	50%	Arm muscle circumference	18.9 cm
		% Arm muscle circumference	79%
• SGA	Medium-level malnutrition		
• ODA	Medium-level malnutrition		
• Somatometry	Medium-level malnutrition		
• BEE	1,125.6 kcal/day		
• TEE	1,350 kcal/day (active factor, 1.0; stress factor, 1.2)		
• Nutrient dosage			
Protein: 48.6 g/day (nonprotein calories/nitrogen: 150)		Fat: 30.3 g/day (fat%: 20%)	
Carbohydrate: 223.7 g/day	Water: 1,527 ml/day	NaCl: 5 g/day	

Patient 2

• Physical status			
Height	153.5 cm	Weight	40.4 kg
Tricep skinfold thickness	4 mm	Arm circumference	16.2 cm
% Tricep skinfold thickness	40%	Arm muscle circumference	14.9 cm
		% Arm muscle circumference	77%
• SGA	Low-level malnutrition		
• ODA	Medium-level malnutrition		
• Somatometry	Medium-level malnutrition		
• BEE	918.1 kcal/day		
• TEE	1,101.7 kcal/day (active factor, 1.0; Stress factor, 1.2)		
• Nutrient dosage			
Protein: 30.6 g/day (nonprotein calories/nitrogen: 200)		Fat: 24.5 g/day (fat%: 20%)	
Carbohydrate: 189.7 g/day	Water: 1,500 ml/day	NaCl: 5 g/day	

Upper, first nutritional assessment of patient 1; lower, first nutritional assessment of patient 2.

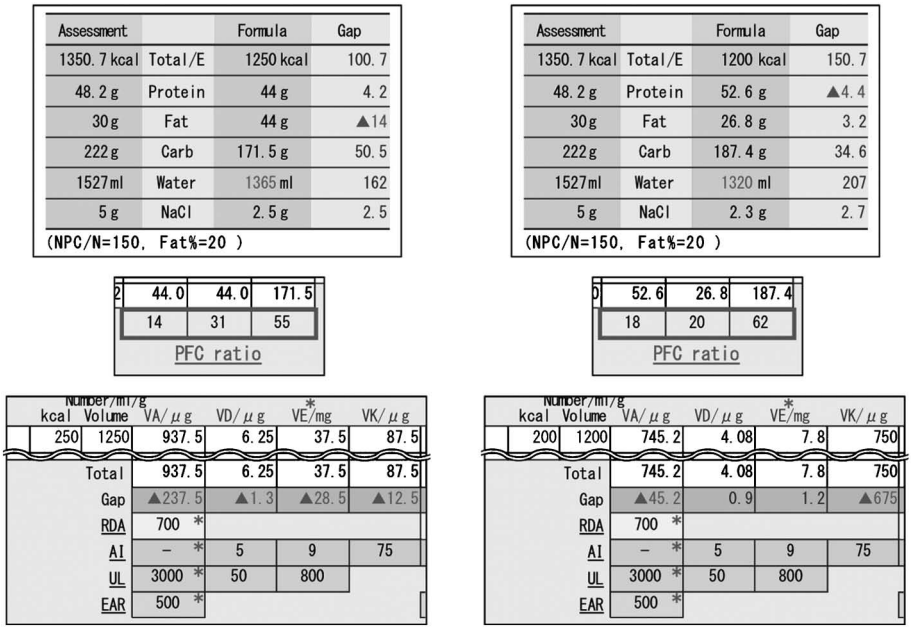

Fig. 5. Comparison of 1200 kcal of Racol (right side) with 1250 kcal of Ensure Liquid (left side)

Upper boxes, comparison of the nutrient contents of the two products; middle boxes, comparison of the P : F : C ratio of the two products, where the P : F : C ratio shows, from left to right, protein, fat, and carbohydrate, respectively; lower boxes, comparison of the quantity of fat-soluble vitamins in the two products.

propriateness of the administered nutrient values and EN solution was evaluated with the NPSS (Fig. 5). EN solutions intended as medicines are less costly to patients than EN solutions intended as food. Because ESL, the EN solution administered before admission, was intended as a medicine, it was compared with Racol (RCL; Otsuka Pharmaceuticals, Tokyo, Japan), another medical EN solution used in our hospital. After the energy to be consumed through ESL was increased to 1250 (250 kcal/250 ml/can, 5 cans) from 1000 kcal/day because of insufficient nutrient values, ESL was compared with 1200 kcal/day of RCL (400 kcal/400 ml/pack, 3 packs). The *n*-6 and *n*-3 fatty acid values of ESL were 25167.5 and 572.5 mg/day, respectively; the *n*-6/*n*-3 ratio was 43.96; and the protein : fat : carbohydrate (P : F : C) ratio was 14 : 31 : 55. For RCL, the *n*-6 and *n*-3 fatty acid values were 5700 and 1800 mg/day, respectively; the *n*-6/*n*-3 ratio was 3.17; and the P : F : C ratio was 18 : 20 : 62. Thus ESL has a higher percentage of fat and a higher *n*-6/*n*-3 value. Most of the fatty acids were long-chain fatty acids. In contrast, RCL has low fat and high protein energy ratios, a high *n*-3 fatty acid value, and a low *n*-6/*n*-3 ratio. To improve the nutritional status and treat the decubitus in this patient with inflammatory disease and a history of heart disease, we considered RCL more appropriate and recommended it to his primary-care physician because the target fat ratio in the Dietary Reference Intakes in Japanese patients is $<25\%$ (for men of 30 years or older).[2] In addition, a low-fat/high-carbohydrate diet reduces the risk of coronary artery disease,[3] a high-protein diet is recommended for patients with decubitus,[4] *n*-3 fatty acids have anti-inflammatory effects,[5,6] and medium-chain fatty acids[7–9] are readily digested and absorbed. However, because the patient was receiving warfarin, we had to consider the content of vitamin K, which inhibits warfarin. The vitamin K content of the ESL prescribed before admission was 70 μg/1000 kcal. This content was similar to the Dietary Reference Intake. RCL contains 750 μg of vitamin K/1200 kcal. Therefore, when RCL is administered, care must be taken to avoid blood clotting due to vitamin K excess. For this reason, while the prothrombin time-international normalized ratio (PT-INR) was carefully monitored, the warfarin dose was adjusted in cooperation with the primary-care physician. The warfarin dose at the time of NST consultation was 1 mg/day. Subsequently, the primary-care physician requested that the PT-INR be increased to 2.5; the warfarin dose was finally increased to 3.25 mg/day, which was close to the target value.

Changes in clinical examination values, the warfa-

rin dose, and the decubitus are shown in Fig. 6. All values improved. The decubitus gradually healed after 47 days. Treatment at home was started after 51 days.

Patient 2 PN therapy was started on admission. After the combination of PN and dietary therapies, nutritional management with the NPSS was performed for PN therapy and the combination of PN and EN therapies, and, finally, for the transition to EN from PN therapy.

The nutritional status was evaluated, and TEE was calculated. The results of a nutritional survey at the time of consultation are shown in Table 1. Evaluation by the NST showed an activity factor of 1.0 and a stress factor of 1.2. The calculated TEE was 1101.7 kcal/day. On the basis of this value, TPN solution was prescribed. However, because of the patient was elderly, there was a risk of refeeding syndrome. Therefore peripheral PN (PPN) solution providing 800 kcal/day was prescribed (Fig. 7–①). After 5 days, symptoms improved, and oral feeding became possible. Therefore a prescription for the transition period was calculated. The total energy intake in the PN solution was reduced to 620 kcal/day, while 600 kcal/day was added in the form of mixer food to the EN solution; thus the total energy intake was 1220 kcal/day.

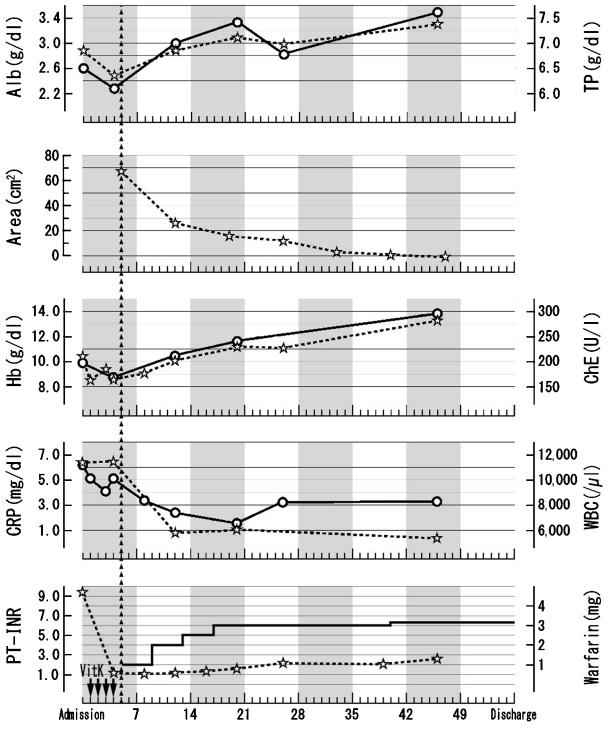

Fig. 6. Time-course of Changes in Several Variables after Consultation by the NST in Patient 1

Nutritional consultation by the NST started on day 5. Dotted lines, stars indicate albumin (Alb), decubitus area, hemoglobin (Hb), C-reactive protein (CRP), and PT-INR; solid lines, open circles indicate total protein (TP), cholinesterase (ChE), white blood cells (WBC), and doses of warfarin.

Because dysphagia subsequently developed, nutritional management with TPN was started. Her total energy intake was 1120 kcal/day. In this prescription, minimizing the difference between the target and prescribed values is important, and attention should also be paid to the levels of electrolytes administered. The NPSS was designed to display variables to determine whether the values of electrolytes, such as Na^+, K^+, and Cl^-, are appropriate. At the time of consultation, hyponatremia, hypochloremia, and hyperkalemia were present. These electrolytic imbalances were attributed to the decreased secretion of mineral corticoids often observed in elderly patients,[10] and so additional NaCl administration was avoided. As shown in Table 2, EN therapy with an elemental diet was started after 40 days along with PN therapy with a gradual decrease in its nutrient doses, and changes in nutrient values were observed until the discontinuation of PN therapy after 48 days. Finally, an EN solution (1200 kcal/day) alone was administered *via* the gastric fistula (Fig. 7–②).

In EN therapy, NaCl is sometimes added to prevent insufficient intakes of water and Na^+. For such supplementation, a special input space was included in

①

Assessment			Formula	Gap
1101.7kcal		Total energy	820kcal	281.7
979.3kcal		Non-P energy	700kcal	279.3
(NPC/N=200)	30.6g	Amino acids	30g (NPC/N=149)	0.6
(Fat%=20)	24.5g	Fat	20g (Fat%=22)	4.5
189.7g		Glucose	127.2g	62.5
1500ml		Water	1600ml	▲100
(85mEq)	5g	NaCl	3.1g (52.5mEq)	1.9

②

Assessment		Formula	Gap
1101.7kcal	Total/E	1200kcal	▲98.3
30.6g	Protein	48g	▲17.4
24.5g	Fat	33.6g	▲9.1
189.7g	Carb	174g	15.7
1500ml	Water	1500ml	0
5g	NaCl	3.4g	1.6
(NPC/N=150, Fat%=20)			

Fig. 7. Example of Total Energy Calculated with the NPSS in Patient 2

① days 0～4 and days 17～33: peripheral PN (PPN) alone; ② days 48～64: EN alone.

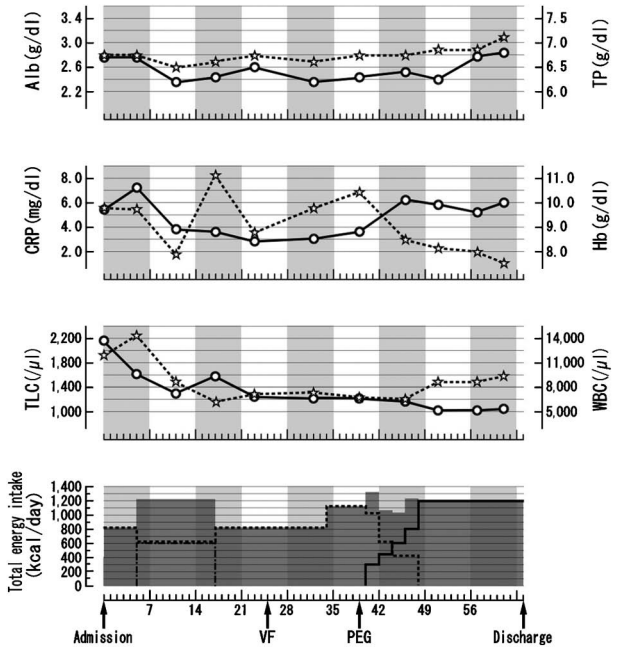

Fig. 8. Time-course of Changes in Several Variables after Consultation by the NST in Patient 2

Nutritional consultation by the NST was started at admission. Dotted lines, stars indicate albumin (Alb), C-reactive protein (CRP), and the total lymphocyte count (TLC); solid lines: open circles indicate total protein (TP), hemoglobin (Hb), and white blood cells (WBC). The lowermost graph shows the day-to-day variations in the infusion route of nutrients and injected total nutrients needed. ·····, Nutrients needed with PN therapy; — · —, nutrients needed with a fluid diet; ———, nutrients needed with EN solutions. The gray area indicates the total energy intake per day. VF, videofluoroscopic examination of swallowing; PEG, percutaneous endoscopic gastrostomy.

the EN prescription window. Changes in laboratory values as nutritional variables and daily changes in the method of nutrient administration and total energy intake after consultation are shown in Fig. 8. Each laboratory variable began to improve after 40 days, and the patient was transferred without complications to a geriatric healthcare facility.

In Japan, physicians generally prescribe TPN solutions, and pharmacists dispense and inspect the solutions according to formulas. Therefore pharmacists have little experience in prescribing TPN solutions, and doing so takes them considerable time. In addition, due to the development of kits for infusion *via* CVC and TPN in Japan, preparing mixed TPN solutions has been simplified but also contributes to pharmacists' lack of experience in prescribing TPN solutions.

Therefore we developed a prescription support system with which solutions for TPN and EN therapies can be readily prescribed and automatically analyzed for their nutrient content. This system enables the effective management of patients' nutritional information. Unlike the separate and parallel systems used by physicians, pharmacists, and nutritionists, the NPSS allows nutritional information to be shared among staff members in different specialities and thereby helps reduce workloads. The most recent version of the NPSS has the following improvements to enhance its clinical usefulness:

1) Before PN and EN solutions are prescribed, the nutritional status should be assessed and nutrient requirements calculated. Therefore the management of patient information has been improved.

2) EN therapy continues to be recognized as extremely useful[11,12] and is now increasingly prescribed instead of PN therapy. In 2005, the Dietary Reference Intakes were significantly revised, and nutritional management based on this revision has become necessary. Therefore additions were made to the NPSS for EN prescription.

3) To evaluate the usefulness of the NPSS, we asked many medical institutions to assess it. They requested a NPSS that could be used during the transition period to EN from PN therapy. Therefore the NPSS was modified to facilitate its use during the transition period.

We presented a patient for whom the EN prescription function of the NPSS was used and another patient for whom prescriptions for the transition period to EN from PN therapy were devised. The NPSS system was applied to NST work and proved useful for comprehensive nutritional management. In patient 1, important considerations were the treatment and prevention of decubitus and the interaction between warfarin and vitamin K. In the treatment of decubitus, systemic nutritional management is indispensable, and the doses of nutrients administered and the route and contents of administration are important. Solutions for EN include various products that are used as medicines or food, and selecting the most appropriate EN solution for each case can be difficult. In addition, the Dietary Reference Intakes should be considered. Traditionally in Japan, EN solutions considered to be medicine have been managed by pharmacists, whereas solutions considered to be food have been managed by nutritionists; therefore comprehensive nutritional management of all EN solutions was not possible. The NPSS allows information about vitamins and minerals, whose requirements according to the Dietary Reference Intakes

change with age, sex, and other factors, to be easily and quickly obtained; furthermore, EN solutions can be selected, and doses can be determined on the basis of appropriate nutritional evaluation. With the NPSS, pharmacists and nutritionists of the NST can work together to select the most appropriate EN solutions.

For patient 2, frequent modifications of nutritional therapy were necessary as the pathologic condition changed. In Japan, pharmacists have usually been involved in PN therapy, whereas nutritionists have usually been involved in EN therapy; as a result, information sharing during the transition to EN from PN therapy has been difficult. The NPSS allows information regarding changes in the pathologic condition and nutritional management methods to be easily shared among all members of the NST. In particular, as shown in Table 2, rapid solution selection and dose determination were necessary from 40 to 48 days after the start of consultation. Therefore the constant involvement of pharmacists in serial nutritional management is important. Because the total energy provided during the transition period to EN from PN therapy can be evaluated in real-time with the NPSS, prescription requirements can be rapidly fulfilled.

Because of recent efforts to decrease medical expenditure in Japan, the diagnostic-related group/prospective payment system has been introduced. Many large hospitals have introduced electronic medical record systems to improve efficiency; however, medium-sized or small hospitals may find introducing such systems to be financially impossible. Since the establishment of elderly medical insurance, care for the elderly in Japan has been shifting from hospitals to residential facilities and homes, and inexpensive systems are necessary for effective nutritional management. In the future, the NPSS should be further developed to facilitate the sharing of nutritional information among members of the NST in each hospital and with other medical institutions in the community.

CONCLUSION

We have developed an NPSS as a nutritional assessment system with the emphasis on prescription and analysis. This NPSS allows the simple, efficient prescription of PN and EN preparations in nutritional therapy. The comprehensive management of EN solutions intended as medicines or food and the transition to EN from PN therapy are possible. This system is useful for simplifying the prescription of EN and PN solutions and the sharing of nutritional information among staff members. In the future, we expect this system to be useful for establishing community networks for nutritional management.

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Table 2. Changes in Nutrients and Water Needed Due to the Shift from PN to EN between Hospital Days 39 and 49

	Day 39	Days 40–41	Days 42–43	Days 44–45	Days 46–47	Day 48
PN solution	TPN		PPN+fat	PPN		—
Energy (kcal)	1,120	1,020	620	420	420	0
Water volume (ml)	1,500	1,000	1,100	1,000	1,000	0
EN solution	GFO+water	Nutrition component+GFO+water			EN+water	
Energy (kcal)	0	300	450	600	800	1,200
Water volume (ml)	500	600	750	900	875	1,500
Total energy (kcal)	1,120	1,320	1,070	1,020	1,220	1,200
Total water volume (ml)	2,000	1,600	1,850	1,900	1,875	1,500

GFO (Otsuka Pharmaceuticals, Tokyo, Japan), EN solution made from mixing glutamine, fiber, and oligosaccharide.

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