



Importance of target calorie intake in hospitalized patients

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ABSTRACT

Background/Aims: To evaluate the feasibility and clinical outcome of a nutritional algorithm based on target calorie intake commenced as enteral nutrition (EN) alone or in combination with supplemental parenteral nutrition (SPN) among hospitalized patients.

Materials and Methods: In total, 301 hospitalized patients who were provided with nutritional support, including EN (n=125) or EN+SPN (n=176), due to various medical conditions during their hospitalization were included in this study conducted at Antalya Training and Research Hospital. All the patients were evaluated during their hospitalization under nutritional support until discharge or in-hospital death. Data on the length of stay (LOS) and serum pre-albumin and C-reactive protein (CRP) levels and records for feeding days considering nutritional risk screening (NRS) 2002 scores were collected.

Results: Overall, 85.7% of patients achieved the target calorie intake within a median of 4.0 days, while discharge and in-hospital death rates were 58.1% and 41.9%, respectively. Of the 5719 feeding days recorded during follow-up, 1076 (18.8%) days were associated with failure to achieve the target calorie intake with hemodynamic instability (33.3%), procurement problems (33.3%), and oral reluctance (23.0%).

Conclusion: Our findings emphasize the role of keeping the intake closer to the target calorie intake and immediate use of SPN whenever full EN fails to achieve the target calorie intake for improving the adequacy of clinical nutrition in the early phase of critical illness. The EN and EN+SPN groups were found to be similar in terms of rates of target achievement, mortality, and discharge, while a lower mortality rate and improved nutritional status were evident in achievers than in non-achievers of the target calorie intake regardless of the type of nutrition.

Keywords: Enteral nutrition, supplemental parenteral nutrition, target calorie intake, nutritional status

INTRODUCTION

Provision of adequate nutritional support to critically ill patients remains challenging due to difficulties in determining the optimal caloric intake as well as controversies regarding the most appropriate timing, best route of administration, and optimal energy intake for a favorable clinical outcome reported in clinical trials (1-6).

Enteral nutrition (EN) is considered to be the first choice of nutritional support for critically ill patients (5-7). However, the achievement of less than prescribed volumes

of EN as well as frequently encountered intolerance to EN in clinical practice poses an indication for a supplemental parenteral nutrition (SPN) strategy to correct the energy deficit due to delivery and tolerance problems associated with full EN, which otherwise leads to a poor clinical outcome (3,8,9).

While SPN enables the delivery of almost 100% of the estimated daily nutrition requirements, conflicting data exist regarding the benefits of increased caloric delivery provided via this method on clinical outcomes in the

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early phase of critical illness (7,10-12). Current guidelines call for an early initiation of nutrition, whereas the timing of SPN remains controversial (3,9). The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend the addition of SPN within 24 h to 48 h in patients who are expected to be intolerant to EN within 72 h of admission and state that the energy provision target should be achieved within 2-3 days (5). In contrast, the American Society for Parenteral and Enteral Nutrition (ASPEN) recommends postponing the initiation of PN until day 8 after intensive care unit (ICU) admission (6). Hence, the exact clinical effects and best practice for the early achievement of energy targets in the critically ill patients, particularly when EN is not indicated or poorly tolerated, remain controversial and undefined (3,7).

The present study was therefore designed to evaluate the feasibility and clinical outcome of a nutritional algorithm based on the target calorie intake commenced as EN alone or in combination with SPN among hospitalized patients.

MATERIALS AND METHODS

Study Population

A total of 301 hospitalized patients [mean standard deviation (SD) age, 64.7 (18.1) years; 57.1% males] who were provided with nutritional support including EN (n=125) or EN+SPN (n=176) due to various medical conditions during their hospitalization in the ICU (n=235) and general wards (n=66) were included in this prospective study conducted at Antalya Training and Research Hospital between January and December 2014. Patients >18 years of age and provided with nutritional support based on recommendations of our Nutritional Support Team were included in the study, while patients on nutritional support based on methods other than those recommended by the nutritional support team were excluded.

Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study, which was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by the institutional ethics committee.

Assessments

Data on patient demographics (age and gender), hospitalization unit (ICU and general ward), diagnosis group (surgical, internal medicine, and neurological), and type of clinical nutrition (EN or EN+SPN) were recorded for each patient at baseline. All patients were evaluated during their hospitalization under nutritional support until discharge or in-hospital death in terms of length of stay (LOS), weekly measurements of serum pre-albumin, and C-reactive protein (CRP) levels, along with records for feeding days for each patient, including nutritional risk screening (NRS) 2002 scores, achievement of the target calorie intake, and reasons for failure to achieve the target calorie intake. Data on LOS, outcome (discharge and in-hospital death),

and laboratory parameters (pre-albumin and CRP) were evaluated with respect to achievement of the target calorie intake in the overall study population as well as with respect to type of clinical nutrition, underlying diagnosis, and hospital unit. The reasons for failure to achieve the target calorie intake (technical problems [i.e., dislodgement of nasogastric tube or catheter or infusion pump malfunction], hemodynamic instability [i.e., hypotension, increased need for ventilator support, fluid restriction, and electrolyte imbalance], gastrointestinal intolerance [vomiting, excess residual volume, and severe diarrhea], procurement problems [skipped by healthcare staff and delay in product supply], oral reluctance, and metabolic complications) were analyzed based on the total number of feeding days recorded with failure to achieve the target daily calorie intake in the overall study population, in clinical nutrition groups and in patients with or without the final achievement of the target calorie intake during the course of hospitalization.

Assessment of Nutritional Status

Nutritional risk screening 2002 scoring system was used to detect the presence or risk of undernutrition in the hospital setting (13). All NRS 2002 scores were recorded for all patients within 24 h after admission based on assessments of the nutritional status (body mass index [BMI], <18.5, 18.5-20.5, and >20.5 kg/m²), weight loss history [over 5% in 3 months, over 5% in 2 months, or over 5% in 1 month], and reduced food intake as a proportion in the preceding week [0%-25%, 25%-50%, 50%-75%, and >75%], disease severity, and age. The total NRS-2002 score (range 0-7) is the sum of the nutritional status score, the disease severity score, and the age adjustment score (14). Patients with a NRS 2002 score of ≥3 and those with scores <3 with planned major surgery were considered nutritionally at risk and considered appropriate to be included in the nutritional support program.

Timing of Clinical Nutrition and Determination of Energy Target

In accordance with ESPEN guidelines, we commenced EN with or without SPN within 24-48 h after admission. The energy provision target was aimed to be as close as possible to the total energy need calculated using Schofield Equation (basal metabolic rate in calories estimated based on gender, age, and weight with consideration of stress and activity; 20-30 kcal/kg body weight/day and to be achieved within 2-3 days) (15).

Statistical Analysis

Statistical analysis was conducted using the computer software Statistical Package for Social Sciences version 21.0 (IBM Corp.; Armonk, NY, USA). Fisher's exact test and Pearson chi-square analysis were performed for categorical variables. Mann-Whitney U, Wilcoxon signed ranks, and Kruskal-Wallis test were used for comparison of quantitative variables with non-normal distribution, while Student t-test and paired t-test were used for normally distributed variables. Data were expressed as "mean (SD)", "n (%)" and "median (minimum and maximum)" values, where appropriate. A p value of <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics (n=301)

Enteral nutrition was applied in 41.5% of patients, while EN+SPN in 58.5% of patients. Hospitalizations were primarily in the ICU (78.1%) and for an internal medicine (39.9%) disease. Of 301 patients, 85.7% (84.0% in EN and 86.9% in EN+SPN groups) achieved the target calorie intake within median 4.0 days, while discharge and in-hospital death rates were 58.1% and 41.9%, respectively. Mean (SD) LOS was significantly higher in the EN+SPN than in the EN group (25.5 [19.0]) vs. 16.0 [13.5] days; $p<0.001$) (Table 1).

Outcome and Laboratory Parameters with Respect to Achievement of Target Calorie Intake (n=301)

Overall, significantly higher mean (SD) LOS (23.7 [18.0] vs. 8.7 [4.2]) days, $p<0.001$ and lesser likelihood of in-hospital death (37.6% vs. 67.4%; $p<0.001$) were noted in patients with than those without achievement of the target calorie intake. From baseline to discharge, a significant increase in mean (SD) pre-albumin levels (from 11.4 [6.0] to 13.9 [7.4]; $p<0.001$) and significant decrease in CRP levels (from 99.4 [69.4] to 76.9 [65.7]; $p<0.001$) were noted in patients who achieved the target calorie intake. However, no significant change occurred in the pre-albumin and CRP levels during clinical nutrition in patients who failed to achieve the target calorie intake (Table 2).

Similarly, in both EN and EN+SPN groups, longer LOS ($p<0.001$, for each) and lesser likelihood of in-hospital death ($p=0.004$ and $p=0.013$, respectively) were noted in patients with than in those without achievement of the target calorie intake, along with significant increase in pre-albumin levels ($p<0.001$ and $p=0.002$, respectively) and significant decrease in CRP ($p=0.001$ for each) levels from baseline to discharge only in patients with achievement of the target calorie intake (Table 2).

Outcomes and Laboratory Parameters with Respect to Underlying Diagnosis and Hospital Unit (n=301)

No significant difference was noted in the rate of achievement of the target calorie intake, LOS outcome, and laboratory parameters with respect to underlying diagnosis. However, longer LOS (23 [18.6] days vs. 16.5 [11.5] days; $p=0.021$), higher in-hospital mortality rate (51.1% vs. 9.1%; $p<0.001$), and lower percentage of patients with decreased CRP levels (60.2% vs. 75.9%; $p=0.028$) were noted in the ICU than in general ward hospitalizations (Table 3).

Clinical Nutrition, Outcome, and Laboratory Parameters among Patients who Achieved the Target Calorie Intake According to Time (N=258)

Of the 258 patients who achieved the target calorie intake, 150 (58.1%) achieved the target calorie intake within 5 days and 108 (41.9%) within ≥ 5 days. The average time to achieve the target calorie intake was 5.0 (2.9) days, 4.3 (2.2) days, and 5.4 (3.3) days in the overall study population and the EN and EN+SPN groups, respectively.

Table 1. Data on demographic and clinical characteristics

Age (year), mean (SD)	64.7 (18.1)
Gender, n (%)	
Female	129 (42.9)
Male	172 (57.1)
Nutritional support, n (%)	
EN	125 (41.5)
EN+SPN	176 (58.5)
Diagnosis, n (%)	
Surgical disease	101 (33.5)
Internal medicine	120 (39.9)
Neurological disease	80 (26.6)
Hospital unit, n (%)	
ICU	235 (78.1)
General ward	66 (21.9)
LOS, mean (SD)	
Overall (n=301)	21.6 (17.5)
EN (n=125)	16.0 (13.5)
EN+SPN (n=176)	25.5 (19.0)*
Target calorie intake, n (%)	
Overall (n=301)	
Not achieved	43 (14.3)
Achieved	258 (85.7)
EN (n=125)	
Not achieved	20 (16.0)
Achieved	105 (84.0)
EN+SPN (n=176)	
Not achieved	23 (13.1)
Achieved	153 (86.9)
Time to achievement (days)	
Mean (SD)	5.4 (3.4)
Median (minimum-maximum)	4 (1-20)
Daily records	
Overall number of feeding days	5719
Feeding days with failure to achieve the daily target calorie intake	1076
Outcome, n (%)	
Overall (n=301)	
Discharge	175 (58.1)
In-hospital death	126 (41.9)
EN (n=125)	
Discharge	79 (63.2)
In-hospital death	46 (36.8)
EN+SPN (n=176)	
Discharge	96 (54.5)
In-hospital death	80 (45.5)

EN: enteral nutrition; ICU: intensive care unit; LOS: length of hospitalization; SD: standard deviation; SPN: supplemental parenteral nutrition
* $p<0.001$ compared with EN (Mann-Whitney U test)

Table 2. Outcome and laboratory parameters with respect to achievement of target calorie intake in overall study population and clinical nutrition groups (n=301)

	Overall (n=301)		EN (n=125)		EN+SPN (n=176)	
	Target calorie intake		Target calorie intake		Target calorie intake	
	Not achieved (n=43)	Achieved (n=258)	Not achieved (n=20)	Achieved (n=105)	Not achieved (n=23)	Achieved (n=153)
LOS (days), mean (SD)	8.7 (4.2)	23.7 (18.0)	8.1 (4.1)	17.4 (14.1)	9.3 (4.4)	27.9 (19.1)
p ¹	p<0.001		p<0.001		p<0.001	
Outcome, n (%)						
Discharge	14 (32.6)	161 (62.4)	7 (35.0)	72 (73.0)	7 (30.4)	89 (58.2)
In-hospital death	29 (67.4)	97 (37.6)	13 (65.0)	33 (37.0)	16 (69.6)	64 (41.8)
p ²	p<0.001		0.004		0.013	
Pre-albumin (mg/dL), mean (SD)						
Baseline	10.2 (5.1)	11.4 (6.0)	11.7 (5.8)	11.8 (6.0)	9.1 (4.5)	11.1 (6.0)
Discharge	10.2 (5.3)	13.9 (7.4)	10.4 (6.2)	15.2 (7.8)	10.2 (4.7)	13.1 (7.1)
p ³	0.753	p<0.001	0.610	p<0.001	0.318	0.002
CRP (mg/L), mean (SD)						
Baseline	106.6 (73.1)	99.4 (69.4)	68.7 (52.5)	92.2 (64.7)	137.8 (74.3)	105.7 (72.6)
Discharge	95.2 (69.6)	76.9 (65.7)	90.1 (80.1)	69.2 (68.5)	99.2 (62.7)	82.2 (63.7)
p ³	0.727	p<0.001	0.507	0.001	0.227	0.001

CRP: C-reactive protein; EN: enteral nutrition; LOS: length of hospitalization; SD: standard deviation; SPN: supplemental parenteral nutrition

¹Mann-Whitney U test, ²Chi-Square test, ³Wilcoxon signed-rank test**Table 3.** Outcome and laboratory parameters with respect to underlying diagnosis and hospital unit (n=301)

	Diagnosis			p	Hospital unit		
	Surgical (n=101)	Internal medicine (n=120)	Neurology (n=80)		ICU (n=235)	General ward (n=66)	p
Target calorie intake							
Not achieved (n=43)	12 (27.9)	22 (51.2)	9 (20.9)	0.261 ¹	38 (88.4)	5 (11.6)	0.078 ¹
Achieved (n=258)	89 (34.5)	98 (38.0)	71 (27.5)		197 (76.4)	61 (23.6)	
LOS (days)	21.7 (16.5)	19.4 (15.4)	24.8 (21.2)	0.300 ²	23 (18.6)	16.5 (11.5)	0.021
Outcome							
Discharge (n=175)	61 (34.9)	62 (35.4)	52 (29.7)	0.148 ²	115 (48.9)	60 (90.9)	p<0.001
In-hospital death (n=126)	40 (31.7)	58 (46.0)	28 (22.2)		120 (51.1)	6 (9.1)	
Pre-albumin level							
Decreased (n=89)	32 (36.0)	35 (39.3)	22 (24.7)	0.874 ²	72 (35.1)	17 (29.3)	0.409
Increased (n=174)	57 (32.8)	72 (41.4)	45 (25.9)		133 (64.9)	41 (70.7)	
CRP level							
Decreased (n=168)	56 (33.3)	67 (39.9)	45 (26.8)	0.879 ²	124 (60.2)	44 (75.9)	0.028
Increased (n=96)	33 (34.4)	40 (41.7)	23 (24.0)		82 (39.8)	14 (24.1)	

CRP: C-reactive protein; ICU: intensive care unit; LOS: length of hospitalization

¹Chi-square test, ²Kruskal-Wallis test

The likelihood of achieving the target calorie intake later (≥ 5 days) was higher in case of EN+SPN than EN (47.1% vs. 34.3%; $p=0.041$). Apart from the significantly longer LOS (26.9 [19.8]

vs. 21.4 [16.2] days; $p=0.015$) in later than in earlier achievers of the target calorie intake, the two groups had similar outcome in terms of discharge and death rates. Significant increase pre-

albumin levels ($p<0.001$ and $p=0.002$, respectively) and decline in CRP levels ($p=0.001$, for each) were noted in both groups from baseline to discharge (Table 4).

Table 4. Clinical nutrition, outcome, and laboratory parameters among patients who achieved target calorie intake ($n=258$)

	Patients achieved target calorie intake	
	Within <5 days (n=150)	Within ≥5 days (n=108)
Clinical nutrition type, n (%)		
EN (n=105)	69 (65.7)	36 (34.3)
EN+SPN (n=153)	81 (52.9)	72 (47.1)
p value ¹	0.041	
LOS (days), mean (SD)	21.4 (16.2)	26.9 (19.8)
p ²	0.015	
Outcome, n (%)		
Discharge (n=161)	94 (58.4)	67 (41.6)
In-hospital death (n=97)	56 (57.7)	41 (42.3)
p ¹	0.918	
Pre-albumin (mg/dL), mean (SD)		
Baseline	12.1 (6.1)	10.6 (5.7)
Discharge	16.2 (7.7)	12.6 (6.9)
p ³	0.000	0.002
CRP (mg/L), mean (SD)		
Baseline	92.6 (64.6)	108.8 (74.9)
Discharge	70.0 (60.3)	85.8 (71.3)
p ³	0.001	0.001

CRP: C-reactive protein; EN: enteral nutrition; LOS: length of stay; SD: standard deviation;
SPN: supplemental parenteral nutrition

¹Chi-square test, ²Mann-Whitney U test, ³Wilcoxon signed-rank test

CRP: C-reactive protein; EN: enteral nutrition; LOS: length of stay; SD: standard deviation; SPN: supplemental parenteral nutrition

¹Chi-square test, ²Mann-Whitney U test, ³Wilcoxon signed-rank test

Reasons for Failure to Achieve the Target Calorie Intake Based on Daily Records with Respect to Clinical Nutrition

Of the 5719 feeding days recorded during follow up, 1076 (18.8%) days were associated with failure to achieve the target calorie intake. Of the 1076 records with failure, 690 (64.1%) were from the EN+SPN nutrition group, while 386 (35.9%) were from EN group. The analysis of reasons for failure in these records revealed that hemodynamic instability (33.3%), procurement problems (33.3%), and oral reluctance (23.0%) were the main reasons for failure to achieve target on a daily basis. Hemodynamic instability (44.1% vs. 14.0%) was more common, whereas procurement problems (25.2% vs. 47.7%) and oral reluctance (19.9% vs. 28.5%) were less likely in the EN+SPN than in the EN group ($p<0.001$ for each) (Table 5).

Overall, hemodynamic instability (41.7% vs. 29.7%) and oral reluctance (32.1% vs. 19.1%) were more common among patients who failed to achieve the target calorie intake, while procurement problems (39.9% vs. 17.8%) and technical problems (4.5% vs. 1.9%) were more common on daily records from patients achieving the target calorie intake ($p<0.001$ for each) (Table 5).

Reasons for Failure to Achieve the Target Calorie Intake Based on Daily Records with Respect to Diagnosis

Overall, technical problems in the clinical nutrition of patients with neurology-based diseases (62.5%), hemodynamic instability, and oral reluctance (55.9%) in internal medicine-based diseases (53.1%), and procurement problems in neurology- (35.8%) and surgery (35.2%) based diseases were more commonly noted reasons for failure to achieve the target calorie intake ($p<0.001$ for each). The analysis of subgroups of patients with and without achievement of the target calorie intake also revealed similar distribution of reasons for failure (Table 6).

Table 5. Reasons for failure to achieve target calorie intake based on daily records with respect to clinical nutrition

Reasons for failure, n (%)	Overall records ($n=1076$)			Records from EN ($n=386$)			Records from EN+SPN ($n=690$)		
	Total	Target calorie intake		Total	Target calorie intake		Total	Target calorie intake	
		Achieved	Not achieved		Achieved	Not achieved		Achieved	Not achieved
Technical problems	40 (3.7)	34 (4.5)	6 (1.9) ⁺	16 (4.1)	11 (4.5)	5 (3.5)	24 (3.5)	23 (4.5)	1 (0.6)
Hemodynamic instability	358 (33.3)	224 (29.7)	134 (41.7) ⁺	54 (14.0)	22 (9.1)	32 (22.4)	304 (44.1)*	202 (39.5)	102 (57.3)
Gastrointestinal intolerance	70 (6.5)	49 (6.5)	21 (6.5)	22 (5.7)	16 (6.6)	6 (4.2)	48 (7.0)	33 (6.4)	15 (8.4)
Procurement problems	358 (33.3)	301 (39.9)	57 (17.8) ⁺	184 (47.7)	141 (58.0)	43 (30.1)	174 (25.2)*	160 (31.3)	14 (7.9)
Oral reluctance	247 (23.0)	144 (19.1)	103 (32.1) ⁺	110 (28.5)	53 (21.8)	57 (39.9)	137 (19.9)*	91 (17.8)	46 (25.8)
Metabolic complications	3 (0.3)	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.4)	3 (0.6)	0 (0.0)
Total	1076 (100.0)	755 (100.0)	321 (100.0)	386 (100.0)	243 (100.0)	143 (100.0)	690 (100.0)	512 (100.0)	178 (100.0)

EN: enteral nutrition; SPN: supplemental parenteral nutrition

Chi-square test

* $p<0.001$ compared with total records from EN group

⁺ $p<0.001$ compared with records from achievers in the overall records

Table 6. Reasons for failure to achieve target calorie intake based on daily records with respect to diagnosis and hospital unit

Reasons for failure, n (%)	Target calorie intake											
	Overall				Not achieved				Achieved			
	Surgery	Internal medicine	Neurology	Total	Surgery	Internal medicine	Neurology	Total	Surgery	Internal medicine	Neurology	Total
Technical problems	6 (15.0)	9 (22.5)	25 (62.5)*	40 (100.0)	1 (16.7)	1 (16.7)	4 (66.7)*	6 (100.0)	5 (14.7)	8 (23.5)	21 (61.8)*	34 (100.0)
Hemodynamic instability	129 (36.0)	190 (53.1)*	39 (10.9)	358 (100.0)	51 (38.1)	79 (59.0)*	4 (3.0)	134 (100.0)	78 (34.8)	111 (49.6)*	35 (15.6)	224 (100.0)
Gastrointestinal intolerance	26 (37.1)	26 (37.1)	18 (25.7)	70 (100.0)	10 (47.6)	9 (42.9)	2 (9.5)	21 (100.0)	16 (32.7)	17 (34.7)	16 (32.7)	49 (100.0)
Procurement problems	126 (35.2)	104 (29.1)*	128 (35.8)	358 (100.0)	26 (45.6)*	19 (33.3)	12 (21.1)	57 (100.0)	100 (33.2)	85 (28.2)*	116 (38.5)	301 (100.0)
Oral reluctance	44 (17.8)	138 (55.9)*	65 (26.3)	247 (100.0)	4 (3.9)	63 (61.2)*	36 (35.0)	103 (100.0)	40 (27.8)	75 (52.1)*	29 (20.1)	144 (100.0)
Metabolic complications	0 (0.0)	3 (100.0)	0 (0.0)	3 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)	0 (0.0)	3 (100.0)
Total	331 (30.8)	470 (43.7)	275 (25.6)	1076 (100.0)	92 (28.7)	171 (53.3)	58 (18.1)	321 (100.0)	239 (31.7)	299 (39.6)	217 (28.7)	755 (100.0)

Reasons for failure, n (%)	Target calorie intake								
	Overall			Not achieved			Achieved		
	Intensive care unit	General ward	Total	Intensive care unit	General ward	Total	Intensive care unit	General ward	Total
Technical problems	39 (97.5)*	1 (2.5)	40 (100.0)	6 (100.0)*	0 (0.0)	6 (100.0)	33 (97.1)*	1 (2.9)	34 (100.0)
Hemodynamic instability	311 (86.9)*	47 (13.1)	358 (100.0)	134 (100.0)*	0 (0.0)	134 (100.0)	177 (79.0)*	47 (21.0)	224 (100.0)
Gastrointestinal intolerance	64 (91.4)*	6 (8.6)	70 (100.0)	21 (100.0)*	0 (0.0)	21 (100.0)	296 (98.3)*	5 (1.7)	301 (100.0)
Procurement problems	353 (98.6)*	5 (1.4)	358 (100.0)	57 (100.0)*	0 (0.0)	57 (100.0)	43 (87.8)*	6 (12.2)	49 (100.0)
Oral reluctance	127 (51.4)	120 (48.6)	247 (100.0)	53 (51.5)	50 (48.5)	103 (100.0)	74 (51.4)	70 (48.6)	144 (100.0)
Metabolic complications	0 (0.0)	3 (100.0)	3 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (100.0)	3 (100.0)
Total	894 (83.1)	182 (16.9)	1076 (100.0)	271 (84.4)	50 (15.6)	321 (100.0)	623 (82.5)	132 (17.5)	755 (100.0)

*p<0.001 compared with other diagnosis or general ward (chi-square test)

Reasons for Failure to Achieve the Target Calorie Intake Based on Daily Records with Respect to Hospital Unit

Overall, technical problems (97.5% vs. 2.5%), hemodynamic instability (86.9% vs. 13.1%), gastrointestinal intolerance (91.4% vs. 8.6%), and procurement problems (98.6% vs. 1.4%) were more commonly recorded reasons for failure to achieve the daily target caloric intake in the ICU than in the general wards ($p<0.001$ for each). The analysis of sub-groups of patients with and without achievement of the target calorie intake also revealed similar distribution of reasons for failure (Table 6).

NRS 2002 Scores with Respect to Clinical Nutrition, Outcome, and Laboratory Parameters

Mean (SD) NRS 2002 scores were significantly higher in patients without than in those with achievement of the target calorie intake in the overall study population (3.9 [0.9] vs. 3.6 [0.8]; $p=0.037$) and in the EN+SPN group (4.1 [1.0] vs. 3.6 [0.8]; $p=0.014$), while no significant difference was noted between patients with and without achievement of the target calorie intake (3.7 [0.9] vs. 3.7 [0.6], respectively; $p=0.718$) in the EN group.

In-hospital death was associated with significantly higher NRS 2002 scores compared with discharge (3.9 [0.8] vs. 3.5 [0.8]; $p<0.001$). No significant difference was noted in the NRS 2002

scores with respect to time to achieve the target calorie intake (3.7 [0.8] vs. 3.6 [0.8] for longer vs. shorter than 5 days, respectively; $p=0.199$), change in pre-albumin (3.7 [0.8] vs. 3.7 [0.9] for decreased vs. increased levels, respectively, $p=0.629$), or CRP levels (3.6 [0.8] vs. 3.7 [0.9] for decreased vs. increased levels, respectively, $p=0.399$) and reasons for failure to achieve the target calorie intake (3.9 [0.9] for technical problems, 3.8 [0.9] for hemodynamic instability, 3.6 [0.8] for gastrointestinal intolerance, 3.7 [0.8] for procurement problems, and 3.7 [1.0] for oral reluctance; $p=0.278$).

DISCUSSION

Our findings revealed achievement of the target calorie intake in majority of hospitalized patients via the nutritional algorithm focused on achieving the target calorie intake within 3 days either via full EN or via prompt commencement of SPN whenever EN fails to meet the energy demands. The EN and EN+SPN groups had similar rates of target calorie achievement, mortality, and discharge, while the EN+SPN group had prolonged LOS. Among achievers of the target calorie intake, lower mortality rate and significantly increased pre-albumin levels were noted regardless of the type of nutrition. Poorer NRS 2002 scores were evident among non-achievers than among achievers of the target calorie intake only in the EN+SPN group.

Our findings support the favorable clinical outcome. Decreased hospital LOS with early EN commenced within 24 h to 48 h after ICU admission. This appears consistent with the consideration of EN as the preferred route of clinical nutrition over PN whenever possible (9,16,17). Early SPN commencement revealed similar rates of achievement of the target calorie intake, mortality, and discharge in the EN group. This appears in agreement with the statement that commencing early SPN is not associated with improved clinical outcome in terms of reduced mortality or hospital LOS, while it improves the provision of calories and promotes the achievement of energy targets, leading to a more optimal intake of calories to avoid further energy deficit in critically ill patients when full enteral support fails to achieve calorie targets (3,9,11,18-23).

Supplemental parenteral nutrition was implemented by a well-trained and experienced nutrition team in our cohort based on an algorithm that insisted on achieving the target calorie intake within the first 3 days of the nutritional plan. Besides, SPN was promptly introduced when EN failed to achieve the target calorie intake.

Hence, our findings emphasize the benefits of individualized early SPN if enteral feeding fails in critically ill patients when promptly commenced by a trained team based on an energy target for relevant indications with matching intake closer to the target calorie intake in accordance with good clinical practices and recommendations that are likely to minimize the risk of PN-related complications and allow a safe use of SPN or exclusive PN (3,12,24-26).

Indeed, studies comparing calorie administration via full EN with exclusive PN or EN+SPN in critically ill patients have revealed inconsistent findings (3,9). Increased mortality risk in late SPN than in EN, higher percentage of alive discharge from ICU in the late PN than in early PN, no difference in ICU and in-hospital mortality between late and early PN, prolonged or shorter hospital LOS in early PN than in late PN, as well as shorter stay in the EN group than in the PN groups and increased ICU stay but improved hospital mortality in the EN+SPN strategy than in the EN strategy were reported (9,10,18-20,27-30).

Notably, while the EN and EN+SPN groups had similar mortality rates in our cohort, a lower mortality rate and improved nutritional status in terms of CRP and pre-albumin levels were noted among achievers than among non-achievers of the target calorie intake in our cohort regardless of the type of clinical nutrition.

This appears to emphasize the importance of a precise determination of the energy target as well as the likelihood of achieving an improved nutritional status by using a nutritional algorithm that focused on achieving the target calorie intake within 3 days via full EN or immediate use of SPN, whenever EN fails to meet energy needs (3,31).

In a previous study regarding full EN followed for a total of 750 feeding days, patients with a delayed target time were reported to have a higher mortality rate than those with a target time of <4 days (32). Although NRS 2002 scores were poorer in cases with in-hospital mortality than with cases of discharge and in achievers than non-achievers of target calorie in the EN+SPN group in our cohort, no significant difference was noted in early (≤ 5 day) versus late (>5 day) achievers of the target calorie intake in terms of discharge and mortality rates as well as NRS 2002 scores. Also, data from a meta-analysis of 16 studies involving 3473 critically ill patients showed no survival benefit in the delivery of increased calories via the enteral route, with or without SPN (33).

Overall, hemodynamic instability, procurement problems, and oral reluctance were the main reasons for failure to achieve the target calorie intake in our cohort on feeding days. Along with higher in-hospital mortality rate and lesser likelihood of improved CRP levels, the ICU unit was associated with a higher likelihood of almost all problems encountered during clinical nutrition compared with the general ward in the present cohort. This appears consistent with the consideration of maximum of 52%-70% of prescribed calories to be actually delivered through EN in the ICU patients due to factors limiting continuity of nutrition, such as frequent radiologic or endoscopic investigations, inadequate routine nursing procedures, surgery, and technical problems regarding nutrition pumps or feeding tubes (26,34-36).

An analysis of factors leading to a reduction in EN prescribed by a nutritional support team in a past study has revealed that 80% of the target feeding volume was achieved on day 4 by 80% of the patients (36). While the nutritional support was implemented by a well-trained and experienced nutrition team based on a protocol insisting on achieving the target calorie intake within the first 3 days of nutritional plan, the intake was achieved at an average of 5 days in our cohort with records of failure to achieve target calorie in 18.8% of feeding days. Achievers of the target calorie intake via this algorithm had a lower mortality rate and improved nutritional status in terms of CRP and pre-albumin levels as well as NRS 2002 scores compared with non-achievers, emphasizing the timely elimination of problems limiting the achievement of daily calorie target in a better clinical outcome.

In this regard, higher frequency of hemodynamic instability and oral reluctance on feeding days failed to achieve the target calorie intake, while procurement problems and technical problems on daily records with achievement of the target calorie intake seem notable. This seems to emphasize the higher potential of patient-related factors, such as hemodynamic instability and oral reluctance, compared to external factors, such as procurement problems and technical difficulties, in causing inadequate intake and failure to achieve full caloric needs.

Besides higher prevalence of procurement problems, such as skipped application by healthcare staff or delay in product supply in case of EN than EN+SPN nutrition seems to emphasize more careful implementation of SPN by healthcare personnel possibly due to higher likelihood of PN rather than EN to be perceived as a medical intervention.

The major strength of this study seems to be the provision of adequate nutritional support by a well-trained and experienced nutrition team and based on an algorithm that insisted on achieving the target calorie intake within the first 3 days of nutritional plan, which may contribute to extend the knowledge achieved in improving adequacy of clinical nutrition among hospitalized patients. However, certain limitations to this study should be considered. First, it is impossible to establish any cause and effect relationships due to the cross-sectional design. Second, relatively low sample size might prevent us to achieve the statistical significance concerning the clinical outcome with respect to timing of achieved the target calorie intake.

In conclusion, our findings emphasize the role of precise determination of the energy target and keeping intake closer to target calories alongside the immediate use of SPN, whenever full EN fails to achieve the target calorie intake, in improving adequacy of clinical nutrition in the early phase of critical illness. Lower mortality rate and improved nutritional status in achievers than in non-achievers of the target calorie intake regardless of the type of nutrition seems to emphasize the benefits of using a protocol that insists on achieving the target calorie intake within the first 3 days of the nutritional plan. Further studies on the provision of adequate nutritional support among critically ill patients are needed addressing clinical outcomes associated with the timing and the route of administration to enable an optimal level of nutritional support matching the nutrition requirements of patients.

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Informed Consent: Written informed consent was obtained from patients who participated in this study.

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