ORIGINAL RESEARCH

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Association Between Achievement of Nutritional Goals and Refeeding Syndrome in Patients Receiving Enteral or Parenteral Nutrition

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Abstract

Objective: The aim of this study was to compare the frequency of refeeding syndrome (RS) in achieving nutritional goals in patients planned to receive enteral nutrition (EN) or parenteral nutrition (PN) treatment, and to compare outcomes between patients aged older and younger than 60 years.

Materials and Methods: This retrospective study included patients who received EN or PN and were followed up at Hacettepe University Faculty of Medicine Adult Hospital between January 2023 and December 2024. Patients were grouped as achieving ≥70% or <70% of the target in clinical nutrition therapy (NT). A serum phosphorus level <2.5 mg/dL was considered RS.

Results: A total of 723 patients were evaluated, comprising 350 (48.4%) females and 373 (51.6%) males, with a median (interquartile range) age of 62.3 (17.0) years. Based on the rate of goal attainment, 432 patients (59.7%) achieved <70% of the target in clinical NT. RS was significantly more frequent in patients who achieved ≥70% of the target ($p = 0.035$). In the EN group, RS was more common among patients who met ≥70% of the target ($p = 0.023$). The multivariate regression analysis results showed that after adjusting for age, sex, body mass index, chronic obstructive pulmonary disease, length of hospital stay and type of NT, achieving ≥70% of the target increased the risk of developing RS (odds ratio :1.86, 95% confidence interval: 1.051-3.316, $p = 0.03$).

Conclusion: The higher risk of RS in patients who achieve the target in clinical nutrition, especially among those receiving EN, appears to be a barrier. While caloric goals are being achieved, patients receiving clinical NT should be monitored with respect to RS.

Keywords: Enteral nutrition, hypophosphatemia, older adults, parenteral nutrition, refeeding syndrome

Introduction

Malnutrition (MN) is defined as a condition involving changes in body composition, particularly a reduction in fat-free mass, and a decrease in body weight due to inadequate nutrient intake, which leads to deterioration in physical and mental functions and worsened clinical outcomes, according to the European Society for Clinical Nutrition and Metabolism (ESPEN) (1). Early identification of MN contributes to the reduction of healthcare costs, morbidity, and mortality (2,3). Refeeding syndrome (RS) is a severe electrolyte or fluid imbalance that occurs in malnourished patients when nutrition therapy (NT) (oral, enteral, or parenteral) is initiated too aggressively after a period of inadequate nutrition (1). RS was first identified in the 1940s among starved prisoners of war who developed complications after refeeding (4). In the literature, the overall prevalence of RS has been reported across a wide range due to variations in

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diagnostic criteria and differences in patient populations (5). More specifically, multicentre randomized studies conducted on hospitalized acute medical patients have shown that the incidence of RS during NT in malnourished individuals ranges from 8% to 14.6% (6).

RS is primarily driven by an insulin surge following carbohydrate intake, leading to intracellular shifts of phosphate, potassium, and magnesium (7). Following MN, high-calorie nutritional intake may lead to electrolyte imbalances (particularly hypophosphatemia, hypokalemia, and hypomagnesemia), decreased vitamin levels (particularly vitamin B1, thiamine), fluid imbalances, and salt retention. These conditions may present with cardiac and neurological side effects, impaired organ function, and, in severe cases, death and prolonged hospital stay (6). Hypophosphatemia, a hallmark feature of this syndrome may result in a wide range of clinical manifestations, including rhabdomyolysis, haemolysis, respiratory failure, musculoskeletal impairments, and reduced cardiac contractility (8).

A number of factors heighten the risk of RS. Individuals with a body mass index (BMI) under 16 kg/m^2, those who have lost more than 15% of their body weight unintentionally within the past 3-6 months, those who have experienced prolonged inadequate intake, or those who begin NT with already reduced phosphate, potassium, or magnesium levels are considered particularly vulnerable. Additional risk factors include a history of alcohol misuse or the use of certain medications such as insulin, chemotherapy, antacids, or diuretics (9).

Clinical guidelines recommend early initiation of nutrition in critically ill and malnourished patients (10). However, rapid progression to full caloric intake increases the risk of RS (11). Studies have shown that aggressive refeeding, particularly during the first 72 hours, correlates with higher morbidity (12). Given that a gradual increase in caloric intake could mitigate the risk of RS-related complications, risk stratification and individualized caloric advancement protocols are crucial. The aim of this study was to compare the frequency of RS in patients receiving enteral nutrition (EN) or parenteral nutrition (PN), with particular emphasis on success in achieving individualized nutritional goals. By evaluating the incidence of RS and its relationship to nutritional outcomes in each group, it is hoped to contribute to evidence-based guidance in the selection and management of NTmodalities.

Materials and Methods

The study protocol complied with the principles of the Helsinki Declaration. The study was approved by Hacettepe University Health Sciences Research Ethics Committee (approval no: 2025/11-35, date: 20.05.2025). As this was a retrospective study, no written informed consent was obtained from participants.

This retrospective study included 723 patients who received EN or PN therapy and were followed up at Hacettepe University Faculty of Medicine Adult Hospital from January 2023 to December 2024. The patients were categorized based on the proportion of their targeted nutritional intake achieved: those who attained ≥70% of their nutritional goals and those who achieved <70%. The <70% and ≥70% thresholds were selected in accordance with current recommendations and previous studies as pragmatic markers of nutritional goal achievement (13-15). RS was defined as a serum phosphorus level <2.5 mg/dL occurring within the first 5 days following the initiation of EN or PN. Routine blood electrolyte levels were monitored daily, allowing for the timely identification and documentation of any decrease in phosphorus levels to <2.5 mg/dL. This systematic approach ensured that all occurrences of RS following the initiation of NTwere accurately captured. Patients receiving EN were then compared with those receiving PN. Under the supervision of a dietician, individual nutritional targets were set according to the clinical characteristics and metabolic requirements of each patient. In the absence of indirect calorimetry, caloric goals were determined using a weight-based approach of 25-30 kcal/kg/day, consistent with current recommendations (9,13). In accordance with these recommendations supporting the gradual advancement of NT, the achievement of nutritional goals was assessed within the first 5 days after the initiation of NT (16,17). Both the EN and PN groups were further subdivided into groups based on their success in nutritional targets (achieving ≥70% or <70%).

Patients were excluded from the study if they were younger than 18 years, had primary hyperparathyroidism, were taking insulin or diuretics, were undergoing continuous haemodiafiltration for acute kidney failure during NT, or had incomplete data.

Data on each patient's MN assessment results, nutritional therapies, age, sex, educational status, marital status, occupation, living arrangements, and chronic diseases were extracted from patient files in the hospital records system.

Nutritional Assessment

Nutritional status was assessed using the Nutritional Risk Screening (NRS-2002). This is a validated screening tool for MN in adults, which is recommended for use in hospitalized patients to ensure that NT is initiated promptly, thereby helping to prevent potential complications (18-20). The NRS-2002 scale begins with an initial screening comprising four questions. If any of these questions are answered with "yes," indicating a significant deviation from normal, a final screening is performed. This final screening assesses the severity of nutritional impairment and of disease. Each parameter is scored on a scale from 0 to 3. During the validation process, a total score of 3 or more indicates that the patient would benefit from an NT plan (19). Patients with an NRS score of ≥3 were classified as high NRS. Anthropometric data were collected as part of a routine nutritional assessment,

with standardized measurements of weight and height obtained using a digital scale and stadiometer. BMI was calculated as weight divided by height squared (kg/m^2).

Statistical Analysis

Data obtained in the study were analyzed using SPSS v.25.0 (Statistical Package for the Social Sciences). Categorical variables were presented as number (n) and percentage (%). Continuous variables were expressed as mean ± standard deviation values for normally distributed data or as median and interquartile range (IQR) values for non-normally distributed data. Conformity of the data to normal distribution was assessed using the Kolmogorov-Smirnov or Shapiro-Wilk tests and histograms. Between-group comparisons of categorical variables were performed using the chi-square test or Fisher's exact test. The Student's t-test was used to compare two groups of normally distributed continuous variables, and the Mann-Whitney U test was applied to non-normally distributed continuous variables. Relationships between variables were examined using Pearson correlation for normally distributed variables and Spearman correlation for non-normally distributed variables. Variables were initially assessed using univariate analyses comparing patients who developed RS with those who did not. Only variables with a p-value <0.05 in univariate analysis were subsequently entered into the multivariate binary logistic regression model. Binary logistic regression analyses using a backward-selection method were performed in the two groups and were adjusted for confounding variables based on the univariate analysis. A value of $p < 0.05$ was accepted as the level of statistical significance.

Results

Evaluations were made of a total of 723 patients comprising 350 (48.4%) females and 373 (51.6%) males with a median (IQR) age of 62.3 (17.0) years. In the whole sample, 33.2% received EN, and 10.8% developed RS. According to the rate of goal attainment, 432 (59.7%) of the patients achieved <70%, and 291 (40.3%) achieved ≥70% of the target in clinical NT. The comparisons of clinical characteristics and metabolic complications between groups achieving <70% and ≥70% of the target in clinical NT are summarized in Table 1. RS developed in 38 (8.8%) of the patients achieving <70% of the target and in 40 (13.7%) of the

Table 1. Comparisons of the clinical characteristics and metabolic complications between the groups achieving <70% and ≥70% of the target in clinical nutrition therapy.

		Achieving <70% of the target (n = 432)	Achieving ≥70% of the target (n = 291)	p
Age, years, median [IQR]		63.9 [16.3]	60.0 [17.7]	**0.003**
Sex, female, n (%)		215 (49.8%)	135(46.4%)	0.37
BMI, kg/m^2, median [IQR]		23.4 [6.1]	22.1 [8.0]	**0.001**
Nutrition type, enteral, n (%)		130 (30.1)	110 (37.8)	**0.031**
NRS score, median [IQR]		5.0 [2.0]	5.0 [1.0]	**0.031**
Follow up period, days, median [IQR]		11.0 [14.0]	20.0 [23.0]	**<0.001**
Department/unit, n (%)	**Medical ward**	203 (47.0%)	146 (50.2%)	0.078
	Surgical ward	115 (26.6%)	85 (29.2%)	
	ICU	114 (26.4%)	60 (20.6%)	
Comorbidities				
Presence of ≥1 comorbidity, n (%)		304 (70.4%)	181 (62.4)	**0.026**
Diabetes mellitus, n (%)		111 (25.7%)	58 (19.9)	0.14
Hypertension		157 (36.3%)	77 (26.5%)	**0.005**
Coronary arterial disease, n (%)		63 (14.6)	34 (11.7)	0.26
Heart failure, n (%)		23 (5.3)	21 (7.2)	0.30
COPD, n (%)		39 (9.0%)	12 (4.1%)	**0.012**
Chronic renal disease, n (%)		21 (4.9)	18 (6.2)	0.44
Metabolic complications (electrolyte imbalance)				
Hypernatremia		11 (2.5)	5 (1.7)	0.46
Hypokalemia		3 (0.7)	4 (1.4)	0.45
Hyperglycemia		3 (0.7)	1 (0.3)	0.65
Hypophosphatemia		38 (8.8)	40 (13.7)	**0.035**

The variables are presented as number (percentage), median [IQR] or mean ± standard deviation) values. Bold indicates $p < 0.05$.
COPD: Chronic obstructive pulmonary disease, BMI: Body mass index, ICU: Intensive care unit, NRS: Nutritional risk screening, IQR: Interquartile range.

patients achieving ≥70% of the target (p = 0.035). No significant differences were found between the groups with respect to other electrolytes.

Comparisons of clinical characteristics and metabolic complications between in patients receiving EN and PN are summarized in Table 2. No significant difference was found between the EN and PN groups in terms of electrolyte disorders.

The comparisons of metabolic complications between patients achieving <70% and ≥70% of the nutritional target, according to the EN and PN subgroups, are summarized in Table 3. Of the patients receiving EN, the incidence of RS was higher in those who achieved ≥70% of the nutritional target (p = 0.023). In the PN group, no significant differences were found between groups defined according to rates of target achievement. The clinical characteristics and metabolic features were also compared between geriatric and non-geriatric patients, defined as adults aged ≥60 years and <60 years, respectively (Table 4). The non-geriatric group achieved ≥70% of the nutritional target significantly more frequently than the geriatric group (p = 0.006).

The results of the multivariate regression analysis showed that after adjusting for age, sex, BMI, chronic obstructive pulmonary disease (COPD), length of hospital stay and type of NT, achieving ≥70% of the nutritional target increased the risk of developing RS [odds ratio (OR): 1.86, 95% confidence interval (CI): 1.051-3.316, p = 0.03]. Other risk factors for RS development were identified: BMI and the presence of COPD (OR: 0.93, 95% CI: 0.882-0.987, p = 0.015; OR: 2.85, 95% CI: 1.181-6.898, p = 0.02, respectively). The results of the regression analysis are shown in Table 5.

Discussion

The results of this study showed that the rate of RS was higher in patients who achieved ≥70% of the energy goals compared to those who achieved <70%. The development of RS was found to be significantly related to achieving ≥70% of the target independently of age, female gender, BMI, COPD, length of hospital stay and type of NT. This finding suggests that a more aggressive approach to meeting nutritional goals in high-risk patients may be associated with an increased risk of RS.

Previous studies have identified several factors associated with RS, including the amount of energy administered through PN or EN (15,21-24). In a retrospective study that examined hospitalized adults receiving PN, it was indicated that higher energy delivery was independently associated with the development of RS (21). Marvin et al. (15) reported a significantly higher incidence of RS in patients who received more than 70% of their daily energy requirements from PN within the first 24 hours of initiation. From the results of recent studies, RS is thought to result particularly from higher caloric targets and carbohydrate-rich feeding, which triggers increased insulin secretion (22,23). Similarly, reaching

Table 2. Comparisons of the clinical characteristics and metabolic complications in patients receiving EN and PN.

	Patients receiving PN (n = 483)	Patients receiving EN (n = 240)	p
Age, years, median [IQR]	62.0 [22.0]	70.5 [20.0]	**<0.001**
Sex, female, n (%)	235 (48.7%)	115 (47.9%)	0.85
BMI, kg/m², median [IQR]	22.9 [6.4]	22.9 [7.5]	0.49
Presence of ≥1 comorbidity,n (%)	302 (62.5%)	183 (76.6)	**<0.001**
Hypernatremia	9 (1.9)	7 (2.9)	0.42
Hypokalemia	3 (0.6)	4 (1.7)	0.17
Hyperglycemia	1 (0.2)	3 (1.3)	0.10
Hypophosphatemia	49 (10.1)	29 (12.1)	0.44

The variables are presented as number (percentage), median [IQR] or mean ± SD values. Bold indicates p < 0.05.
EN: Enteral nutrition, PN: Parenteral nutrition, IQR: Interquartile range, BMI: Body mass index, SD: Standard deviation.

Table 3. Comparisons of the metabolic complications between patients achieving <70% and ≥70% of the target in the EN and PN groups.

	Patients receiving EN (n = 280)			Patients receiving PN (n = 483)		
	Achieving <70% (n = 130)	Achieving ≥70% (n = 110)	p-value	Achieving <70% (n = 302)	Achieving ≥70% (n = 181)	p-value
Hypernatremia	4 (3.1)	3 (2.7)	1.00	7(2.3)	2 (1.1)	0.34
Hypokalemia	2(1.5)	2(1.8)	1.00	1(0.3)	2 (1.1)	0.55
Hyperglycemia	2 (1.5)	1 (0.9)	1.00	1 (0.3)	0 (0)	1.00
Hypophosphatemia	10 (7.7)	19 (17.3)	**0.023**	28 (9.3)	21 (11.6)	0.41

The variables are presented as number (percentage), median [IQR] or mean ± SD valuess. Bold indicates p < 0.05.
EN: Enteral nutrition, PN: Parenteral nutrition, IQR: Interquartile range, SD: Standard deviation.

the energy goals in the current study was associated with an increased risk of RS.

Age has also been identified as a contributing factor to the development of RS, with incidence rising with age. A systematic review has shown that RS can occur in older adults regardless of the rate of refeeding (20). In the current study, older adults (≥60 years) were less likely to achieve nutritional targets compared with younger adults. This finding was consistent with age-related physiological barriers such as the anorexia of aging, reduced appetite, early satiety and slower gastrointestinal motility (25). These changes limit caloric and protein intake, making it more difficult for older adults to meet therapeutic goals. Advanced age also increases vulnerability to RS due to diminished physiological reserves and a high prevalence of chronic MN. Therefore, clinicians must initiate NT cautiously with slower caloric advancement and close electrolyte monitoring, although reaching the full target can be further delayed (26). Although no significant difference in RS incidence was observed between the geriatric and non-geriatric populations in the current study, ageing remains a substantial barrier to achieving nutritional goals because of impaired intake capacity and the need for conservative refeeding strategies.

A low BMI and the presence of COPD were identified as additional risk factors for RS. Consistent with many previous studies and various guidelines, these findings also showed that lower BMI is a risk factor for RS (15,27). In a study investigating the impact of COPD on RS risk, malnourished patients with COPD who received hypocaloric nutrition were found to have a lower risk of RS and more favourable outcomes (28). In COPD patients, the combination of chronic under-nutrition, systemic inflammation, metabolic alterations, and electrolyte depletion makes them particularly susceptible to RS. Hypoxia contributes to altered glucose and lipid metabolism, and metabolic adaptations during starvation exacerbate electrolyte depletion. Rapid reintroduction of nutrition can lead to significant metabolic shifts when insulin is reactivated (28,29). Many COPD patients,

Table 4. Comparisons of the clinical characteristics and metabolic features between geriatric and non-geriatric patients (adults aged ≥60 and <60 years).

	Geriatric group (n = 439)	Non-geriatric group) (n = 284)	p
Age, years, median [IQR]*	72.0 [12.0]	46.0 [20.0]	**<0.001**
Sex, male, n (%)	234 (53.3%)	139 (48.9%)	0.252
BMI, kg/m², median [IQR]	23.66 [7.03]	21.48 [6.92]	**<0.001**
Nutrition type, enteral, n (%)	177 (40.3%)	63 (22.2%)	**<0.001**
Achieving ≥70% of the target	159 (36.2%)	132 (46.5%)	**0.006**
Presence of ≥1 comorbidity, n (%)	345 (78.8%)	140 (49.3%)	**<0.001**
Diabetes mellitus, n (%)	122 (27.8%)	47 (16.5%)	**0.001**
Hypertension	196 (44.6%)	38 (13.4%)	**<0.001**
Coronary artery disease, n (%)	89 (20.3%)	8 (2.8%)	**<0.001**
Heart failure, n (%)	39 (8.9%)	5 (1.8%)	**<0.001**
Chronic renal disease, n (%)	33 (7.5%)	6 (2.1%)	**0.002**
COPD, n (%)	45 (10.3%)	6 (2.1%)	**<0.001**
Hypophosphatemia	50 (11.4%)	28 (9.9%)	0.517

*Age is presented as median [Q1-Q3] for the geriatric group (72 [67-79] years) and the non-geriatric group (48 [38-55] years). Bold indicates $p < 0.05$.
BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, IQR: Interquartile range.

Table 5. The binary regression analysis results of risk factors for Refeeding syndrome

	Odds ratio	95% CI	p
Sex, female	0.872	0.501-1.518	0.629
BMI	0.933	0.882-0.987	**0.015**
Follow-up period, days	0.990	0.973-1.006	0.223
COPD	2.854	1.181-6.898	**0.020**
Age, years	1.006	0.989-1.023	0.513
Type of nutrition therapy, enteral	0.885	0.482-1.623	0.692
Achieving ≥70% of the target	1.867	1.051-3.316	**0.033**

Bold indicates $p < 0.05$.
BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, CI: Confidence interval.

particularly those in advanced stages, have reduced caloric intake for extended periods because of dyspnea while eating, fatigue, or depression; this meets one of the key RS risk criteria (i.e., little or no nutritional intake for more than 10 days). This supports the hypothesis that NT in COPD patients carries a higher risk of RS and should be managed carefully. As these patients are at high-risk of MN due to their underlying disease and altered catabolism, NT should be tailored to mitigate catabolic effects and prevent overfeeding (30).

According to the current study findings, RS in the EN group was more frequently observed among patients who achieved ≥70% of their nutritional target, whereas no significant difference was found in the PN group. RS has been reported in EN at rates more than two-fold higher than in PN (31). Regardless of the method used to estimate calorie targets (e.g., Harris-Benedict equation, kcal/kg, etc.), the importance of avoiding overfeeding has been emphasised (31). Incretins are hormones secreted from the gut in response to food intake that enhance insulin secretion from the pancreas (32). During EN, increased incretin activity may amplify the insulin response, resulting in accelerated electrolyte shifts and an increased risk of RS. The incretin effect, first described in the 1960s, refers to the greater insulin secretion observed when glucose is administered orally rather than intravenously. This phenomenon is attributed to the production of enteral hormones such as gastric inhibitory polypeptide and glucagon-like peptide-1, which enhance insulin secretion from pancreatic β-cells (33). Therefore, careful adjustment of the glycemic content and feeding rate is especially important in EN (34). Further research is needed to clarify the clinical significance and optimal management of NT via enteral or parenteral routes. It is important for clinicians to assess the risk of RS and take appropriate preventive measures.

One recommended practices is to initiate energy intake at a maximum of 50% of the planned target (500-1000 kcal/day). Starting at 20 kcal/hour on the first day, energy intake should be gradually increased over the course of a week until full nutritional requirements are met and the patient is metabolically stable (10). In addition, the American Society for Parenteral and EN (ASPEN) recommends starting NT at a reduced caloric intake (approximately 10 kcal/kg/day) for patients at high-risk of RS, with careful monitoring and gradual increases over several days (4). NICE recommends providing no more than 50% of the estimated target energy and protein requirements during the first two days of feeding in seriously ill or injured individuals receiving tube feeding or PN (22). It is known that critically ill patients are more frequently exposed to overnutrition than to undernutrition (35). In a study comparing restricted and continuous standard calorie intake during the management of RS in critically ill adults, a protocol for restricted calorie intake was shown to be a suitable option in terms of avoiding RS (12). Another study conducted on intensive care unit (ICU) patients reported that higher mortality was observed in those receiving high caloric intake (≥66%), while moderate caloric intake (33-65% of the target) was associated with the most favourable outcomes (36). Although various guidelines have been published, there is no definitive evidence identifying a specific feeding rate and target calories, which would reliably prevent the development of RS (4,10,37). While no significant association with RS was found among ICU patients in the current study, ≥70% of the energy target was identified as a risk threshold in the overall population. Although current nutritional guidelines consistently recommend initiating energy delivery at a reduced rate and gradually increasing to meet target requirements, healthcare professionals seem to lack awareness regarding the risks associated with RS. The most important preventive or protective measures are adequate assessment of high-risk patients and proper treatment planning and follow-up. It is vital that the refeeding protocol be adapted to suit each patient's clinical condition, rather than simply focusing on their calorie target. Thus, it is imperative to implement a controlled hypocaloric nutritional intake strategy in order to mitigate the risk of RS (38). This approach is essential and must be administered by a multidisciplinary team of healthcare professionals.

Study Limitations

The majority of previous studies have incorporated hypophosphatemia, either as a defined cutoff or as a relative decrease from baseline, as a component of their definitions (the range varied from phosphate <1 mmol/L (below the normal range) to <0.32 mmol/L, or as a decrease from baseline >30% or >0.16 mmol/L). However, relying exclusively on hypophosphatemia to identify risk may lead to misclassification, as there are many other potential causes of reduced serum phosphate levels. Although the ASPEN consensus recommendations propose a broader definition of RS based on proportional decreases in serum phosphorus, potassium, and/or magnesium levels following nutritional replenishment, there is currently no universally accepted diagnostic definition of RS (5,39). Notably, ESPEN guidelines do not provide specific diagnostic cutoffs or formal diagnostic criteria for RS. Instead, hypophosphatemia has consistently been described as the hallmark biochemical abnormality of the syndrome and has been widely used in observational studies and systematic reviews as an operational definition. Furthermore, a systematic review demonstrated substantial heterogeneity among published definitions, with most studies incorporating hypophosphatemia either as an absolute threshold or as a relative decline from baseline (5). Given the retrospective design of the currrent study and the limited availability of all ASPEN diagnostic components, hypophosphatemia (serum phosphorus <2.5 mg/dL) was used as a pragmatic surrogate marker for RS (8). An important limitation of this study was that the retrospective design prevented a comprehensive assessment of several potential confounding

factors associated with RS, including malignancy burden, infection or sepsis status, ICU-related interventions, baseline serum phosphate levels, and the use of corticosteroids, alcohol, antacids, or chemotherapeutic agents. Therefore, residual confounding cannot be excluded. Another limitation of the study was that, had it been designed prospectively, the incidence of RS over time could have been evaluated more objectively, and there would have been an opportunity to observe RS that patients developed during the follow-up period. Because the study was retrospective, detailed data on specific nutritional formulations, macronutrient composition, and stepwise caloric advancement protocols were not systematically recorded in patient files, since EN and PN decisions were made at the discretion of the treating clinical team in accordance with current guidelines. The effect of feeding rate on RS development could not be evaluated separately. Nevertheless, all RS cases were assessed within the first 5 days after the initiation of NT, a period recognized as the highest-risk window for RS.

One of the strengths of this study was the large sample size and the use of electronic medical records for data collection, which together ensured data accuracy and reliability. The onset of RS was reported while electrolyte concentrations were monitored daily during the follow-up period. This allowed RS to be detected as soon as it developed. In many studies, patients receiving EN or PN have been analyzed separately. However, the inclusion of both groups in the current study's patient population allowed a more objective and comprehensive comparison. The use of the NRS in all patients was another strength of this study. Rather than using BMI, weight loss, or dietary intake history in isolation, combining these individual variables into a single NRS score provides a practical and accessible tool for identifying patients at risk of RS due to MN.

Conclusion

The main finding of this study was that the risk of RS was higher in patients receiving NT with higher energy targets (≥70% of the goal). RS was seen to be significantly associated with achieving ≥70% of the target independently of age, female gender, BMI, COPD, length of hospital stay and type of NT. Given that the risk appears particularly relevant in EN, further large-sample studies are needed to define optimal initiation and progression protocols specific to enteral NT routes. While achieving caloric goals is fundamental in NT, a cautious and personalized approach is required to avoid RS. Awareness, prevention, and vigilant monitoring can allow for safe advancement in NT without compromising patient safety. Further prospective studies are needed to validate these findings and establish optimal feeding strategies to prevent the development of RS.

Ethics

Ethics Committee Approval: The study protocol complied with the principles of the Helsinki Declaration. The study was approved by Hacettepe University Health Sciences Research Ethics Committee (approval no: 2025/11-35, date: 20.05.2025).

Informed Consent: As this was a retrospective study, no written informed consent was obtained from participants.

Footnotes

Authorship Contributions

Concept: E.S.A., P.K., Design: E.S.A., P.K., Data Collection or Processing: E.S.A., P.K., Analysis or Interpretation: E.S.A., P.K., Literature Search: E.S.A., P.K., Writing: E.S.A., P.K.

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