Original Article

Relationship between energy intake, prognosis and related indicators in adults after cardiac, thoracic, and vascular surgery: A prospective observational study

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Background and Objectives: The study aimed to explore the association between energy intake (EI), the proportion of enteral nutrition intake (EN%), and prognostic-related indicators. **Methods and Study Design:** This was a prospective observational study. Patients aged 18-80 years old, who had undergone cardiothoracic surgery, were enrolled between January 2017 and January 2018. The measured REE (mREE) was evaluated by indirect calorimetry (IC). The observational data on EI, EN% and EI/mREE% were collected following admission to ICU, ICU discharge, and prior to discharge. **Results:** A total of 160 patients (60.6% male) were studied. The prealbumin and total protein were positively correlated with EN% at the time of ICU discharge; liver function index levels were negatively correlated with EI/mREE% at discharge ($p<0.05$). Multiple linear regression indicated that ALT levels as well as EI/mREE% were related to the duration of mechanical ventilation; ALT, AST, APACHE II were related to the ICU duration; EN% and EI/mREE% were related to the length of stay (LOS) following ICU discharge. EN% was related to the LOS in the hospital. **Conclusions:** The patients treated cardiothoracic surgery demonstrated associations of EN% with LOS in the hospital. Increased EN% and EI/mREE% were associated with higher serum protein levels and maintain normal liver function.

Key Words: energy intake, postoperative period, length of stay, indirect calorimetry

INTRODUCTION

Nutritional support plays an important role in critically ill patients.[1-5] Insufficient energy intake has been shown to be associated with longer durations of ventilator dependency, hospital and ICU stay. It is also related to disease complications and mortality.[6-8] It has been shown that nutritional support of patients following gastrointestinal surgery can improve their disease prognosis, whereas when this is applied to patients who have undergone non-gastrointestinal surgery, the exploration of optimum nutritional support mode is still limited.[9] Up to now, the exact way by which reasonable nutritional support affects the disease status remains controversial. It has been suggested that appropriate nutritional support should be provided according to the patient clinical status. Excessive nutritional support is not conducive to disease prognosis.[10-12] The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N) recommends that critically ill patients with a BMI of ≥30 kg/m^2 should receive 50-70% of the estimated energy requirements.[11] With regard to nutritional support, early postoperative resumption of oral intake is safe and should be encouraged within enhanced recovery protocols. However, in the case of severe postoperative complications or poor tolerance of oral food following the operation, supplementary artificial nutrition should be immediately initiated.[3,13] Although total parenteral nutrition is successful in meeting adequate and complete nutritional needs, it is associated with several potential complications.[1,14,15]

LOS is one of the major factors, which affect hospital

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Manuscript received 30 August 2021. Initial review and accepted 01 September 2021.
doi: 10.6133/apjcn.202109_30(3).0003

costs. According to the previous literature, plasma protein, liver function, and other biochemical indexes in perioperative patients can reflect the changes in the patient's condition and prognosis.[16-25] Here, we call them "prognostic indicators." However, these "prognostic indicators" are not well studied in the LOS of patients after cardiothoracic surgery, the relationship between these indicators and energy intake is not clear. For patients after cardiothoracic surgery, what is the role of postoperative nutritional support, especially enteral nutrition? Can it benefit the prognosis? If the improvement of nutritional intake is related to LOS, is it improving "prognosis indicators"?

Previous studies have used the energy predictive equations to determine the nutritional needs of patients following surgery. It has been shown that the results derived from the predictive equations are very different from those derived from the measured results.[26-30] However, due to the limited conditions, the indirect calorimetry cannot be fully developed, as shown in several previous studies, which may lead to inaccurate research results. IC is a gold standard used in REE measurement. Currently, the development of specific IC equipment has enabled the successful applications of IC.

In the present study, mREE measurement was used as the standard to evaluate energy intake. The purpose of the present study was to describe prognostic-related indicators and energy intake by determining energy consumption and calculating energy intake of patients. Moreover, we aimed to identify risk factors associated with LOS in order to assess the prognostic-related indicators and the nutritional strategy that can be used with disease prognosis.

METHODS

Patients

Patients with esophageal or heart disease who were admitted to the Department of Cardiothoracic Surgery in a hospital during January 2017 and January 2018 underwent thoracic surgery and were subsequently transferred to the cardiothoracic surgery ICU. Patients with valvular disease were operated by valvuloplasty or valve replacement. Coronary artery bypass grafting (CABG) was performed in patients with coronary heart disease. Patients with esophageal disease were treated with tumor resection. The inclusion criteria were the following: (1) cardiothoracic surgery patients operated at a hospital; (2) patients who received mechanical ventilation (Drägerwerk AG & Co. Evita 4, Lübeck, German) following surgery; (3) patients who satisfied conditions of REE measurement and completion of measurements on the day of admission to the ICU; (4) patients aged 18–80-years old. The exclusion criteria were the following: (1) patients with respiratory instability who required frequent adjustment of mechanical ventilation parameters; (2) patients with surgical complications who required timely treatment, which resulted in interruption or reduced accuracy of REE measurements; (3) patients who could not cooperate with the dietary survey due to hearing impairment or mental problems; (4) patients who experienced at least one rescue after operation; (5) patients who died during hospitalization.

The present study was approved by the Ethics Committee of the Hospital with the approval number XHEC-C-2017-086. The researchers fully communicated with the patients and obtained informed consent prior to the study. The study design flow chart is shown in Figure 1.

Measured energy expenditure (mREE)

The mREE measurement was completed by three medical nutrition experts whose work experience was 1, 3, and 10 years, respectively. Inspiratory and expiratory gases were sampled via a sole port to tracheal intubation and measured by the analyzer of the machine (GE Datex-Ohmeda S/5tm), which was calibrated according to the manufacturer's specifications prior to each measurement. The data

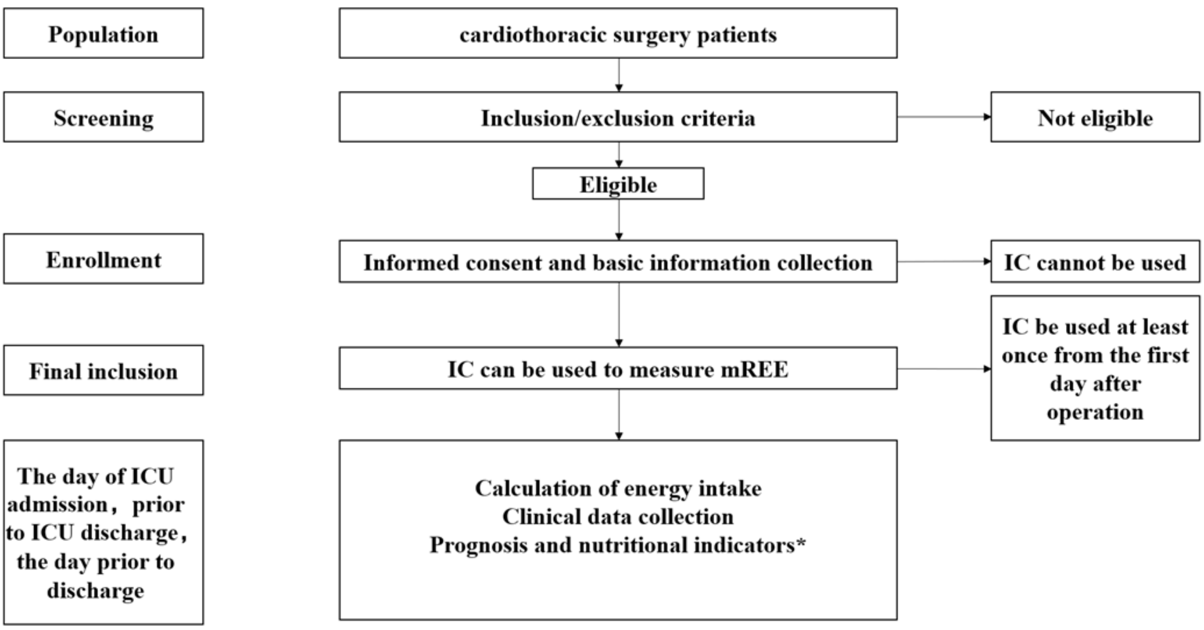

Figure 1. Study design flow chart. *Prognosis and related indicators: duration of mechanical ventilation, ICU duration, LOS following ICU discharge, LOS in hospital; blood glucose, lactic acid, HB, albumin, pre-albumin, total protein, ALT, AST, total bilirubin, direct bilirubin, urea nitrogen, urea creatinine.

were expressed in the form of 24-h energy consumption (kcal/d).[30,31] The first measurement was carried out on the day of admission to ICU when the situation was initially stable. Provided the patients met the conditions of the determination, the REE was measured once a day from 10 to 12 am. The final mREE was the average of all the aforementioned results.

Calculation of energy intake

Oral and enteral nutrition and intravenous rehydration programs were implemented by a cardiothoracic surgeon with 10-year work experience in the cardiothoracic surgery intensive care unit. In case of requiring "all-in-one" parenteral nutrition, the program was implemented by a nutrition medical expert unrelated to the present study with 20-year work experience. Energy intake included oral or digestive tract intake of nutrients and energy-containing intravenous administrations, including "all-in-one" PN, glucose, and amino acid injection. The EN formula was a mass-produced commercial preparation. The hospital meals were prepared by the chefs working in the Nutrition Department of the hospital according to the production standards. Nutrition medical staff used 24-hour recall methods, medical records and received the assistance of the patient family and ward staff to record nutrition intake. The nutrition medical experts who calculated nutrition intake held the qualification of registered dietitian (RD) issued by the Chinese Nutrition Society and had 10-year work experience in the field. The energy intake was calculated at three different time points--the day of ICU admission, the day of ICU discharge, and the day prior to discharge. The final results were expressed in kcal/d.

Clinical data collection

Personal data, including gender, body height, body weight (BW), disease, diagnosis, treatment, acute physiology and chronic health evaluation II (APACHE II) score, were recorded according to the patients' medical history. Weight and height were measured by trained nurses using the same equipment under standard procedures following hospitalization of the patients. The body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Obesity or overweight (OB/OW) status was defined as BMI ≥24.0 kg/m^2, whereas malnutrition was defined as BMI <18.5 kg/m^2 and normal weight as 18.5≤ BMI <24.0 kg/m^2. Fasting blood samples were extracted from nurses and sent to the laboratory department of the hospital for determination of serum pre-albumin, total protein, albumin, urea nitrogen, and creatinine levels. Blood glucose and lactate levels in the fasting state were measured by a blood gas analyzer at 6 pm on the day of ICU admission. Blood glucose and blood gas were measured at 10 am on the day of ICU discharge, 3h prior to the last meal of the patients. The specific indices reflecting prognoses, such as length of hospital stay and ICU stay, the duration of mechanical ventilation, and length of hospital stay following ICU discharge, were obtained from medical records.

Statistical analysis

Statistical analysis was performed using SPSS Statistics version 25.0 statistical software (IBM Co., Armonk, NY, USA). Categorical variables are reported as numbers and percentages (%) and continuous data as mean (SD), in case the data followed a normal distribution pattern, or as median (interquartile range [IQR]) in case the data were not normally distributed. The Shapiro-Wilk test was used for assessing the normality of the sample distribution. Categorical variables were compared using the Chi-square test. One-way analysis of variance (ANOVA) was used to compare the difference of patients' characteristics among different types of the operation group; Repeated measures analysis of variance (repeated measure ANOVA) was also used to compare the difference among the energy intake (EI) of the same individual on the day of ICU admission, on the day of ICU discharge and on the day prior to discharge. In the case of equal variance, the LSD method was used for multiple comparisons; in the case of unequal variance, the Dunnett's T3 method was used. Partial correlation analysis was used to assess the correlation between EI and prognosis and other nutritional indicators after controlling variables. Multivariate linear regression was used to explore the indicators associated with prognosis. $p<0.05$ indicated statistically significant differences.

RESULTS

Characteristics of all the subjects

According to the type of operation, the patients were divided into coronary surgery group, valve surgery group, and esophageal surgery group. Significant differences were noted in the parameters age, height, body weight, BMI, LOS in hospital following ICU discharge, duration of mechanical ventilation, and LOS in ICU among the different groups (all $p<0.05$). No significant differences were noted in the parameters operative time, mREE, APACHE II score, and LOS in hospital among groups (all $p>0.05$). The Chi-square test indicated that the obesity rate of the coronary artery bypass group was higher than that of the valve surgery group (χ^2=8.976, p=0.003) and the esophageal surgery group (χ^2=12.318, p=0.0001). In contrast, no significant differences were noted between the valve surgery and the esophageal surgery groups (χ^2=2.411, p=0.120). No significant differences were noted in the malnutrition rate among the three groups (χ^2=0.102, p=0.749; χ^2=2.188, p=0.139; χ^2=3.650, p=0.056). The differences between the groups are noted in Table 1.

Characteristics of energy intake and related indicators

Repeated measure ANOVA was performed. The total protein derived from the patients following operation was gradually increased ($p<0.05$). No significant differences were noted with regard to albumin and pre-albumin levels ($p>0.05$). The levels of CRP, blood glucose, and lactic acid exhibited a downward trend post-surgery (all $p<0.05$). Urea nitrogen levels were increased on the day of ICU discharge and subsequently decreased ($p<0.05$). No significant differences were noted with regard to urinary creatinine levels ($p>0.05$).

The changes in energy intake (EI) and nutritional indicators were observed at three different time points, namely the day of ICU admission, the day of ICU discharge,

Table 1. Characteristics of all the subjects between different surgery groups

	Coronary artery bypass (n=57)	Valve surgery (n=78)	Esophagus surgery (n=25)	Total (n=160)	*p*-value
Age (years)	64.2±9.58	55.8±11.1†	65.6±8.37‡	60.3±11.1	<0.001
Male, n (%)	44 (77.2)	33 (42.3)†	20 (80.0)‡	97 (60.6)	-
Weight (kg)	67.7±9.68	62.4±11.5†	60.6±9.98†	64.0±11.0	0.004
Height (cm)	168±7.05	163±7.00†	167±7.56‡	165±7.42	<0.001
BMI (kg/m^2)	24.0±2.58	23.3±3.25	21.6±3.12†‡	23.3±3.09	0.005
BMI classification, n (%)					
OB/OW	33 (57.9)	25 (32.1)†	4 (16.0)†	62 (38.8)	
Normal	22 (38.6)	50 (64.1)†	17 (68.0)†	72 (55.6)	
Malnutrition	2 (3.5)	3 (3.8)	3 (16.0)	5 (5.6)	
Operative time (min)	249±54.3	254±48.7	252±60.8	252.1±52.4	0.892
mREE (kcal/d)	1862±387	1956±413	1794±542	1898±429	0.192
APACHE II	7.81±2.39	6.92±2.41†	7.56±1.81	7.34±2.34	0.083
Duration of mechanical ventilation (d)	0.94 (1.25)	0.99 (1.15)	0.27 (0.48) †‡	0.93 (1.14)	<0.001
LOS in ICU (d)	3.82 (3.5)	3.76 (2.97)	0.83 (1.08)†‡	3.69 (3.82)	<0.001
LOS following ICU discharge (d)	7.63 (3.01)	8.90 (5.68) †	10.9 (3.06) †‡	8.71 (4.92)	<0.001
LOS in hospital (d)	17.5 (10.0)	20.9 (13.7)	19.7 (5.66)	19.9 (10.02)	0.143

BMI: The body mass index was calculated as weight/height^2 (kg/m^2); OB/OW: obesity or overweight was defined as BMI ≥24.0 kg/m^2; malnutrition was defined as BMI <18.5 kg/m^2; mREE: measured Energy Expenditure; APACHE II: acute physiology and chronic health evaluation II; LOS: length of stay.
†Compared with coronary artery bypass group, the differences were statistically significant.
‡Compared with valve surgery group, the differences were statistically significant.

and the day prior to discharge. The parameters EI at the different time postoperative periods were 518±230 kcal/d, 1916±471 kcal/d, and 1779±379 kcal/d, respectively. The parameter EI/mREE% was 28.5±14.0%, 105±33.5%, and 97.2±28.5% for the three different groups, respectively. The parameter EN% was estimated to 0%, 73.8±28.8%, and 97.0±15.8% for the three groups, respectively. EI (kcal/d), EN (kcal/d), and EN% were increased, while PN (kcal/d) and PN% were decreased following operation (all $p<0.05$). The results are shown in Table 2 and Figure 2.

Correlation analysis of energy intake and prognostic indicators

Following adjustment for age and gender, the partial correlation analysis indicated that the EI/mREE% and EN% variables were associated with prognostic indicators (duration of mechanical ventilation, ICU duration, LOS following ICU discharge, LOS in hospital) at different time points following operation. A certain correlation was noted between enteral nutrition feeding indices and specific prognostic -associated indices. A correlation was noted between lower EI/mREE% and higher liver function.

The correlation coefficient and p-value are shown in Figure 3. EN% was also related to plasma protein, prealbumin, and total protein levels. The relationship between them is shown in Figure 4.

Multiple linear regression analysis

Multiple linear regression was used to evaluate the prognostic factors. The data indicated that ALT and blood glucose levels, as well as EI/mREE%, were related to the duration of mechanical ventilation. In addition, the parameters ALT, AST, HB, APACHE II score, blood glucose were related to ICU time; EN%, urea nitrogen, and EI/mREE% were related to LOS following ICU discharge. The variables EN% and urea creatinine were associated

Table 2. The characteristics of nutritional indicators and other related indicators at different post-surgical time periods

	The day of ICU admission	The day of ICU discharge	The day prior to discharge	*p*-value
Prealbumin (mg/ L)	196±41.2	180±49.9	188±43.6	0.150
Total protein (g/ L)	57.5±7.64	59.9±5.78†	62.2±5.86†‡	<0.001
Albumin (g/ L)	36.6±4.20	36.4±3.75	35.6±3.54	0.601
CRP (mg/ L)	55.5±29.6	58.3±43.4	25.2±19.1†‡	0.001
HB (g/ L)	113±17.9	102±17.0†	109±17.9†‡	<0.001
ALT (U/ L)	25.0 (19)	24.5 (32.3)	29.5 (43.3)	0.328
AST (U/ L)	62.0 (68)	29.5 (23.8)	26.0 (22.3)	0.343
Total bilirubin (μmol/ L)	17.4 (13.7)	13.7 (10.7)†	10.6 (8.70)†‡	<0.001
Direct bilirubin (μmol/ L)	6.75 (6.58)	5.15 (5.00)†	3.95 (3.68)†	0.006
Urea nitrogen (mmol/ L)	7.67 (3.76)	8.59 (5.19)†	7.51 (4.00)‡	<0.001
Urea creatinine (μmol/ L)	70.0 (32.0)	65.5 (26.8)	68.0 (39.0)	0.144
Blood glucose (mmol/ L)	9.20 (5.13)	8.25 (3.28)†	-	0.027
Lactic acid (mmol/ L)	2.45 (3.28)	1.70 (1.00)†	-	<0.001

ICU: intensive care unit; CRP: C-reactive protein; HB: hemoglobin; ALT: alanine aminotransferase; AST: aspartate aminotransferase.
†Compared with "The day of ICU admission" group, the difference was statistically significant.
‡Compared with "The day of ICU discharge" group, the difference was statistically significant.

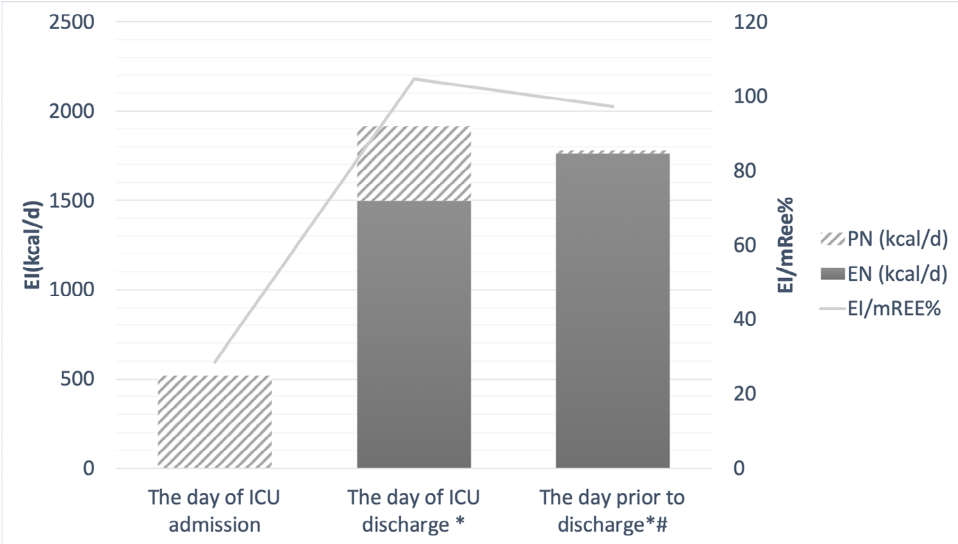

Figure 2. The characteristics of energy intake post-surgery. *Compared with "The day entering ICU" group, the difference was statistically significant. #Compared with "The day leaving ICU" group, the difference was statistically significant. EI: Total energy of oral or enteral nutrition intake and parenteral nutrition intake. EN%: Percentage of oral or enteral energy intake in EI. EI/mREE%: Percentage of total energy intake in measured REE.

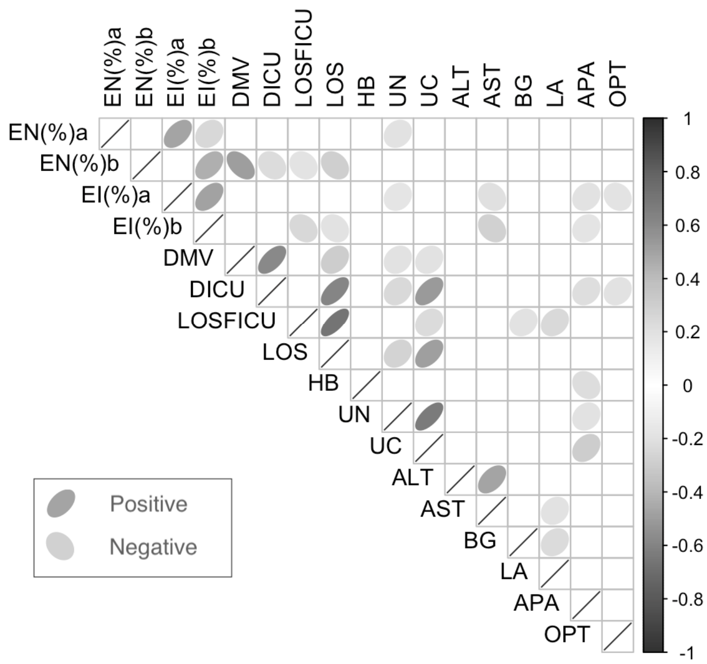

Figure 3. Partial correlation coefficients between analysed variables. Only significant correlations are shown (p<0.05). Colour intensity and size of the ellipse are proportional to the correlation coefficients. a: refers to the data on the day prior to ICU discharge; b: refers to the data on the day prior to discharge. DMV: duration of mechanical ventilation (d). DICU: ICU duration (d). LOSFICU: LOS following ICU discharge (d). LOS: LOS in hospital (d), OPT: operative time (min). APA: APACHEII score. EI%: EI/mREE (%). UN: urea nitrogen (mmol/L). UC: urea creatinine (μmol/ L). BG: blood glucose (mmol/ L). LA: lactic acid (mmol/ L).

with the LOS in the hospital. The results are listed in Table 3.

DISCUSSION

The present study recorded and calculated the energy intake of patients undergoing thoracotomy in cardiothoracic surgery and assessed the association between energy intake and prognostic indicators. The present study supports the conclusion that energy intake, especially EN%, is related to the improvement of LOS and prognosis-related indicators of patients who have undergone cardiac, thoracic, and vascular surgery; besides, insufficient nutrition intake was associated with higher levels of liver function and lower levels of pre-albumin and total protein.

Previous studies have found that reasonable energy intake is helpful for the prognosis of patients with different diseases and ages.[1,2,9,32-34] Early enteral nutrition is associated with decreased morbidity and mortality.[1] Enhanced Recovery After Surgery (ERAS) protocols effectively reduce morbidity and LOS following major surgery.[2] Well-managed nutritional support was identified as an independent factor associated with a reduced number of postoperative surgical site infections (SSIs).[9] An additional study indicated that low energy intake at one week following hospitalization in older adults with pneumonia

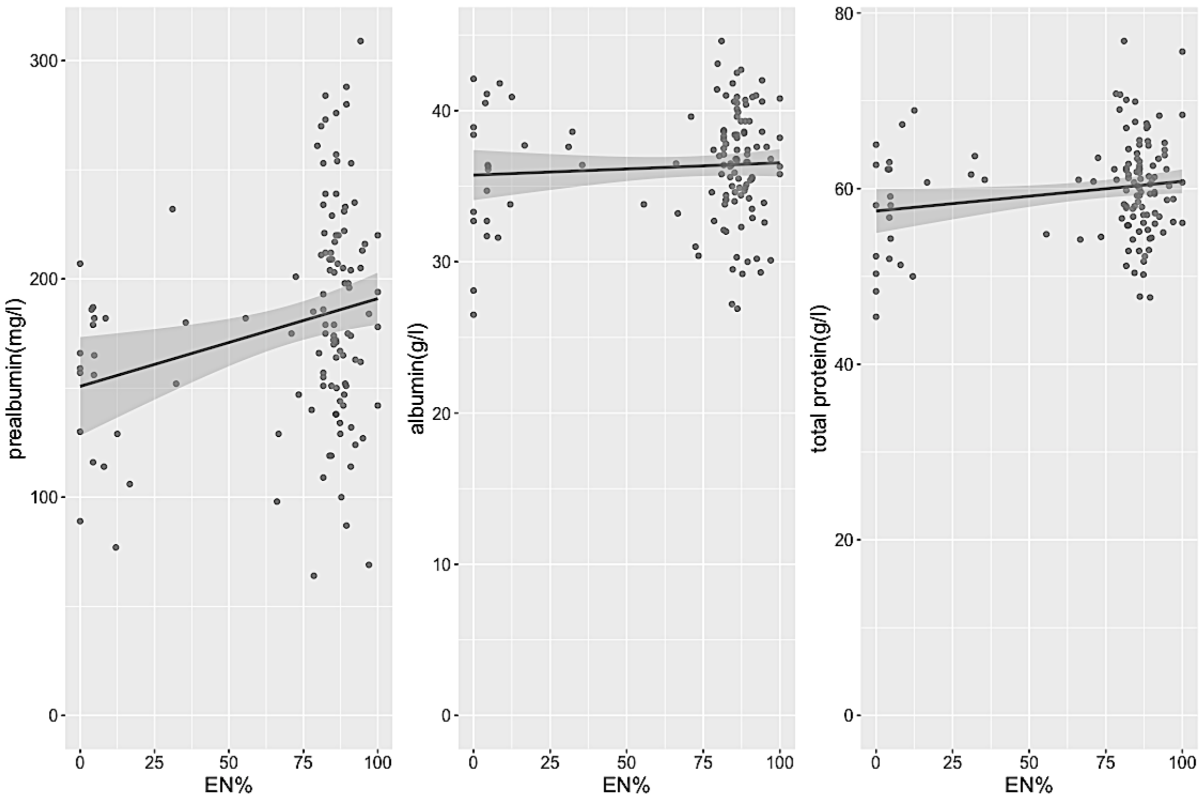

Figure 4. Relationship between EN% prior to ICU discharge and pre-albumin, albumin and total protein. EN%: percentage of oral or enteral energy intake in EI.

Table 3. Statistics of multiple linear regression

Factors	Standardization coefficient β	p	R	R^2	Adjusted R^2
Duration of mechanical ventilation (d)					
ALT†	0.487	<0.0001	0.557	0.333	0.316
Blood glucose†	0.230	0.001			
EI/mREE%†	0.164	0.018			
HB†	-0.136	0.048			
ICU duration (d)					
AST†	0.365	<0.0001	0.605	0.366	0.344
ALT†	0.285	0.001			
HB‡	-0.201	0.012			
APACHE II	0.166	0.038			
LOS following ICU discharge (d)					
EN%§	-0.519	<0.0001	0.712	0.506	0.488
Urea nitrogen‡	0.263	0.001			
EI/mREE%§	-0.226	0.008			
LOS In hospital (d)					
EN%§	-0.275	0.009	0.427	0.182	0.162
Urea creatinine‡	0.266	0.011			

ALT: alanine aminotransferase; AST: aspartate aminotransferase; EI: energy intake; mREE: the measured REE; EN%: Percentage of oral or enteral energy intake in EI; APACHE II: acute physiology and chronic health evaluation II; HB: hemoglobin.
†Data of the day of ICU admission.
‡Data the day prior to ICU discharge.
§Data of the day prior to discharge.

was an independent risk factor for mortality, difficult at-home recovery, and pneumonia recurrence.[32] Although patients with low nutritional risk do not benefit from high energy intake, it is recommended that patients with high nutritional risk take at least 800 kcal per day to reduce their mortality in intensive care units.[33] The present study further confirmed the benefits of nutritional support for disease prognosis. In addition, the present study evaluated the association between the proportion of enteral nutrition and prognosis; the nutritional indicators and energy intake were evaluated at different time periods following the operation. In the present study, we found that in the early stage following surgery, the changes in the prognostic indicators caused by primary disease or physiological stress were associated with prognosis, notably with regard to ICU time and mechanical ventilation time. In the following period, energy intake, notably enteral nutrient intake, was associated with shorter length of stay following ICU discharge and the overall length of stay in the hospital. The LOS following ICU discharge reflects the speed of patient recovery. The increase in EI, notably EN%, can improve the diagnostic value of this index and patients can benefit from its application.

The present study also explored the association between the proportion of enteral nutrition intake and nutrition-related indicators. EN% was associated with higher total protein and pre-albumin levels. In the early postoperative period, the enteral nutrient intake was low, and then the proportion of enteral nutrient intake was increased rapidly, which was consistent with the changes in the expression levels of the total protein and pre-albumin in the blood. In addition, the indices of liver function were higher when the proportion of energy intake was low. This finding was consistent with previous studies.[14,15] Cardiopulmonary bypass is required in the operation of patients with valvular disease, which may cause organ injury. This can partly explain the abnormal liver function of certain patients.[35-37] Cardiopulmonary bypass-induced acute microcirculatory perfusion disturbances persist in the first three postoperative days. These microcirculatory alterations may play a role in the development of postoperative organ dysfunction and prolonged hospital stay.[38]

Postoperative abdominal distension and gastroesophageal reflux have been observed in previous study, these conditions will affect the implementation of the enteral nutrition program.[39] In this study, the nutrition support team and clinicians jointly managed the patient's nutrition plan to avoid unreasonable nutrition support.[6,40] In this study, we found that the increase of nutritional intake, especially the proportion of enteral nutrition intake, is related to prognosis-related indicators, and nutritional support is likely to promote the rehabilitation of patients through this way. In the present study, all patients exhibited intestinal integrity. Even in patients with esophageal cancer undergoing radical surgery, the intestinal function was not significantly affected. Therefore, the process of nutrient absorption and utilization through the digestive tract was not affected. Based on the characteristics of the nutritional support noted in the present study, total energy intake was low in the early postoperative period, and the total energy intake was acceptable on the day of ICU discharge.

Nevertheless, the present study has some limitations when interpreting the results. This is a single-center prospective study with a small sample size. The gradual recovery of the disease following ICU discharge may increase the activity of certain patients. Moreover, the impact of the activity on energy consumption was not fully evaluated. Following ICU discharge, due to displaying the instruments used to assess the patient conditions, the patients could not be re-evaluated for REE. This could limit the generalizability of our findings. Moreover, the follow-up time was limited due to the period of postoperative hospitalization, and the follow-up of the patients following discharge was not monitored. Several patients lacked optimal nutritional support following discharge, resulting in a poor long-term prognosis. Future research studies should focus on reasonable nutrition management in different periods following the operation. In addition, patients with severe illness were not included in this study due to many interference factors. Therefore, the current research results can not be used to explain patients with severe conditions.

Conclusion

We discussed the association between energy intake and energy intake indicators, as well as the association between energy intake and prognostic indicators. In the present study, the IC method was used to evaluate REE of patients following surgery; the energy intake was assessed in patients at different stages following cardiac, thoracic, and vascular surgery. The results indicated that enteral nutrient intake could improve the prognostic value of specific indicators.

ACKNOWLEDGEMENTS

We thank all participants in the present study and the medical staff of the Department of Cardiothoracic Surgery, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, for their support. We thank Mr. Zhongliang Jin for his help in making figures.

AUTHOR DISCLOSURES

The authors declare no conflict of interest.

The present study was supported by grants from the Shanghai Key Laboratory of Pediatric Gastroenterology and Nutrition (17dz2272000) and the Foundation of Shanghai Municipal Health Commission (Key weak discipline construction project2019ZB0101).

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