Short Communication

Energy intake in the first week in an emergency intensive care unit may not influence clinical outcomes in critically ill, overweight Japanese patients

Satomi Ichimaru PhD, RD, CNSC[1], Maren Sono MD[2], Ryutaro Seo MD[2], Koichi Ariyoshi MD, PhD[2], Teruyoshi Amagai MD, PhD[3]

[1]*Department of Nutrition Management, Osaka Saiseikai Nakatsu Hospital, Osaka, Japan*
[2]*Department of Emergency Medicine, Kobe City Medical Center General Hospital, Kobe, Japan*
[3]*Department of Food Sciences and Nutrition, School of Environmental Sciences, Mukogawa Women's University, Nishinomiya, Japan*

Background and Objectives: The American Society for Parenteral and Enteral Nutrition recommends hypocaloric feeding for critically ill patients with a BMI of ≥30.0 kg/m^2. However, the cut-off value of obesity in Japan is BMI >25.0 kg/m^2, due to the higher prevalence of type 2 diabetes mellitus, and cardiovascular risk factors, even at a lower BMI than in Western populations. Thus, the optimal energy intake for critically ill, overweight Asian patients is unknown. **Methods and Study Design:** A retrospective chart review was conducted in patients with BMI of ≥25.0 kg/m^2 in an emergency intensive care unit (EICU). Patients were categorized into two groups by average daily energy intake during the first week in the EICU, with Group A at <50% of requirement and Group B at ≥50%. **Results:** A total of 72 patients with a median BMI of 27.5 kg/m^2 were included in the study. No significant differences between the groups were observed for all-cause mortality, ICU-free days, or length of hospital stay. The number of ventilator-free days (VFDs) was significantly higher in Group A than Group B (20.0 [15.5-24.5] vs 17.0 [2.0-21.0] days; p=0.042). On multiple adjusted analysis, however, we found that %energy intake/requirement was not independently associated with VFDs (regression coefficient=0.019; 95% confidence interval, −0.115–0.076). **Conclusions:** Energy intake in the first week in the EICU did not influence clinical outcomes in critically ill, overweight Japanese patients. Confirmation of these results in larger, randomized trials is required.

Key Words: critical illness, body mass index, obesity, overweight, energy intake

INTRODUCTION

Overweight and obesity, conditions characterized by an excess of body fat, are global and growing health problems. The World Health Organization (WHO) recommends an international cut-off point of BMI of ≥25.0 kg/m^2 for overweight and ≥30.0 kg/m^2 for obesity.[1] In critically ill conditions, obesity increases the risk of comorbidities (eg, insulin resistance, sepsis, infections, deep venous thrombosis, organ failure),[2,3] and the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) accordingly recommends that critically ill patients with a BMI of ≥30.0 kg/m^2 receive 50%-70% of estimated energy requirements.[4]

In contrast, the Japanese Society for the Study of Obesity (JASSO) has defined obesity as any BMI greater than 25.0 kg/m^2,[5] because Asian populations develop negative health outcomes such as type 2 diabetes and cardiovascular diseases at a lower BMI than Western people.[6,7] To our knowledge, the optimal energy intake for critically ill, obese/overweight Asian patients remains unclear.

Here, to examine whether energy intake influences the mortality and morbidity of critically ill, overweight/obese Asian patients, we conducted a retrospective chart review of Japanese patients with a BMI of more than 25.0 kg/m^2 in an EICU.

METHODS

Study population

This single-center retrospective chart review was conducted in an 8-bed emergency intensive care unit (EICU) of our institution, a tertiary teaching hospital. The EICU is a ward for emergency admissions, in which patients with serious emergency medical or surgical conditions receive intensive care. Critically ill patients transferred from general wards or who had undergone elective surgery are admitted to other ICUs. The study received approval from the ethics committee of our institution (Ap-

Corresponding Author: Dr Satomi Ichimaru, Department of Nutrition Management, Osaka Saiseikai Nakatsu Hospital, 2-10-39 Shibata Kitaku Osaka, 530-0012, Japan.
Tel: +81-6-6372-0333; Fax: +81-6-6372-0339
Email: s_ichimaru@nakatsu.saiseikai.or.jp
Manuscript received 11 April 2016. Initial review completed 04 July 2016. Revision accepted 26 July 2016.
doi: 10.6133/apjcn.022017.01

proval No. 150707). Owing to the characteristics of the study, informed patient consent was not required.

For eligibility, we analyzed consecutive patients admitted to the EICU from August 2011 to July 2014. Among all critically ill adult patients, we included those whose BMI was >25.0 kg/m^2, underwent mechanical ventilation within the first 48 h of admission, and remained in the EICU for 72 h or more. Exclusion criteria were as follows: age <18 years, pregnant or lactating woman, readmittance to the EICU within the same period of hospitalization, mask ventilation, withdrawal from treatment within the first week, and initiation of oral nutrition within the first week of admission to the EICU.

Data collection

All data were obtained from medical records. The following baseline data were recorded: age, sex, body weight and height on admission, and BMI. The following baseline clinical characteristics were also recorded: Acute Physiology and Chronic Health Evaluation (APACHE) II Score;[8] surgical or medical admission; admission from the emergency department, emergency ward, surgical theater, or other hospital; primary diagnosis in the EICU for cardiovascular, vascular, respiratory, gastrointestinal, neurological disorders, trauma, sepsis, burn, metabolic disorder, or renal disorder; Charlson Comorbidity Index;[9] and comorbidities including diabetes mellitus, cardiac disease, dialysis-dependent renal failure, and chronic obstructive pulmonary disease. The following nutritional characteristics were recorded: energy requirement and energy and protein intake during the first week in the EICU. Total energy intake was considered to include energy from EN, intravenous fluid, as well as lipids delivered via sedatives (e.g. propofol). In contrast, we excluded glucose infusions used for drug dilution and correction of hypoglycemia from calculations of energy intake.

In this hospital, indirect calorimetry was not available for all patients. Therefore, according to the guidelines from A.S.P.E.N.,[4] energy requirements were estimated based on the Penn State University 2010 predictive equation, or the modified Penn State equation if the patient was aged over 60 years.[4,10] Patients were categorized into two groups by average daily energy intake during the first week in the EICU, with Group A at <50% of requirements and Group B at ≥50%. The cutoff value of 50% was established on the basis of the ASPEN recommendation to provide 50%-70% of estimated energy requirements for critically ill obese patients.[4]

Clinical outcomes

Clinical outcomes in Groups A and B were compared. The following variables were analyzed:

1. All-cause mortality in the hospital and EICU.
2. ICU-free days, defined as the number of days between successful transfer to a general ward and Day 28 after EICU admission. ICU-free days were 0 if the patient died before Day 28 or stayed in the EICU or other ICU for ≥28 days.
3. Length of hospital stay; this analysis excluded patients who died during hospitalization.
4. Ventilator-free days (VFDs), defined as the number of days between successful weaning from mechanical ventilation (MV) and Day 28 after EICU admission. VFDs were 0 if the patient died before Day 28 or required MV for ≥28 days.
5. Number of patients requiring continuous or intermittent MV via tracheostomy at hospital discharge.
6. Number of patients undergoing tracheostomy in the EICU or hospital.
7. Antibiotic-free days, defined as the number of days during the 28 days after surviving patients were admitted to the EICU in which they did not receive any antibiotics as treatment for infection or as prophylaxis.
8. Inflammatory index, defined as maximum plasma C-reactive protein (CRP) level during the first 28 days after EICU admission.
9. Number of patients exhibiting liver dysfunction, defined as a total bilirubin level of >1.2 mg/dL during the first 28 days after EICU admission.
10. Number of patients exhibiting renal dysfunction, as determined by an increase in serum creatinine level of >1.2 mg/dL or need for renal replacement therapy during the first 28 days after EICU admission.
11. Number of patients receiving insulin therapy and their average daily insulin dose in the first week after EICU admission. Target glucose level was between 100 and 180 mg/dL.

Statistical analysis

Statistical analyses were performed using SPSS statistical software v. 21 (IBM, Armonk, NY, USA). Baseline characteristics and clinical outcomes in the two groups were summarized by providing the median and interquartile range for continuous variables and numbers and percentages for categorical variables. *p* values were calculated using the Mann-Whitney U test for continuous data and Fisher's exact test for categorical data. To reveal the impact of %energy intake/requirement on patient outcomes after controlling for differences in patient baseline characteristics, multiple regression analysis was carried out using VFDs as the dependent variable, and %energy intake/requirement during the first week in the EICU, admission category, and primary EICU diagnosis as the independent variables.

RESULTS

Among the 1,993 patients who were assessed for eligibility, 72 met the criteria and were included in the study. Reasons for exclusion were as follows: aged <18 years (n=12), EICU length of stay <72 h (n=1,265), no MV within 48 h of admission (n=218), re-admittance to the EICU during the same hospitalization period (n=20), pregnant or lactating (n=3), withdrawal from treatment during the first week (n=68), oral intake within the first week (n=80), BMI <25.0 kg/m^2 (n=234), and lack of BMI data (n=21).

Patient characteristics

Table 1 shows the baseline demographic, clinical, and nutritional characteristics of Groups A and B. Although BMI was similar between the two groups, height and weight were significantly larger in Group A. Therefore, the energy requirement calculated by the Penn State equa-

Table 1. Demographics, clinical characteristics, and nutritional characteristics of Group A and Group B

Characteristic	Group A (n=45) Energy intake/requirement <50%	Group B (n=27) Energy intake/requirement ≥50%	*p* value
Demographic			
Age, years; median (IQR)	59.3 (49.9-71.0)	69.1 (58.8-74.8)	0.126
Sex; n (%)			0.244
Women	15 (33)	12 (44)	
Men	30 (67)	15 (56)	
Height, cm; median (IQR)	165 (157.5-170.8)	160 (150.0-165.0)	0.039
Weight, kg; median (IQR)	75.1 (68.9-87.1)	70.1 (62.5-75.0)	0.042
BMI, kg/m^2; median (IQR)	27.4 (26.4-30.9)	27.5 (26.0-28.5)	0.446
Clinical characteristic			
APACHE II score; median (IQR)	22.0 (18.5-26.0)	25.0 (20.0-29.0)	0.128
Admission category; n (%)			0.078
Medical	13 (29)	14 (52)	
Surgical	32 (71)	13 (48)	
Source of admission; n (%)			0.269
Emergency department	19 (42)	17 (63)	
Emergency ward	1 (2)	1 (4)	
Operating room	21 (47)	7 (26)	
Other hospital	4 (9)	2 (7)	
Primary EICU diagnosis; n (%)			0.015
Cardiovascular or vascular disorder	0 (0)	3 (11)	
Respiratory disorder	2 (4)	5 (19)	
Gastrointestinal disorder	2 (4)	0 (0)	
Neurologic disorder	31 (69)	11 (41)	
Sepsis	2 (4)	2 (7)	
Trauma	3 (7)	5 (19)	
Metabolic disorder	2 (4)	0 (0)	
Hematologic disorder	2 (4)	0 (0)	
Burn	1 (2)	1 (4)	
Comorbidity			
Charlson comorbidity index; median (IQR)	4.0 (3.0-6.0)	4.0 (4.0-7.0)	0.189
Diabetes mellitus; n (%)	13 (29)	8 (30)	0.576
Cardiac disease; n (%)	4 (9)	4 (15)	0.342
Dialysis-dependent renal failure; n (%)	1 (2)	0 (0)	0.625
Chronic obstructive pulmonary disease; n (%)	0 (0)	0 (0)	1.000
Nutritional characteristic during first week in EICU; median (IQR)			
Energy requirement, kcal/day	1817 (1620-2067)	1623 (1386-1928)	0.024
Average daily energy intake/requirement, %	36.6 (27.7-45.9)	73.0 (58.3-85.1)	<0.001
Average daily energy intake, kcal	632 (473-785)	1139 (1021-1375)	<0.001
Average daily energy intake, kcal/kgABW	8.3 (6.1-11.2)	16.8 (14.2-18.4)	<0.001
Average daily protein intake, g	26.5 (17.6-36.4)	53.8 (44.0-67.8)	<0.001
Average daily protein intake, g/kgABW	0.3 (0.2-0.5)	0.8 (0.6-1.0)	<0.001

ABW: actual body weight on EICU admission; APACHE II: The Acute Physiology and Chronic Health Evaluation II; EICU: emergency intensive care unit; IQR: interquartile range.
Data are presented as median and interquartile range for continuous variables and as number and percentage for categorical variables. Mann-Whitney U test was used for continuous data and Fisher's exact test for categorical data.

tion was also significantly larger in Group A (1817 [1620–2067] vs 1623 [1386–1928] kcal/day; p=0.024). The APACHE II score did not significantly differ between groups. The number of surgical patients was higher in Group A than in Group B, albeit without statistical significance. Primary EICU diagnosis was significantly different between the Groups: 69% of patients in Group A had a neurologic disorder, while 41%, 19%, and 19% of patients in Group B had a neurologic disorder, respiratory disorder, and trauma, respectively. Charlson Comorbidity Index and the incidence of comorbidities including diabetes mellitus, cardiac disease, dialysis-dependent renal failure, and chronic obstructive pulmonary disease did not significantly differ between the groups.

Average daily energy intake/requirement in the first week of EICU admission were 36.6% (27.7%-45.9%) in Group A and 73.0% (58.4%-85.1%) in Group B. Average daily energy and protein intakes per actual body weight (ABW) during the first week of EICU admission were lower in Group A than in Group B (8.3 [6.1–11.2] vs 16.8 [14.2–18.4] kcal/kgABW; p<0.001, 0.3 [0.2–0.5] vs 0.8 [0.6–1.0] g/kgABW; p<0.001, respectively).

Outcomes

Table 2 shows patient outcomes. There were no significant differences between the two groups in all-cause mortality in the EICU or hospital, ICU-free days, or length of hospital stay. VFDs were significantly greater in Group A (20.0 [15.5–24.5] vs 17.0 [2.0–21.0] days; p=0.042). No significant differences were noted between the two groups regarding the requirement for MV at hospital discharge, tracheostomy, antibiotic-free days, serum CRP

Table 2. Unadjusted clinical outcomes between Group A and Group B

Outcome	Group A (n=45) Energy intake/ requirement <50%	Group B (n=27) Energy intake/ requirement ≥50%	*p* value
All-cause mortality; n (%)			
In EICU	3 (7)	3 (11)	0.402
In hospital	9 (20)	5 (19)	0.567
Length of stay; median (IQR)			
ICU-free days, days	19.0 (9.5-22.0)	18.0 (7.0-21.0)	0.504
Length of hospital stay, days	44.4 (31.3-59.1)	42.1 (30.6-61.2)	0.936
Mechanical ventilation			
Mechanical ventilation-free days, days; median (IQR)	20.0 (15.5-24.5)	17.0 (2.0-21.0)	0.042
Requirement for mechanical ventilation at hospital discharge; n (%)	1 (3)	3 (14)	0.148
Tracheostomy; n (%)			
In EICU	18 (40)	14 (52)	0.572
In hospital	23 (51)	11 (41)	0.573
Antibiotic-free days, days; median (IQR)	12.0 (6.5-16.5)	12.0 (6.0-18.0)	0.641
Highest CRP, mg/dL; median (IQR)	16.3 (10.2-25.2)	18.3 (12.2-29.7)	0.295
Liver and kidney dysfunction; n (%)			
Liver dysfunction (serum bilirubin >1.2 mg/dL)	17 (38)	10 (37)	0.577
Renal dysfunction (serum creatinine>1.2 mg/dL) or requirement for RRT	20 (44)	13 (48)	0.475
Glycemic control			
Received insulin administration in first week in EICU; n (%)	17 (38)	20 (74)	0.003
Average daily insulin dose in first week in EICU (units); median (IQR)	13.1 (6.1-20.2)	21.7 (11.4-30.0)	0.240

CRP: C-reactive protein; EICU: emergency intensive care unit; ICU: intensive care unit; IQR: interquartile range; RRT: renal replacement therapy.
Data are presented as median and interquartile range for continuous variables and as number and percentage for categorical variables. Mann-Whitney U test was used for continuous data and Fisher's exact test for categorical data.

level, or incidence of liver or renal dysfunction. The number of patients who received insulin administration in the first week in the EICU was smaller in Group A than in Group B (38% vs 74%, p=0.003), but average daily insulin dose did not significantly differ (13.1 [6.1-20.2] vs 21.7 [11.4-30.0] units, p=0.240).

When multiple adjusted analyses was performed, however, we found that %energy intake/requirement was not independently associated with VFDs (regression coefficient=0.019; 95% confidence interval, −0.115–0.076).

DISCUSSION

In this study in critically ill Japanese patients with a BMI ≥25.0 kg/m^2, we found no statistically significant difference in all-cause mortality, ICU-free days, or length of hospital stay between those who received <50% or ≥50% of energy requirements during their first week in the EICU. Although the number of VFDs was significantly higher in those receiving <50% of energy requirements, this association was lost on multivariable analyses with adjustment for confounders. To our knowledge, this study is the first to evaluate the influence of energy intake on mortality and morbidity in obese/overweight and critically ill Asian patients.

According to data from the Organisation for Economic Co-operation and Development (OECD), only about 3.6% of the Japanese population is classified as obese using the WHO criteria of BMI >30.0 kg/m^2.[11] When the JASSO values are used, however, the prevalence of obesity (BMI >25.0 kg/m^2) in Japan is 24.7%.[12]

Dickerson et al. showed a benefit to hypocaloric feeding, in terms of decreased ICU stay, fewer days of antibiotics, and a trend toward fewer days of mechanical ventilation.[13] Choban et al demonstrated no difference in mortality or length of hospital stay in hospitalized obese patients who received hypocaloric parenteral nutrition (PN) when compared with eucaloric PN.[14] However, a large observational study indicated a higher mortality rate in critically ill obese patients who received hypocaloric feeding.[15] Guidelines for critical care from A.S.P.E.N. recommend hypocaloric feeding for critically ill patients with BMI of ≥30.0 kg/m^2.[4] Our present study examined whether hypocaloric feeding should be used for critically ill obese/overweight Japanese patients. On evaluation of the influence of energy intake on mortality and morbidity in critically ill patients with BMI ≥25.0 kg/m^2, we found no statistically significant increase in all-cause mortality, ICU-free days, or length of hospital stay. Energy requirements as calculated by the Penn State equation were lower in Group B due to the smaller physical characteristics than in Group A. The lower energy requirement might have resulted in Group B receiving greater %energy intake/requirement. The average daily energy intake/requirement was 36.6% in Group A and 73.3% in Group B. A.S.P.E.N. recommends the administration of 50%-70% of estimated energy requirement for critically ill obese patients.[4] The lack of differences in the outcomes of our two groups might have been because we compared patients who received very low energy with those who received low energy. The median BMI of patients in the present study was 27.5 kg/m^2. This is within the "overweight" range according to the WHO criteria and A.S.P.E.N. does not recommend hypocaloric feeding in this population. It would likely have been preferable to conduct this study in patients with BMI >30.0 kg/m^2, but this would have been difficult due to the low prevalence of obese patients in Japan.[11,12] Indeed, among our 76 patients with a BMI >25.0 kg/m^2 in this study, only 17 (22%)

had a BMI >30.0 kg/m^2.

Several limitations of our study warrant mention. First, the study size was small and the design was retrospective. A better design would be a prospective study with obese/overweight patients who are randomized to either a hypocaloric or eucaloric intake. Second, the energy target was estimated using a predictive equation rather than in direct calorimetry. Most studies recommend the use of indirect calorimetry because energy expenditure is influenced by many factors, such as age, body composition, thyroid hormones, catecholamines, ambient and body temperature, disease states and treatments; however, some patients do not meet valid testing criteria, and most Japanese facilities do not have indirect calorimeters. Therefore we used the predictive equation in this study. Although the Penn State equation has not been validated for determining the energy needs of critically ill Japanese patients, no other formula for estimating energy requirements in critically ill obese/overweight Asian patients has yet been developed. Third, the weight change during EICU stay could not be assessed because non-nutritional factors such as fluid balance and inflammatory status may influence actual body weight early in the clinical course. Finally, although we focused on energy intake in the present study, outcomes might also have been affected by the low protein intake in the two groups.[16] Thus, a conclusive answer as to whether energy intake in the first week in the EICU influences clinical outcomes in critically ill, overweight Japanese patients requires large multicenter prospective studies with random patient assignment.

Conclusion

The results of this single-center, retrospective chart analysis demonstrated that energy intake in the first week in an EICU did not influence clinical outcomes in critically ill, overweight Japanese patients. Further large randomized trials are needed to confirm the results of this study.

ACKNOWLEDGEMENTS

The authors thank the EICU staff for their support, collection of data, and review of this manuscript.

AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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