



Safety of Early Enteral Nutrition for Cardiac Medical Critically Ill Patients

— A Retrospective Observational Study —

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Background: Early intervention with enteral nutrition (EN) is the standard of care in many medical intensive care units (ICUs). However, few studies have addressed the use of early EN for critically ill patients in the cardiac ICU (CICU). In this study we explored the indications for early EN for patients admitted to a CICU.

Methods and Results: This retrospective observational study included 63 consecutive patients admitted to the CICU who were diagnosed with cardiovascular disease. Early EN was initiated in these patients as per the hospital's nutrition protocol. Mean Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores at admission were 18.8 and 9.1, respectively. All patients were admitted to the medical CICU with a diagnosis of cardiovascular disease and/or cardiopulmonary arrest. Enteral feeding was initiated in 59 patients (94%) within 5 days of admission. Fifty-two patients (83%) achieved the energy intake goal at Day 7 of their CICU admission either by enteral feeding or oral intake; 49 patients (78%) survived to time of discharge. The patients experienced several minor complications, including minor reflux (4 patients; 6%) and diarrhea (8 patients; 13%). None of the patients developed aspiration pneumonia or bowel ischemia.

Conclusions: The present retrospective observational study indicates that early EN for critically ill patients in a medical CICU can be achieved safely with no major complications.

Key Words: Cardiac intensive care unit; Early enteral feeding; Nutrition

Nutrition support therapy is an important component of care for critically ill patients. There are published guidelines that can be used to provide enteral nutrition (EN) with the goal of improving overall outcomes.^{1,2} EN is recommended as a first choice for nutritional therapy in an intensive care unit (ICU) setting. Recent studies have indicated that early EN reduces the rate of infectious complications compared with outcomes when EN is delayed.³ Similarly, intervention with early EN resulted in a reduced rate of infectious complications, length of ICU stay, and number of hospital days compared with early parenteral nutrition (PN).^{4–8} However, these studies primarily included patients diagnosed with sepsis, trauma, head injury, severe acute pancreatitis, or those who underwent surgery. One recent study reported that initiation of EN for cardiovascular patients was typically later than for non-cardiovascular patients in the ICU, and that energy provided by EN for cardiovascular patients was less than that provided to those with non-cardiovascular diagnoses.⁹

Most patients admitted to a medical cardiac ICU (CICU) are those with hemodynamic disorders secondary to cardiovascular disease. As such, the number of medical CICU patients who are dependent on catecholamines, inotropic agents, or mechanical circulatory support is typically higher than in the general ICU (GICU) or post-surgical ICU (SICU) population. However, once hemodynamically stabilized, medical CICU patients may benefit from early EN despite a dependence on mechanical circulatory support.

Few studies have addressed the efficacy of early EN for critically ill medical CICU patients. As such, we investigated EN as an early intervention in patients who were admitted to a medical CICU.

Methods

The present study was a single-center retrospective observational study. The study was approved by the Ethics Committee of Hyogo Prefectural Amagasaki General Medical Center (Approval no. 1-109).

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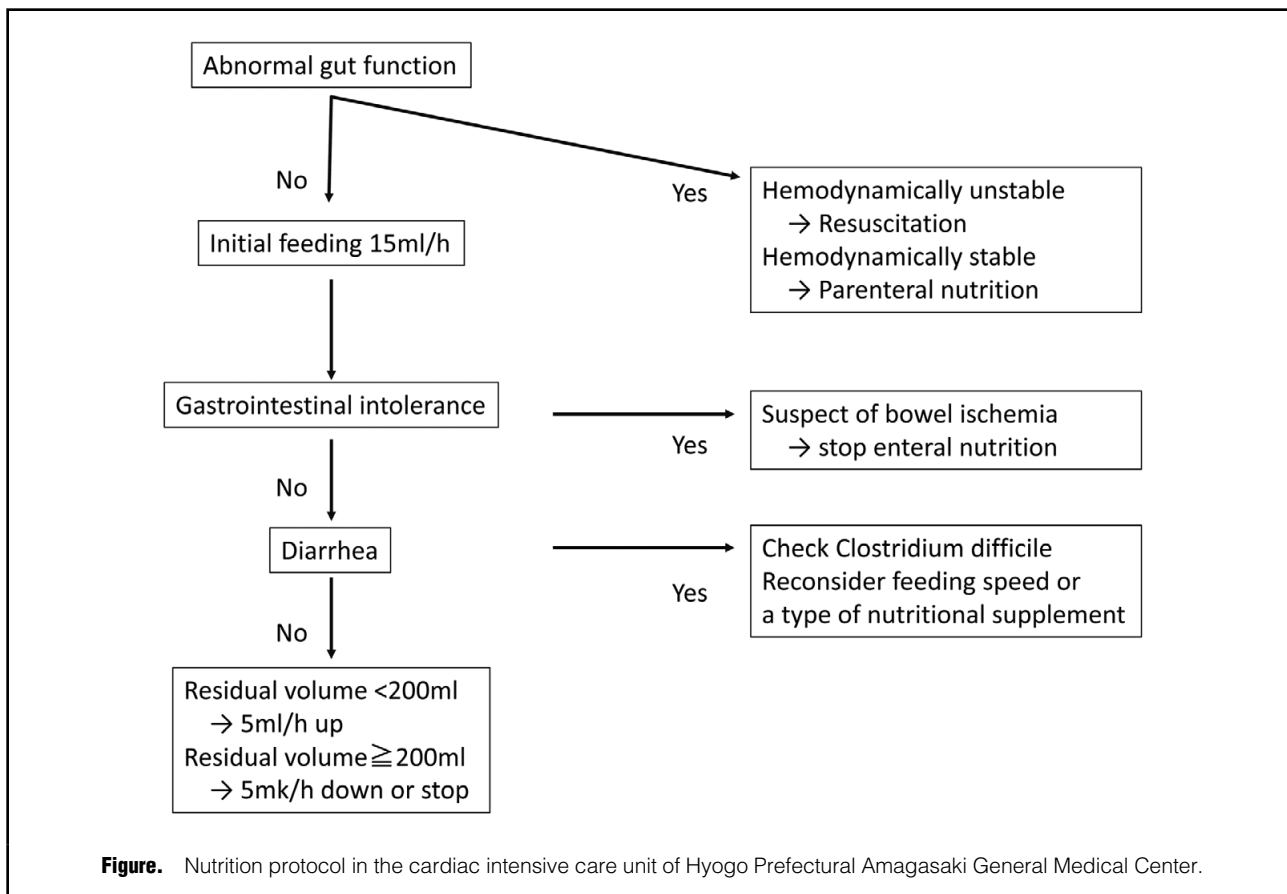
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The study enrolled 63 consecutive mechanically ventilated patients aged >18 years who stayed in the medical CICU of Hyogo Prefectural Amagasaki General Medical Center for 48 h or longer between April 2018 and July 2019. On admission, details regarding a patient's current and past medical history and drug regimens were reviewed. Patient admission data were collected, including the Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, and the use of an intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), vasopressors, or renal replacement therapy. Body height and weight, systemic blood pressure, and heart rate were also recorded. Body mass index (BMI) was calculated as body weight, in kilograms, divided by height, in meters, squared. Left ventricular ejection fraction was measured by ventriculography or echocardiography and calculated using the modified 2-dimensional Simpson method or the Teichholz formula.

Laboratory findings upon admission to the CICU included serum hemoglobin, sodium, albumin, creatinine, B-type natriuretic peptide (BNP), total cholesterol, and total peripheral blood lymphocytes. Recently published equations were used to calculate the estimated glomerular filtration rate (eGFR) in Japanese men and women, as follows:

$$eGFR = (194 \times \text{serum creatinine} - 1.094 \times \text{age} - 0.287) \text{ in men}$$

$$eGFR = (194 \times \text{serum creatinine} - 1.094 \times \text{age} - 0.287 \times 0.739) \text{ in women}$$

because the equations used to calculate eGFRs in Western

populations are not generally applicable to patients of Asian heritage. All study procedures were performed in compliance with the principles outlined in the Declaration of Helsinki and the institutional guidelines of Hyogo Prefectural Amagasaki General Medical Center. The authors had full access to and take responsibility for the integrity of the data.

Early EN was provided to all patients as per the hospital's nutrition protocol (Figure), unless specifically contraindicated. Uncontrolled shock, uncontrolled hypoxemia, uncontrolled acidosis, uncontrolled upper gastrointestinal bleeding, bowel ischemia, bowel obstruction, and abdominal compartment syndrome were defined as contraindications for EN. EN was initiated in patients who were hemodynamically stable because of mechanical support or the use of catecholamines. EN was not initiated in patients who required intravenous fluid resuscitation or escalating doses of catecholamine agents to maintain hemodynamic stability. Continuous EN was started at 15 kcal/h, and feeding intolerance (vomiting, abdominal distention, or a gastric residual volume >200 mL) was evaluated every 4 h. EN was increased by 5–10 kcal/h during each of the following 12-h periods as per the institutional protocol unless feeding intolerance developed. PN was chosen if EN was contraindicated, and the dose of PN was also increased gradually as per the protocol. The energy and protein requirements were calculated as 25 kcal and 1.2–1.5 g·kg⁻¹·day⁻¹, respectively. Daily energy and protein targets were discussed with nurses, physical therapists, and nutritionists at each morning conference. The goal to be achieved was 60%

Age (years)	68.8±3.8
Female sex	19 (30)
BMI on Day 1 (kg/m²)	22.9±1.1
Concomitant disease	
Hypertension	41 (65)
Diabetes	16 (25)
Dyslipidemia	20 (32)
Chronic kidney disease	22 (35)
Admission disease	
Heart failure	15 (24)
Acute coronary syndrome	23 (37)
Aortic disease	7 (11)
Cardiopulmonary arrest	28 (44)
APACHE II score	18.8±1.9
SOFA score	9.1±0.98
Vital signs on Day 1	
Systolic blood pressure (mmHg)	112.5±6.7
Heart rate (beats/min)	89.4±5.4
LVEF (%)	49.1±3.8
LVEF <50%	31 (49)
Blood chemistry on Day 1	
Hemoglobin (g/dL)	11.9±0.65
Sodium (mEq/L)	139.8±1.2
eGFR (mL/min/1.73 m ²)	45.4±5.4
BNP (pg/mL)	260.5±119.9
Albumin	3.3±0.1
Total cholesterol	140.7±10.9
Lymphocytes	2,291±650.1
BNP at discharge (pg/mL)	488±459.5

Data are given as the mean±SD or as n (%). APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; BNP, B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; SOFA, Sequential Organ Failure Assessment.

of the daily energy requirement by Hospital Day 7. The extent to which this goal was achieved in each patient was evaluated, together with the rate of survival to discharge and complications related to EN (i.e., aspiration pneumonia, bowel ischemia, vomiting, or diarrhea). Vomiting was divided into minor or major reflux depending on whether EN could be continued (minor) or not (major) in a given patient.

Continuous variables are presented as the mean±SD and categorical variables are presented as percentages. Patients were divided into 2 groups according to whether nutrition therapy was started by EN or PN, and the vital signs (e.g., blood pressure, heart rate, and catecholamine dose and duration) were evaluated. In addition, vital signs were collected within 2 h after the initiation of nutrition therapy, and changes were evaluated. For comparisons between groups, the Chi-squared test was used for qualitative variables, whereas Student's t-test and the Wilcoxon rank-sum test were used for parametric and non-parametric quantitative variables, respectively. The significance of differences in the mean total energy intake from Day 1 to Day 7 was examined using multivariate analysis of variance (MANOVA). All statistical analyses were performed using JMP version 11.0 (SAS Corporation, Cary, NC, USA).

Alive at discharge	49 (78)
Initiation of enteral feeding within	
24 h	31 (49)
48 h	41 (65)
5 days	59 (94)
Energy goal achieved at Day 7	52 (83)
Complications	
Aspiration pneumonia	0 (0)
Bowel ischemia	0 (0)
Interruption of enteral feeding	1 (2)
Minor reflux	4 (6)
Major reflux	0 (0)
Diarrhea	8 (13)

Data are given as n (%).

Results

The baseline characteristics of the patients in this study are given in **Table 1**. The mean APACHE II and SOFA scores were 18.8 and 9.1, respectively. Diagnoses on admission included acute heart failure (25%), acute coronary syndrome (37%), and cardiopulmonary arrest (44%); 49% of these patients had an ejection fraction (EF) <50%.

Patient outcomes were given in **Table 2**. Ten patients who died within 48 h of admission to the CICU were excluded from the analysis. The protocol used to provide EN is shown in **Figure**. Enteral feeding was initiated in 31 patients (49%) within 24 h, in 41 patients (65%) within 48 h, and in 59 patients (94%) within 5 days of admission. EN was contraindicated in three patients (5%) because of concomitant gastrointestinal diseases. Ten patients (16%) were capable of oral intake within 48 h of admission. The total energy intake of EN on the starting day and on Day 7 was 169.5 and 1,100.5 kcal/day, respectively. The total energy intake of PN on the starting day and on Day 7 was 210.2 and 747.3 kcal/day, respectively.

Fifty-two patients (83%) achieved the stated goal by Hospital Day 7 either via enteral feeding or by oral intake, and 78% of patients survived to the time of discharge. No severe complications developed in response to EN. EN was temporarily discontinued in 1 patient due to an observed drop in blood pressure after initiation of enteral feeding; this patient's hemodynamic status stabilized, and enteral feeding was reinitiated several days later. Four (6%) minor reflux events were experienced; enteral feeding was continued without any further dysfunction. Prokinetics were provided to 50 patients (79%), and there were no cases of postpyloric feeding. Diarrhea developed in 8 patients (13%), although only 1 patient experienced diarrhea for more than 2 days. There was no malfunction of the membrane oxygenator in patients with lipid infusion with PN or in hypertriglyceridemic patients after EN. There were no significant differences between the PN and EN groups in terms of changes in vital signs and increases in catecholamine dose as a result of nutrition therapy (**Supplementary Table**). The duration of catecholamine use was longer in the PN group. The energy intake in the 2 groups on each day is shown in **Supplementary Figures 1 and 2**. The mean total energy intake of the EN group was increased gradually from Day 1 to Day 7, whereas the mean total energy

intake of the PN group increased from Day 1 to Day 4 and then decreased from Day 4 to Day 7. However, these changes were not statistically significant (MANOVA, $P=0.11$ and $P=0.13$, respectively).

Thirteen patients (21%) in the study were dependent on venoarterial ECMO (VA-ECMO). Enteral feeding was initiated in 6 patients (46%) within 24h, in 9 patients (69%) within 48h, and in all 13 patients (100%) within 5 days of admission. This was largely tolerated, and 10 patients (77%) reached the energy balance goal at Hospital Day 7. The survival rate of ECMO-dependent patients was 50%. There were no venovenous ECMO-dependent patients enrolled in the study.

Discussion

This study showed that early administration of EN is safe and feasible for patients admitted to the CICU. To the best of our knowledge, this is the first report documenting the use of early EN for critically ill patients diagnosed with cardiovascular disease. Of note, only 51% of patients presented with preserved ventricular EF; designing early EN protocols for these patients was challenging. Interestingly, we found that the rate of complications secondary to early EN in the medical CICU was indistinguishable from that reported in studies in non-cardiac ICUs.³⁻⁶ One previous study reported that increased energy and protein intake was associated with improved clinical outcomes in critically ill patients, particularly among those with a BMI <25 or ≥ 35 kg/m².¹⁰ These data are of particular significance for medical care in Asia, where a national data study reported that there is a larger fraction of the population with a BMI <25 kg/m² in Japan than is typically observed in other countries.⁹

Overall, these studies indicate that EN for cardiovascular patients may be pursued aggressively from as early as the first day of admission. The findings of the present study support the routine use of early EN in a medical CICU as well as in non-cardiac ICUs.

Another recent study revealed that instituting a specific nutrition protocol reduced the time required to achieve target energy intake and generally improved overall tolerance of EN.¹¹ However, the precise nature of an optimized protocol and specific target energy intakes have not been formally established.¹² Indirect calorimetry is the best choice for calculating target energy intake, but this methodology is not widely available. The results of a previous study compared the use of complex equations vs. weight only and found no differences in overall mortality; furthermore, among those surviving, the time to patient discharge was shorter in patients whose intake was determined based on their body weight alone.¹² As such, we also calculated the target energy intake for use in our protocol using the equation based on body weight alone.

The protocol used in this study is original; we generated our own protocol based on careful reference to each guideline.^{1,2} We focused specifically on patient safety; as such, this is not an overly aggressive early nutrition protocol. We chose to focus on enteral feeding due to the low rate of associated infectious complications.⁴⁻⁸ Gastrointestinal complications, including vomiting and diarrhea, are significant problems for those receiving EN, as is aspiration pneumonia. In an effort to prevent these complications, we chose continuous feeding rather than bolus EN¹³ and provided metoclopramide as a prokinetic therapy as a routine

part of the protocol.¹ Furthermore, patients with EN in the present study were maintained in a head-up position at all times.¹⁴ There are few well-designed studies showing the relationship between nutrition therapy and catecholamine dose or index. Therefore, we did not include cut-off values of catecholamine dose or index for the initiation of nutrition therapy. Instead, hemodynamic stabilities were included for the initiation based on each guideline.^{1,2} In the present study, the complications did not differ significantly between the EN and PN groups, and this result is supported by several previous studies.⁴⁻⁸

During acute episodes, cardiovascular disease can be associated with a profound inflammatory reaction.¹⁵ This can promote a hypermetabolic state during which one must avoid overfeeding so as to limit the possibility of dysfunctional responses, including hyperglycemia.^{1,2} In the present study, patients with reduced EF were started on EN with very limited intake, and intake was increased gradually over the course of several days until the target energy goal was reached. Using this protocol, 83% of patients achieved the goal by Day 7 from the date of admission, suggesting that our protocol was safe and readily tolerated by this patient population.

In the present study 21% patients were VA-ECMO dependent. Early EN for these patients was found to be relatively safe; indeed, early EN was associated with reduced mortality in patients with cardiogenic or obstructive shock requiring VA-ECMO¹⁶ and nutritional support for these patients promoted improved long-term survival.¹⁷ Therefore, we conclude that patients who are hemodynamically stabilized with VA-ECMO may also benefit from early EN. Furthermore, EN is possible in approximately 80% of patients undergoing target temperature management.¹⁸ We succeeded in achieving appropriate energy goals using EN in 78% of these patients.

The present study has several limitations. First, this was a retrospective study conducted at a single center with a somewhat small sample size. In particular, the sample size of the PN group was small for comparison. As such, the findings need to be confirmed in a larger, well-designed randomized controlled study. However, in this study we succeeded in establishing a protocol for EN that is suitable for use in a critically ill patient cohort. We showed that this protocol is safe and well tolerated by patients in a medical CICU. As such, the results may help introduce early EN into clinical practice in medical ICUs and elsewhere.

Conclusions

The results of the present single-center retrospective observational study suggest that early EN is safe and feasible for patients admitted to a medical CICU. Nutritionists may work together with cardiologists to introduce early EN for critically ill patients in the medical CICU via means currently in use in most medical ICUs.

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Disclosures

None.

IRB Information

This study was approved by the local Ethics Committee of Hyogo Prefectural Amagasaki General Medical Center (Approval no. 1-109).

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Supplementary Files

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