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Early Enteral Nutrition is Related to Decreased In-hospital Mortality and Hospitalization in Patients with Acute Pancreatitis: Data from the Japanese Diagnosis Procedure Combination Database

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Abstract : Management of early nutrition plays an important role in the treatment of acute pancreatitis patients, but the sample sizes of randomized control trials that have compared enteral and parental nutrition were small. From the data of Diagnostic Procedure Combination, we identified patients who had been diagnosed with acute pancreatitis and discharged from the hospital between 2014 and 2015. We compared the length of hospital stay and hospital mortality among patients with acute pancreatitis that was managed with and without enteral nutrition within 7 days from hospitalization. The results showed a significant decrease in the in-hospital mortality rate of 56% (odds ratio 0.444, 95% confidence interval [CI] 0.358–0.551, $P < 0.001$) and length of hospital stay by 8.6 days (95% CI -9.05 – -8.13, $P < 0.001$) when enteral nutrition was administered within 7 days. According to multivariate analysis, early enteral nutrition was independently associated with in-hospital mortality rate and length of hospitalization. Enteral nutrition is an important management method for the treatment of acute pancreatitis patients.

Keywords : acute pancreatitis, diagnosis procedure combination database, enteral nutrition, in-hospital mortality, length of hospital stay.

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Introduction

Acute pancreatitis is an inflammatory condition of the pancreas. The severe form is a life-threatening disease with hospital mortality rates of approximately 15% and has been reported to comprise approximately 20–30% of the patients [1].

Fluid resuscitation is considered to be an essential part of the management of acute pancreatitis, but management of the disease remains largely supportive [2].

Oral feeding is stopped to suppress the function of the exocrine pancreas, and pain relievers, antiemetics, and oxygen administration might be helpful, but bowel rest owing to fasting is associated with intestinal mucosal atrophy and increased infectious complications because of bacterial translocation from the gut [3]. Damage to the gut-barrier accounts for the initiation of the systemic inflammatory response syndrome, sepsis, and infected pancreatic necrosis [1].

A systematic review showed that, in patients with

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acute pancreatitis, enteral nutrition significantly reduced mortality and the risk of multiple organ failure compared to that in patients who received parenteral nutrition [4]. Enteral nutrition within 48 hours after hospitalization in severe acute pancreatitis patients significantly decreased the risk of multiple organ failure, operative intervention, and systemic infections [5], demonstrating that the management of early nutrition plays an important role in the treatment of patients with acute pancreatitis. All of the randomized control trials (RCT) that compared enteral or parental nutrition were conducted with a small number of subjects, however, and no such RCT has been conducted in Japan. To the best of our knowledge, there are few reports that demonstrate a relationship between enteral nutrition and length of hospitalization in patients with acute pancreatitis based on the Diagnostic Procedure Combination (DPC) database. Therefore, we evaluated the efficacy of enteral nutrition in acute pancreatitis based on the Japanese DPC.

Materials and Methods

Data Source

Diagnostic Procedure Combination (DPC) is an original Japanese case-mix system that has been used since 2003 to calculate payment for treatments at acute care hospitals. Its database contains patient information and detailed procedures for the Japanese National Insurance System [6]. During the period of the present study, 1,181 hospitals participated in a survey for the purpose of research based on DPC. For patients with acute pancreatitis, the prognostic factor score and computed tomography (CT) grade based on contrast-enhanced CT according to the Japanese Severity Scoring System (JSSS) are recorded in the database, which we could use to assess the severity of acute pancreatitis.

Patients and variables

From the data of DPC, we identified patients who were diagnosed with acute pancreatitis (ICD-10 code K85) and were discharged from the hospital between 2014 and 2015.

We included patients whose “main diagnosis” or “hospitalization occasional disease name” or “resource disease name” was acute pancreatitis and whose DPC

data showed that they had been discharged from the hospital between 2014 and 2015. The DPC data allowed us to track if a patient was treated in more than one hospital. If all cases were included, a patient who had been transferred within a few days to another hospital and received treatment there would be considered as two cases, so we only evaluated patients who were hospitalized directly from their homes or nursing homes and discharged from the same hospital. We defined patients in whom enteral nutrition was started within 7 days as the early enteral nutrition cohort, and evaluated patients who survived for more than 7 days. We excluded from the study patients who had developed cholangitis at the time of diagnosis of acute pancreatitis and received endoscopic retrograde cholangiopancreatography (ERCP).

We collected the following data: patients' age and sex, prognostic factor score, CT grade according to the JSSS [7], emergency transport, hemodialysis performed, enteral nutrition within 7 days, ERCP performed, length of hospital stay, and death at discharge.

Acute pancreatitis was diagnosed when the patients showed at least two of the following three features: 1) acute abdominal pain and tenderness in the upper abdomen, 2) elevated levels of pancreatic enzymes in the blood and urine, and 3) abdominal findings of acute pancreatitis as presented by ultrasonography, CT, or magnetic resonance imaging. Severe acute pancreatitis was diagnosed in cases in which the total prognostic factor score was ≥ 3 or the contrast enhanced CT grade was ≥ 2 , in accordance with the JSSS [8] (Table 1).

The primary outcome was the in-hospital mortality rate. The secondary outcomes were the length of hospital stay, the rate of in-hospital mortality, and length of hospital stay according to the severity of acute pancreatitis.

We compared the patient characteristics between the group that started enteral nutrition within 7 days and the group that started enteral nutrition after 7 days. Next, in-hospital mortality rate, which was the primary endpoint, and length of hospital stay were examined based on the presence or absence of early enteral nutrition, and the patients were subsequently divided into two groups: 1) mild group (prognostic factor score ≤ 2 and CT grade ≤ 1), and 2) severe group (prognostic factor score ≥ 3 or CT grade ≥ 2). The severe group

was further divided into three groups: 1) those with prognostic factor score ≥ 3 and CT grade ≤ 1 , 2) those with prognostic factor score ≤ 2 and CT grade ≥ 2 , and 3) those with prognostic factor score ≥ 3 and CT grade ≥ 2 , and we examined the length of hospital stay and in-hospital mortality rate in the presence or absence of early enteral nutrition.

Statistical analysis

Data were expressed as medians (inter quartile range). The differences between the groups were compared using the chi-square or Fisher's exact test and Wilcoxon-Mann-Whitney U test. The generalized linear model analysis was performed by Stata/IC 15.0 (Light Stone®) ($P < 0.05$ being significant).

Results

Patients

A total of 39,192 patients were diagnosed as having acute pancreatitis from the DPC data. Among these patients, 12,825 were excluded because they did not meet the inclusion criteria. We also excluded 389 patients because of insufficient data. The remaining 25,978 patients were classified into the two groups: the group that started enteral nutrition within 7 days ($n = 18,036$) and the group that started enteral nutrition after 7 days ($n = 7,942$). A patient flow chart is shown in Figure 1.

The baseline characteristics of the patients in whom enteral nutrition was started within 7 days and those in whom it was started after 7 days are shown in Table 2, where it can be seen that the two groups had different baseline characteristics. Enteral nutrition was started on day 5 of hospitalization for many patients (16.1%) (data not shown).

Rate of in-hospital mortality: comparison of patients with enteral nutrition started within 7 days

We examined the rate of in-hospital mortality with the administration of enteral nutrition in patients with acute pancreatitis, and noted a 56% reduction in the in-hospital mortality rate when enteral nutrition was provided within 7 days (odds ratio [HR] 0.444, 95% confidence interval [CI] 0.358–0.551, $P < 0.001$) (Table 3, 4). Next, we divided the prognostic factor

Table 1. Japanese scoring system for severity of acute pancreatitis by the Ministry of Health, Labour and Welfare of Japan

Prognostic factors (1 point for each factor)

1. Base excess ≤ -3 mEq/l or shock (systolic blood pressure < 80 mm Hg)
2. $\text{PaO}_2 \leq 60$ mm Hg (room air) or ventilatory failure (ventilator management is needed)
3. $\text{BUN} \geq 40$ mg/dl (or $\text{Cr} \geq 2.0$ mg/dl) or oliguria (daily urine output < 400 ml even after IV fluid resuscitation)
4. $\text{LDH} \geq 2$ times of upper limit of normal
5. Platelet count $\leq 100,000/\text{mm}^3$
6. Serum $\text{Ca} \leq 7.5$ mg/dl
7. $\text{CRP} \geq 15$ mg/dl
8. Number of positive measures in SIRS criteria ≥ 3
9. Age ≥ 70 years

CT Grade by contrast-enhanced CT

1. Extrapancreatic progression of inflammation

Anterior pararenal space	0 point
Root of mesocolon	1 point
Beyond lower pole of kidney	2 points
 2. Hypoenhanced lesion of the pancreas

The pancreas is conveniently divided into three segments (head, body, and tail).

Localized in each segment or only surrounding the pancreas	0 point
Covers 2 segments	1 point
Occupies entire 2 segments or more	2 points
- 1 + 2 = Total scores
- | | |
|-------------------------|---------|
| Total score = 0 or 1 | Grade 1 |
| Total score = 2 | Grade 2 |
| Total score = 3 or more | Grade 3 |

Severe acute pancreatitis: prognostic factor ≥ 3 or CT Grade ≥ 2 . Measures in SIRS criteria include body temperature > 38 or $< 36^\circ\text{C}$, heart rate > 90 beats/min, respiratory rate > 20 breaths/min or $\text{PaCO}_2 < 32$ torr, and white blood cell counts $> 12,000$ cells/ mm^3 , $< 4,000$ cells/ mm^3 , or $> 10\%$ immature (band) forms. BUN: blood urea nitrogen, CRP: C-reactive protein, CT: computed tomography, LDH: lactate dehydrogenase, SIRS: systemic inflammatory response syndrome.

scores and CT grades into groups according to severity and examined the rate of in-hospital mortality. In mild acute pancreatitis, there was a significant reduction of 74% in the in-hospital mortality rate when enteral nutrition was started within 7 days (HR 0.257, 95% CI 0.185–0.357, $P < 0.001$) (Table 3, 4). In severe acute pancreatitis, there was a significant reduction in the in-hospital mortality rate of 50% when enteral nutri-

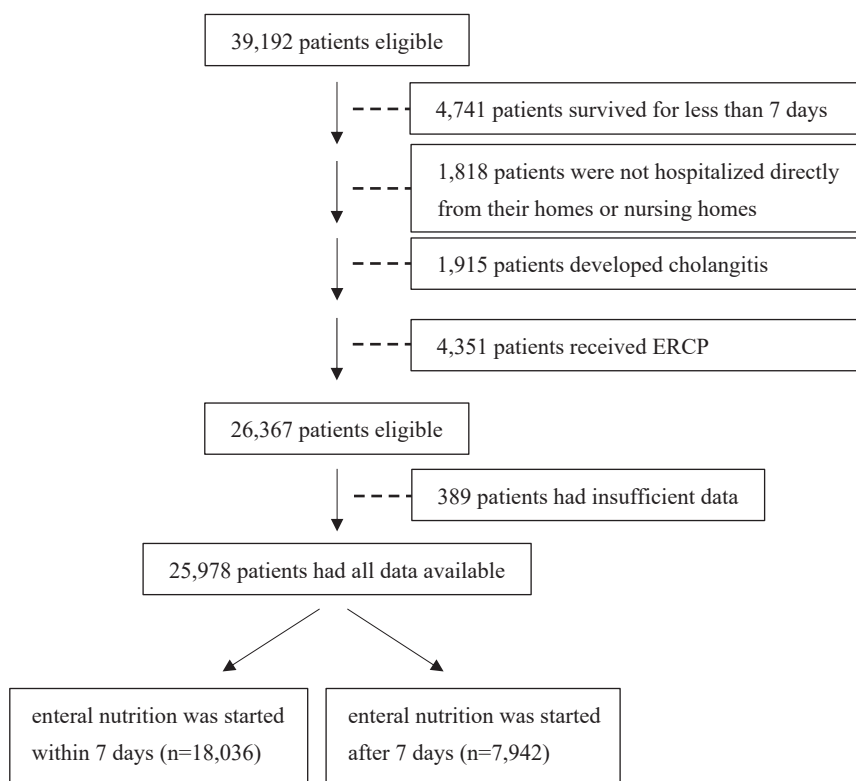


Figure 1. Flow chart of recruitment and participants.

Table 2. Characteristics of the study population

	Early EN (-) n=7,942	Early EN (+) n=18,036	<i>P</i> value
Female patients, n, (%)	2,398 (30.2%)	5,987 (33.2%)	<0.001
Age, years, median (IQR)	61.0 (27)	61.0 (27)	0.914
Prognostic factor score, median (IQR)	1.0 (2)	0.0 (1)	<0.001
CT grade score, median (IQR)	1.0 (2)	0.0 (1)	<0.001
Day of starting EN, median (IQR)	10.0 (5)	5.0 (2)	<0.001
Height, cm, median (IQR)	164.0 (14)	163.0 (15)	<0.001
Body weight, kg, median (IQR)	60.0 (18)	58.2 (17)	<0.001
BMI, kg/m ² , median (IQR)	22.5 (5.4)	22.0 (5.0)	<0.001
Length of stay, days, median (IQR)	20.0 (14)	11.0 (6)	<0.001
Use of emergency medical transport, n, (%)	2546 (32.1%)	4281 (23.7%)	<0.001
Use of catecholamine, n, (%)	437 (5.5%)	520 (2.9%)	<0.001
CHDF, n, (%)	188 (2.4%)	94 (0.5%)	<0.001
Hemodialysis, n, (%)	89 (1.1%)	102 (0.6%)	<0.001
Maintenance dialysis, n, (%)	77 (1.0%)	124 (0.7%)	0.017
Blood purification, n, (%)	21 (0.3%)	5 (0.0%)	<0.001
Death at discharge, n, (%)	128 (1.6%)	139 (0.8%)	<0.001

Variable had a significant difference ($P<0.05$), Chi-square of Fisher's exact test or Mann-Whitney U test. BMI: body mass index, CHDF: continuous hemodiafiltration, CT: computed tomography, EN: enteral nutrition, IQR: interquartile range.

Table 3. Multivariable analysis for factors associated with in-hospital mortality and severity of pancreatitis

Severity	Early EN (+)			
	HR	(95% CI)	<i>P</i> value	
All	0.444	(0.358–0.551)	<0.001	
Mild	0.257	(0.185–0.357)	<0.001	
Severe	0.501	(0.419–0.601)	<0.001	
Severe factor	Prognostic factor score	0.805	(0.467–1.385)	0.433
	CT grade score	0.445	(0.355–0.558)	<0.001
	Prognostic and CT grade score	0.501	(0.419–0.601)	<0.001

Variable had a significant difference ($P<0.05$), Binominal logistic regression analysis. CI: confidence interval, CT: computed tomography, EN: enteral nutrition, HR: hazard ratio.

Table 4. Multivariable analysis for factors associated with in-hospital mortality

Severity	All		Mild		Severe	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Sex, Female	1.040 (0.838–1.290)	0.724	1.378 (0.983–1.932)	0.063	0.874 (0.724–1.056)	0.163
Age	1.058 (1.050–1.067)	<0.001	1.065 (1.051–1.078)	<0.001	1.058 (1.051–1.065)	<0.001
Use of emergency medical transport	0.934 (0.752–1.159)	0.533	1.218 (0.867–1.713)	0.235	1.053 (0.877–1.264)	0.581
Use of catecholamine	10.317 (8.220–12.949)	<0.001	10.452 (7.185–15.206)	<0.001	8.522 (7.032–10.327)	<0.001
CHDF	2.509 (1.762–3.574)	<0.001	7.250 (3.150–16.686)	<0.001	4.112 (3.132–5.400)	<0.001
Hemodialysis	1.881 (1.166–3.034)	0.01	2.494 (0.958–6.490)	0.061	2.101 (1.435–3.078)	<0.001
Maintenance dialysis	3.786 (2.265–6.330)	<0.001	6.545 (3.067–13.968)	<0.001	2.446 (1.561–3.831)	<0.001
Starting EN within 7 days	0.444 (0.358–0.551)	<0.001	0.257 (0.185–0.357)	<0.001	0.501 (0.419–0.601)	<0.001
Prognostic factor score						
1	1.086 (0.803–1.469)	0.592				
2	1.407 (1.001–1.977)	0.049				
3	2.631 (1.831–3.779)	<0.001				
4	2.809 (1.813–4.350)	<0.001				
5	4.410 (2.683–7.249)	<0.001				
6	4.722 (2.740–8.138)	<0.001				
7	8.647 (3.970–18.834)	<0.001				
8	2.872 (1.104–7.472)	0.031				
9	6.190 (1.597–23.989)	0.008				
CT grade score						
1	1.065 (0.798–1.422)	0.670				
2	1.242 (0.946–1.631)	0.119				
3	1.664 (1.127–2.456)	0.010				
4	2.047 (1.298–3.226)	0.002				

Variable had a significant difference ($P<0.05$), Binominal logistic regression analysis. CHDF: continuous hemodiafiltration, CI: confidence interval, CT: computed tomography, EN: enteral nutrition, HR: hazard ratio.

Table 5. Multivariable analysis for factors associated with in-hospital mortality

Severe factor	Prognostic factor		CT grade		Prognostic factor and CT grade	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Sex, Female	1.185 (0.663–2.118)	0.568	0.798 (0.628–1.014)	0.065	0.874 (0.724–1.056)	0.163
Age	1.047 (1.023–1.071)	<0.001	1.051 (1.043–1.060)	<0.001	1.058 (1.051–1.065)	<0.001
Use of emergency medical transport	0.854 (0.495–1.473)	0.570	1.149 (0.913–1.447)	0.236	1.053 (0.877–1.264)	0.581
Use of catecholamine	6.916 (3.843–12.446)	<0.001	6.592 (5.184–8.382)	<0.001	8.522 (7.032–10.327)	<0.001
CHDF	3.964 (1.579–9.951)	0.003	3.687 (2.668–5.096)	<0.001	4.112 (3.132–5.400)	<0.001
Hemodialysis	3.902 (1.098–13.872)	0.035	1.776 (1.139–2.768)	0.011	2.101 (1.435–3.078)	<0.001
Maintenance dialysis	0.097 (0.008–1.169)	0.066	2.775 (1.666–4.622)	<0.001	2.446 (1.561–3.831)	<0.001
Starting EN within 7 days	0.805 (0.467–1.385)	0.433	0.445 (0.355–0.558)	<0.001	0.501 (0.419–0.601)	<0.001

Variable had a significant difference ($P < 0.05$), Binominal logistic regression analysis. CHDF: continuous hemodiafiltration, CI: confidence interval, CT: computed tomography, EN: enteral nutrition, HR: hazard ratio.

tion was provided within 7 days (HR 0.501, 95% CI 0.419–0.601, $P < 0.001$) (Table 3, 4). The results of the in-hospital mortality analysis for each severe group were as follows: 1) prognostic factor score ≥ 3 and CT grade ≤ 1 (HR 0.805, 95% CI 0.467–1.385, $P = 0.433$), 2) prognostic factor score ≤ 2 and CT grade ≥ 2 (HR 0.445, 95% CI 0.355–0.558, $P < 0.001$), and 3) prognostic factor score ≥ 3 points and CT grade ≥ 2 (HR 0.501, 95% CI 0.419–0.601, $P < 0.001$) (Table 3). The results of the multivariate analysis results for each severity category are shown in Table 5.

Length of hospital stay: comparison between patients with enteral nutrition started within 7 days and those with enteral nutrition started after 7 days

We examined the relationship between length of hospital stay and the patients' age, sex, prognostic factor score, CT grade score, use of emergency medical transportation, and hemodialysis/continuous hemodiafiltration (CHDF)/maintenance dialysis, use of catecholamine preparations, and enteral nutrition within 7 days. There was a significant reduction by 8.6 days in the length of hospital stay when enteral nutrition was provided within 7 days for patients with acute pancreatitis (95% CI -9.05–-8.13, $P < 0.001$) (Table 6).

Next, we divided the prognostic factor scores and CT grades into groups and assessed the data. When the prognostic factor score was ≤ 2 and CT grade was ≤ 1 , the length of hospital stay was significantly shortened by 8.6 days in patients who were provided with enteral

Table 6. Generalized linear model analysis for factors associated with length of hospital stay

	Coef.	95% CI	<i>P</i> value
Age	0.1	0.06–0.08	<0.001
Sex, female	1.1	0.35–1.26	<0.001
Use of emergency medical transport	0.8	0.45–1.36	<0.001
Hemodialysis	10.1	6.84–13.37	<0.001
CHDF	8.6	6.10–11.02	<0.001
Maintenance dialysis	4.9	1.95–7.82	0.001
Use of catecholamine	12.6	11.34–13.86	<0.001
Enteral nutrition	-8.6	-9.05–-8.13	<0.001
Prognostic factor score			
1	0.7	0.22–1.22	0.005
2	3.0	2.20–3.70	<0.001
3	5.8	4.65–6.97	<0.001
4	13.7	11.85–15.52	<0.001
5	11.3	8.45–14.20	<0.001
6	19.8	15.74–23.92	<0.001
7	11.0	3.46–18.54	0.004
8	15.1	6.62–23.49	<0.001
9	-1.8	-9.28–5.60	0.628
CT grade score			
1	0.1	-0.36–0.65	0.574
2	2.2	1.60–2.77	<0.001
3	4.2	3.02–5.33	<0.001
4	6.3	4.53–8.00	<0.001

Variable had a significant difference ($P < 0.05$). CHDF: continuous hemodiafiltration, CI: confidence interval, CT: computed tomography.

Table 7. Generalized linear model analysis for factors associated with enteral nutrition and length of hospital stay

	Severity		Severe factor							
	Mild	Severe	Prognostic factor		CT grade		Prognostic factor and CT grade			
	Coef. (95% CI)	<i>P</i> value	Coef. (95% CI)	<i>P</i> value	Coef. (95% CI)	<i>P</i> value	Coef. (95% CI)	<i>P</i> value	Coef. (95% CI)	<i>P</i> value
Age	0.1 (0.06–0.08)	<0.001	0.1 (0.09–0.13)	<0.001	0.1 (0.02–0.28)	0.022	0.1 (0.06–0.11)	<0.001	0.1 (0.07–0.16)	<0.001
Sex, female	0.9 (0.48–1.34)	<0.001	1.2 (0.35–2.14)	0.006	1.2 (–3.50–5.98)	0.608	1.3 (0.41–2.11)	<0.001	1.1 (–0.65–2.810)	0.221
Emergency medical transport	0.8 (0.39–1.29)	<0.001	1.5 (0.65–2.42)	0.001	–1.3 (–5.50–2.83)	0.531	1.1 (0.32–1.97)	0.007	2.5 (0.69–4.27)	0.007
Hemodialysis	3.4 (–0.47–7.37)	0.085	17.2 (12.23–22.19)	<0.001	–6 (–26.72–14.70)	0.570	13.4 (7.57–19.15)	<0.001	22.3 (13.91–30.67)	<0.001
CHDF	6.3 (1.41–11.19)	0.012	13.0 (9.79–16.20)	<0.001	7.1 (–7.50–21.70)	0.340	12.1 (8.24–15.88)	<0.001	12.1 (6.83–17.42)	<0.001
Maintenance dialysis	5.8 (2.77–8.89)	<0.001	6.9 (2.07–11.64)	0.005	3.0 (–12.51–18.44)	0.707	0.6 (–6.74–7.91)	0.875	7.1 (–0.39–14.56)	0.063
Use of catecholamine	10.6 (9.19–11.98)	<0.001	17.9 (15.93–19.81)	<0.001	9.0 (0.75–17.21)	0.032	12.8 (10.36–15.18)	<0.001	19.8 (16.59–22.93)	<0.001
Enteral nutrition	–8.6 (–9.03––8.10)	<0.001	–10.8 (–11.68––9.97)	<0.001	–13.5 (–17.73––9.35)	<0.001	–9.4 (–10.23––8.63)	<0.001	–12.4 (–14.14––10.64)	<0.001

Variable had a significant difference ($P<0.05$). CHDF: continuous hemodiafiltration, CI: confidence interval, CT: computed tomography, Coef.: Coefficient.

nutrition within 7 days (95% CI –9.03––8.10, $P<0.001$) (Table 7). We further divided and evaluated the data in patients with severe acute pancreatitis and found a significant reduction in the length of hospital stay by 10.8 days (95% CI –11.68––9.97, $P<0.001$) when enteral nutrition was provided within 7 days (Table 7). When the prognostic factor score was ≥ 3 and CT grade ≤ 1 , the length of hospital stay was significantly shortened by 13.5 days (95% CI –17.73––9.35, $P<0.001$) (Table 7). When the prognostic factor score was ≤ 2 and CT grade ≥ 2 , the length of hospital stay was significantly shortened by 9.4 days (95% CI –10.23––8.63, $P<0.001$) (Table 7). When the prognostic factor score was ≥ 3 and CT grade was ≥ 2 , the length of hospital stay was significantly shortened by 12.4 days (95% CI –14.14––10.64, $P<0.001$) (Table 7).

Discussion

The results of this study suggested that early administration of enteral nutrition was related to reduced in-hospital mortality and hospitalization regardless of the severity of acute pancreatitis.

Early enteral nutrition for acute pancreatitis is an effective mode of intervention in acute pancreatitis, as recommended in all guidelines [9–11], including the Japanese guidelines [7]. One study has shown that early enteral nutrition, starting within 48 hours after admission, significantly reduced mortality and risk of multiple organ failure, operative intervention, systemic infections, local septic complications, and gastrointestinal symptoms when compared with late enteral nutrition or parenteral nutrition [5]. According to the results of a nationwide questionnaire survey in Japan, however, most enteral nutrition is started on the 7th day of acute pancreatitis onset [12], revealing that it is possible that early enteral nutrition is not performed in Japan. Considering those results, we examined the benefits of providing enteral nutrition within 7 days.

We examined a significant amount of data retrieved from the DPC database. We showed that the length of hospital stay was reduced by 8.6 days when enteral nutrition was started within 7 days in patients with acute pancreatitis. When comparing patient characteristics, the group that was provided enteral nutrition earlier had less severe acute pancreatitis, lower mortality

rates, and less severe symptoms. Therefore, we examined the effects of enteral nutrition according to the severity of acute pancreatitis. Although the length of hospital stay increased with the severity of acute pancreatitis, early administration of enteral nutrition was related to a reduction in the number of days of hospitalization and the hospital stay was shortened regardless of the severity of acute pancreatitis. Furthermore, a 56% reduction in the rate of in-hospital mortality was seen when enteral nutrition was provided within 7 days to patients with acute pancreatitis. In this study, the in-hospital mortality rate increased with increases in severity of acute pancreatitis, and the number of patients using CHDF and catecholamines also increased. Similar to a previous national survey in Japan [13], the prognosis differed depending on the combination of the prognostic factor score and CT grade in severe pancreatitis. As a severity assessment factor, the prognostic factor scores alone correlated with prognosis worse than that associated with the CT grades, and the prognosis was worse when both the prognostic factor score and CT grade indicated more severity. The effects of enteral nutrition on hospital mortality were not significantly different in cases in which the prognostic factor score was ≥ 3 and CT grade ≤ 1 , but detailed data on the treatment approaches were not obtained in this study. Thus, we speculate that even in severe cases, enteral nutrition could help treat acute pancreatitis.

The gut-barrier function is impaired during the course of severe acute pancreatitis, allowing large amounts of bacteria and endotoxins to enter the systemic circulation and cause more severe complications. Prevention of translocation of the gut bacteria is most important in avoiding extraintestinal infection and improving the prognosis in patients with acute pancreatitis [14]. Enteral nutrition is better at maintaining the gut-barrier function and decreasing bacterial translocation of severe acute pancreatitis [15]. Enteral nutrition is also more important for preventing infections rather than for nutrition supply. According to an epidemiological survey in Japan, enteral nutrition was administered to approximately 10% of patients, even in severe acute pancreatitis [7]. It is important to start enteral nutrition as early as possible if there is no severe intestinal obstruction or intestinal ischemia. Our study showed that providing early enteral nutrition is

important in the treatment of acute pancreatitis.

This study has several limitations. Owing to the retrospective study design, several biases might have been introduced, and the quality of this study was inferior to that of other types of studies such as prospective studies or RCTs. Because enteral nutrition is typically started late in the clinical situation (i.e. at around the 7th day of hospitalization), we evaluated enteral nutrition within 7 days, not within 48 h as in the previous RCT. Another limitation is that detailed clinical data could not be extracted from the DPC database. For example, we were unable to procure data regarding the etiology of the patients' acute pancreatitis, the criterion for discharging the patients, their past history of pancreatitis, physiological data, or blood laboratory findings. Moreover, this study did not analyze the treatment methods, such as fluid resuscitation, antibacterial drugs, intervention procedures, and anti-disseminated intravascular coagulation treatment, in patients with pancreatitis, nor were detailed results of the prognostic factors and CT findings available. We also could not obtain data regarding the change in the severity of the patients' condition after hospitalization. Further research is warranted to overcome these limitations. In spite of these limitations, a major strength of the present study is that the data regarding acute pancreatitis in Japan were obtained from a large-scale database based on a large number of low- to high-volume hospitals.

Conclusion

Based on the data obtained from the DPC database, we concluded that enteral nutrition within 7 days was related to decreased in-hospital mortality and hospitalization in patients with acute pancreatitis, suggesting that enteral nutrition is an important method for the treatment of patients with acute pancreatitis, regardless of the severity of the disease.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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