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Effect of home enteral nutrition after pancreaticoduodenectomy

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ABSTRACT

Objectives: Providing home enteral nutrition (HEN) might prevent further deterioration of nutritional status and reduce complication risk after very invasive abdominal surgery. The aim of this study was to assess the effect of HEN after pancreaticoduodenectomy (PD).

Methods: Between January 2013 and July 2016, 150 consecutive patients underwent PD. All patients received postoperative enteral nutrition until discharge. HEN (400 or 800 kcal/d) was introduced in March 2015 for patients with reduced food intake (daily, <15 kcal/kg ideal body weight) at discharge (HEN group). Patients with low intake at discharge treated before March 2015 were considered historical controls (non-HEN group). All patients received postoperative enteral nutrition until discharge. Primary outcomes measures included morbidity rate and nutritional status including body weight and blood examination from discharge until postoperative day (POD) 90.

Results: The HEN and non-HEN groups included 24 and 39 patients, respectively. HEN was provided for a median of 68 d (range, 21–90 d) and two patients (8.4%) developed tube obstruction during HEN. The HEN group showed significantly lower rate of morbidity of Clavien-Dindo grade II from discharge to POD 90 or higher (4 of 24, 16.7% versus 17 of 39, 46.1%; $P = 0.031$) and significantly higher rate of increase in body weight (median: 4.9% versus −4%; $P = 0.003$), serum albumin levels on POD 90 (median: 3.8 versus 3.5 g/dL; $P = 0.020$), and prognostic nutritional index (median: 48.5 versus 42.5; $P = 0.012$). Multivariate logistic analysis demonstrated that body weight at discharge (odds ratio [OR], 0.63; 95% confidence interval [CI], 0.53–0.97) and not receiving HEN (OR, 3.86; 95% CI, 1.81–15.2) were prognostic factors for morbidity after discharge.

Conclusion: HEN is safe and may reduce postdischarge morbidity and improve nutritional status after PD.

Introduction

Pancreaticoduodenectomy (PD) is the only potential curative approach for treating premalignant and malignant neoplasms of periampullary lesions and represents one of the most invasive procedures in the field of abdominal surgery, being associated with postoperative morbidity rates of 30% to 40% [1].

It is well accepted that preoperative malnutrition is an independent risk factor for morbidity and mortality in patients undergoing abdominal surgery, and postoperative nutritional support, including early enteral nutrition (EN), is effective in decreasing postoperative complications [2–6]. Although in-hospital EN in patients with PD, and in those undergoing other gastrointestinal (GI) surgeries, was theoretically expected to improve postoperative clinical outcomes, recent studies reported either no benefit or marginal benefit related to in-hospital feeding [7–9].

In contrast, continuation of EN after hospital discharge (home enteral nutrition [HEN]) and regular monitoring of nutritional status might prevent further deterioration of the nutritional status and decrease postoperative morbidity after GI surgery [10–12]. However, to the best of our knowledge, no report has focused on investigating the effects of HEN after PD.

The aim of the present study was to assess the effects of HEN on postoperative morbidity and nutritional status after discharge in patients with malnutrition after PD.

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Patients and methods

Patients

Between January 2013 and July 2016, a total of 156 adult patients underwent PD at our hospital and were considered for the present study. We excluded six patients who underwent PD via two-stage pancreatojejunostomy because they were readmitted for reconstruction within 90 d from the first surgical procedure. [13] Indications for HEN were daily oral intake <15 kcal/kg and ideal body weight (IBW) at discharge (HEN group), per the guidelines of the Japanese Society for Parenteral and Enteral Nutrition and the Nutritional Risk Screening 2002 system [14,15]. Patients who underwent PD between January 2013 and February 2015, when HEN had not been introduced in our hospital's practice, and had reduced daily oral intake at discharge (<15 kcal/IBW) were assigned to the non-HEN group. Actually, 63 had reduced oral intake at discharge (<15 kcal/IBW), and 30 were treated with HEN after March 2015. Among the 30 patients, HEN was abandoned in 6 because of postoperative diarrhea (n = 2), advanced age (n = 2), or preference of the family to stop HEN (n = 2). The remaining 33 patients were treated before March 2015. Accordingly, 24 patients were included in the HEN group and 39 were included in the non-HEN group. The clinical records of the patients included in the study were retrospectively reviewed. All aspects of the procedures were conducted according to the principles expressed in the Declaration of Helsinki.

Surgical procedures

PD was performed in accordance with the standardized Whipple's procedure. Standard lymph node dissection was performed for patients with malignant tumors but was omitted in some patients with benign or borderline malignant lesions. The portal vein and superior mesenteric vein were resected and reconstructed when these vessels involved tumors. The nerve plexus of the superior mesenteric artery was partly resected in some of the patients with pancreatic ductal carcinoma. The reconstruction was performed in the Child fashion, and enteric anastomosis was performed following either the double Roux-en-Y [13] or antecolic-modified Child methods, with additional Braun anastomosis. A pancreatic tube was placed for external drainage. In all patients who underwent PD, a 9-French feeding surgical jejunostomy tube was inserted into the jejunal limb or from the efferent loop [2]. The anal side of the tube was placed 20 to 25 cm from the GI anastomosis. Data regarding the following intraoperative factors were collected and analyzed: operative time, estimated blood loss, need for blood transfusion, portal resection, resection of nerve plexus surrounding the superior mesenteric artery, and method of reconstruction.

Perioperative management

All patients who underwent PD were preoperatively evaluated for nutritional status including body weight; prognostic nutritional index (PNI); and levels of serum albumin, cholinesterase, total cholesterol, and transthyretin (TTR). PNI was calculated as: PNI = 10 × albumin (g/dL) + 0.005 × total lymphocytes (μL) and was assessed as a nutritional marker according to previous reports [3]. The preoperative oral diet and fluid intake were stopped 18 h and 12 h before PD, respectively. Preoperative biliary drainage was performed for patients with biliary obstruction owing to tumor invasion. Routine postoperative examinations were performed as follows: blood tests (complete blood count, biochemical measurements, and coagulation profiles) were performed daily between postoperative days (POD) 1 and 5 and every few days thereafter, whereas chest and abdominal radiographs were examined daily until POD 5 and every 2 to 5 d thereafter. EN through a surgical jejunostomy tube was started at 10 to 30 mL/h (1 kcal/mL) on POD 1 and increased every 24 h—a maximum of 40 to 60 mL/h. The detail regimen of postoperative EN contained 60% carbohydrates, 20% lipids, 20% protein vitamin, mineral, trace element, and immunonutrition supplements. Oral fluid intake after PD was initiated on POD 2 and modified depending on the occurrence of nausea, awareness, and pain. Oral food intake usually started on POD 3. After the start of oral food intake, the daily amount of the EN was controlled as the combined amount of oral intake and enteral feeding covered the required total energy expenditure calculated using the Harris–Benedict equation by POD 7 [6]. The antiflatulence and pancreatic digestive enzyme replacement were used routinely to prevent diarrhea in most cases, whereas antidiarrheal medication was indicated if diarrhea was prolonged or exacerbated without infection. Before discharge, patients or caregivers were trained in the correct use of HEN in the HEN group.

Postoperative management after discharge

HEN was performed as 400 or 800 kcal/d, which was selected in order to fulfill the total energy expenditure calculated using the Harris–Benedict equation [6]. Because a pack of the product contained 400 kcal, either 400 or 800 kcal/d of HEN was selected for the better compliance of the patients. In principle, 400 kcal/d of HEN was selected when the total energy expenditure calculated using the Harris–Benedict equation was fulfilled, otherwise 800 kcal/d of HEN was selected. The content of HEN included any standard polymeric formula providing 1 kcal/mL with 60% carbohydrates, 20% lipids, and 20% protein. Attending physicians controlled HEN dose and speed according to the patients' condition, willingness, and ability to receive HEN. In general, HEN could be withdrawn after 6 wk from discharge, but could also be stopped earlier if the patient had no intent of continuation or when the amount of the daily oral intake was recovered to fulfill the nutritional requirement calculated by the Harris–Benedict equation. In both the HEN and the non-HEN groups, morbidity after discharge was assessed at the outpatient clinic once every 2 wk until 6 wk after discharge and, if necessary, the patients were readmitted. Thereafter, the patients visited the outpatient clinic every 4 wk until POD 90. From discharge until POD 90, PNI; body weight; body mass index; and the levels of serum albumin, cholinesterase, total cholesterol, and transthyretin were investigated in both groups.

Assessment of postoperative morbidity

In-hospital morbidity and mortality were assessed during hospitalization and after discharge until POD 90. Morbidity data were recorded and graded according to the Clavien–Dindo classification [16]. Additionally, to investigate the efficacy of HEN, we focused on postoperative morbidity and mortality (i.e., developed after discharge). Postoperatively, pancreatic fistula and gastric-delayed emptying were graded according to the guidelines of the International Study Group of Pancreatic Fistula [17] and International Study Group of Pancreatic Surgery [18], respectively, both during hospitalization and after discharge.

Statistical analysis

Categorical variables, expressed as number (%), were compared between the groups using Fisher's exact test. Continuous variables, expressed as median values with range, were compared between the groups using the Mann–Whitney U test. Statistical significance ($P < 0.05$) was assessed using a two-tailed test. Multivariate analysis using a logistic regression model was performed to assess potential risk factors for morbidity after hospital discharge. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each risk factor. The rate of increase in body weight (%) at discharge and on POD 90 were calculated as follows: (value at discharge − value at initiation) / (value at initiation) × 100, and (value on POD 90 − value at discharge) / (value at discharge) × 100, respectively. The cutoff levels for estimated blood loss, albumin levels, and PNI were set at 800 mL, 3.5 g/dL, and 45, respectively, based on previous reports [3,19,20]. Other continuous variables were categorized by the median value. Statistical analysis was performed using JMP (version 11.0.6; SAS Institute Inc., Cary, NC).

Results

Patient characteristics

Table 1 provides a summary of the patients' characteristics. There is no significant difference in preoperative factors. As for intraoperative factors, estimated blood loss (422 versus 670 mL; $P = 0.049$) and prevalence of Roux-en-Y reconstruction (16.7% versus 74.3%; $P < 0.001$) were significantly higher for the non-HEN group. Regarding postoperative factors, oral intake (585 versus 700 kcal/d; $P = 0.008$) and body weight (46.6 versus 52.8 kg; $P = 0.045$) at discharge were significantly lower for the HEN group, whereas the rate of intrapapillary mucinous neoplasm was significantly higher (16.6% versus 0%; $P = 0.018$). There was no difference between the groups in terms of in-hospital morbidity or other nutritional status. None of the patients received radiotherapy treatment during the study period.

HEN outcomes

The median duration of HEN was 63 d (range, 21–90 d). Fourteen patients were started on HEN at 400 kcal/d, and 10 were started at 800 kcal/d. Sixteen patients (67%) continued HEN for >42 d after discharge. HEN was terminated before 42 d after discharge because of tube obstruction in two patients. The remaining six patients stopped HEN within 6 wk after discharge because the oral intake achieved the daily nutritional requirement without HEN. None of the patients experienced new adverse events

Table 1
Characteristics of patients who underwent pancreaticoduodenectomy

Characteristic	HEN group	Non-HEN group	*P*-value
Patients, *n*	24	39	
Patient-related factors			
Age y	71 [39–84]	72 [32–83]	0.782
Sex (male/female)	12/12	22/17	0.415
Body height, cm	161 [139–175]	161 [139–172]	0.651
Body weight, kg	53 [34.6–81.2]	60 [36–85]	0.061
Body mass index, kg/m^2	20.6 [16.5-27.1]	23.2 [17.9-34.9]	0.089
ASA score (1/2/3)	5/1/1	5/32/2	0.696
Preoperative HbA c, %	5.8 [4.7–7.2]	5.9 [3.9–9.4]	0.603
Preoperative total bilirubin, mg/dL	0.8 [0.4–2]	1 [0.4–7.2]	0.185
Preoperative albumin, g/dL	3.8 [3.2–4.7]	3.7 [2.3–4.6]	0.553
Preoperative cholinesterase, mg/dL	257 [137–385]	256 [126–397]	0.916
Preoperative PNI	46.1 [38–55.5]	46.5 [27.5–53.8]	0.632
Preoperative transthyretin, mg/dL	22.0 [13.9–39.7]	21.4 [9.8–36.6]	0.999
Preoperative biliary drainage	11 (45.8)	19 (48.7)	0.823
Preoperative chemotherapy	2 (8.3)	2 (5.1)	0.795
Intraoperative factors			
Operative time, min	574 [417–753]	574 [417–753]	0.921
Estimated blood loss, mL	422 [190–1540]	670 [220–2380]	**0.049**
Blood transfusion	0 (0)	6 (15.4)	0.074
Portal vein resection	5 (20.8)	11 (28.2)	0.566
Plexus dissection	22 (91.6)	32 (82.1)	0.462
Reconstruction (Child/Roux-en-Y)	20/4	10/29	<**0.001**
Postoperative factors			
Postoperative hospital stay, d	24 [16–58]	26 [16–51]	0.45
Surgical site infection	9 (37.5)	10 (25.6)	0.399
Diarrhea	4 (16.7)	3 (7.7)	0.412
Pancreatic fistula grade (≥B)*	7 (29.1)	19 (48.7)	0.237
Delayed gastric emptying grade (≥B)†	9 (37.5)	13 (33.3)	0.808
Clavien–Dindo grade ≥IIIa	5 (20.8)	5 (12.8)	0.485
Albumin at discharge, g/dL	3.3 [2.5–4.4]	3.3 [2.5–4.0]	0.434
Cholinesterase at discharge, mg/dL	200 [100–252]	164 [81–363]	0.245
PNI at discharge	40.2 [31.5–53.5]	39.5 [35.0–50.0]	0.472
Total cholesterol at discharge, mg/dL	115 [78–175]	127 [85–224]	0.281
Transthyretin at discharge, mg/dL	16.4 [9.2–23.3]	13.5 [6.3–22.3]	0.224
Oral intake at discharge, kcal/d	585 [320–950]	700 [440–980]	**0.008**
Body weight at discharge, kg	46.6 [31.5–76.7]	52.8 [35.5–76.3]	**0.045**
Body mass index at discharge, kg/m^2	18.2[25.5–13.8]	23.2[17.9-34.9]	0.053
Rate of increase in body weight, %	−9.8 [−26.6 to −0.2]	−7.0 [−14.9–4.6]	0.103
Pathologic findings			
Pancreatic adenocarcinoma	13 (54.1)	29 (74.4)	0.098
Biliary adenocarcinoma	3 (12.5)	5 (12.8)	0.999
Duodenal papillary adenocarcinoma	3 (12.5)	4 (10.3)	0.999
Intrapapillary mucinous neoplasm	4 (16.6)	0 (0.0)	**0.018**
Neuroendocrine tumor	1 (4.2)	1 (2.6)	0.878
Oncologic management after discharge			
AC	7 (29.2)	15 (38.7)	0.425
Duration of AC until POD 90, d	40 [12–69]	30 [5–56]	0.336
Regimen of AC (TS–1/ GEM)	1/6	3/12	0.887

AC, Adjuvant chemotherapy; ASA, American Society of Anesthesiologists; GEM, gemcitabine; HbA1 c, glycated hemoglobin; HEN, home enteral nutrition; PNI, prognostic nutritional index; POD, postoperative day; TS-1, tegafur-gimeracil-oteracil
HEN was introduced in March 2015 and considered in patients with reduced daily oral intake (<15 kcal/kg ideal body weight) at discharge. Such patients were included in the HEN group, whereas patients treated between January 2013 and February 2015, before introduction of HEN, and with similarly reduced oral intake per day, were defined as the non-HEN group
*Pancreatic fistula was graded postoperatively according to the guidelines of the International Study Group of Pancreatic Fistula.
†Delayed gastric emptying was graded according to the guidelines of the International Study Group of Pancreatic Surgery.

associated with the HEN procedure including stoma-site infection or tube dislocation. One patient experienced diarrhea but it was controlled with antidiarrheal medication.

Postdischarge morbidity and nutritional status after discharge

Table 2 summarizes postdischarge morbidity until POD 90 and nutritional condition on POD 90. After discharge, morbidity of Clavien–Dindo grade II or more was observed significantly less frequently for the HEN group (16.7% versus 43.6%; $P = 0.032$). No deaths were reported even before POD 90 in either group. One patient in the HEN group had morbidity grade IIIA because of hemorrhage from the diverticulum, whereas the rest of the patients were classified as having morbidity grade II. At POD 90, the rate of increase in body weight (4.9% versus −4%; $P = 0.003$), serum albumin levels (3.8 versus 3.4 g/dL; $P = 0.020$), and PNI (48.5 versus 42.5, $P = 0.012$) were significantly higher in the HEN group. Figure 1 shows postoperative changes in body weight and serum albumin levels. Body weight at initiation and discharge were significantly lower in the HEN group but were comparable between the groups on POD 90. Serum albumin levels were comparable between the groups at initiation and discharge but had significantly improved in the HEN group on POD 90.

Table 2
Postoperative outcomes from discharge until postoperative day 90

Outcome	HEN group	Non-HEN group	*P*-value
Patients, *n*	24	39	
Postoperative morbidity after discharge			
Clavien–Dindo grade ≥II	4 (16.7)	17 (43.6)	**0.032**
Cholangitis	2 (8.4)	8 (20.5)	0.135
Anorexia	1 (4.2)	4 (10.3)	0.641
Diarrhea	1 (4.2)	2 (5.2)	0.999
Hemorrhage from diverticulum	1 (4.2)	0 (0.0)	0.381
Lower limb edema	0 (0.0)	2 (5.2)	0.865
Herpes zoster	0 (0.0)	1 (2.6)	0.999
Readmission before POD 90	3 (12.5)	8 (20.5)	0.509
Nutritional status on POD 90			
Body weight, kg	48.4 [30.2–77]	49.4 [33.3–65.4]	0.932
Body mass index, kg/m^2	19.1[14.4–25.6]	18.2 [15.0–23.9]	0.863
Rate of increase in body weight, %	4.9 [−0.1 to 9]	−4.0 [−9.8 to 3.5]	**0.003**
Albumin, g/dL	3.8 [3.2–4.7]	3.4 [2.6–4.6]	**0.020**
Cholinesterase, mg/dL	24 [141–287]	210 [153–316]	0.196
PNI	48.5 [38.3–53]	42.5 [35.5–52.5]	**0.012**
Total cholesterol, mg/dL	148 [108–198]	148 [93–194]	0.917
Transthyretin, mg/dL	20.7 [10.2–25.3]	16.5 [5.2–20.8]	0.723

ASA, American society of anesthesiologists; BMI, body mass index; HEN, home enteral nutrition; PNI, prognostic nutritional index; POD, postoperative day;
HEN was introduced in March 2015 and considered in patients with reduced daily oral intake (<15 kcal/kg ideal body weight) at discharge. Such patients were included in the HEN group, whereas patients treated between January 2013 and February 2015, before introduction of HEN, and with similarly reduced oral intake per day, were defined as the non-HEN group
Values represent median [range], total number, or number (frequency). Values with statistical significance of the intergroup differences are marked in **bold**

Predictive factors for morbidity from discharge until POD 90

Preoperative body weight ≥60 kg (OR, 0.32; 95% CI, 0.09–0.99; $P = 0.049$), preoperative PNI ≥40 (OR, 0.61; 95% CI, 0.25–0.66; $P = 0.032$), body weight at discharge ≥60 kg (OR, 0.18; 95% CI, 0.03–0.84; $P = 0.029$), and not receiving HEN (OR, 2.49; 95% CI, 1.26–7.56; $P = 0.003$) were found to be significantly associated with morbidity after discharge (Table 3). Of these factors, body weight at discharge ≥60 kg (OR, 0.63; 95% CI, 0.63–0.97; $P = 0.042$) and not receiving HEN (OR, 3.86; 95% CI, 1.81–15.2; $P = 0.025$) were independent prognostic factors for morbidity after discharge.

Discussion

The present study demonstrated that HEN was safe and moreover improved morbidity and nutritional status after discharge. Finally, multivariate logistic regression analysis revealed that not receiving HEN was one of the independent prognostic factors for morbidity after discharge.

HEN itself is an established technique for maintaining adequate nutritional status, with acceptable complication rates, especially in patients undergoing major GI surgery [10,11,21]. Gavazzi et al. observed 38 patients with upper GI cancer who received HEN for 2 mo after discharge and noted no specific complications [12]. In our series, two patients who received HEN developed tube obstruction, which prompted interruption of HEN and no further measure; in other words, these patients could be considered to be part of the non-HEN group. In addition, although HEN could be withdrawn after 42 d from discharge, 16 patients (67%) continued HEN for >42 d after discharge; in other words, more than half of the patients who received HEN were both capable and willing to continue HEN beyond the pre-established 6-wk cutoff. Accordingly,

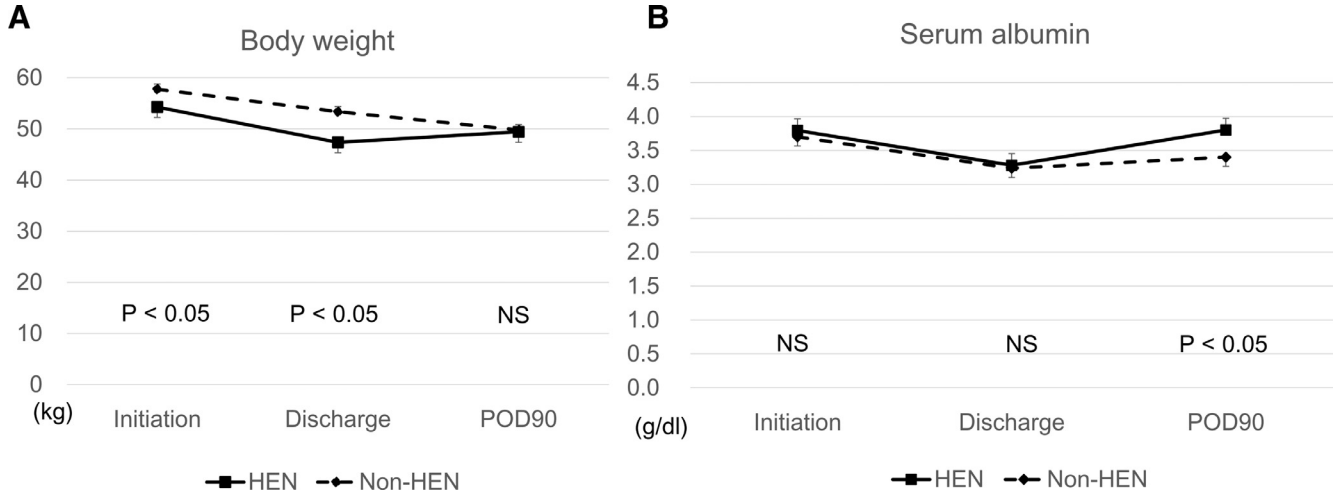

Fig. 1. Changes in nutritional status during follow-up after pancreaticoduodenectomy. (**A**) Postoperative change in body weight at initiation, at discharge, and on POD 90. (**B**) Postoperative change in serum albumin levels at initiation, at discharge, and on POD 90. POD, postoperative day.

Table 3
Univariate and multivariate analysis results for morbidity risk from discharge until postoperative day 90

Risk factor vs reference	Univariate analysis			Multivariate Analysis		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Preoperative factors						
Sex						
Male vs Female	0.77	0.27–2.15	0.620			
Age, y						
≥70 vs ≤69	1.10	0.26–2.18	0.856			
Body weight, kg						
≥60 vs ≤59.9	0.32	0.09–0.99	**0.049**			
ASA score						
≥3 vs ≤2	1.12	0.10–25.1	0.702			
HbA1c, %						
≥5.9 vs ≤5.8	0.29	0.07–1.08	0.067			
Albumin, g/dL						
≥3.5 vs ≤3.4	0.68	0.16–2.48	0.574			
Cholinesterase, mg/dL						
≥201 vs ≤200	0.90	0.17–3.95	0.891			
Transthyletine, g/dL						
≥20 vs ≤19.9	1.09	0.29–3.91	0.893			
PNI						
≥40 vs ≤39	0.61	1.11–12.6	**0.032**			
Preoperative body muscle weight, kg						
≥30 vs ≤29.9	0.41	0.07–1.71	0.228			
Preoperative body cell mass, kg						
≥25 vs ≤ 24.9	1.50	0.39–5.79	0.548			
Preoperative body fat weight, kg						
≥10 vs ≤9.9	0.31	0.04–1.54	0.160			
Preoperative biliary drainage	1.12	0.40–3.14	0.823			
Intraoperative factors						
Operative time, min						
≥600 vs ≤599	2.46	0.50–10.3	0.156			
Estimated blood loss, mL						
≥800 vs ≤799	0.41	0.13–1.27	0.125			
Blood transfusion	0.46	0.07–2.70	0.461			
Portal resection	1.75	0.75–1.76	0.127			
Reconstruction						
Child vs. Roux-en-Y	1.33	0.46–3.90	0.592			
Postoperative factors						
Clavien–Dindo grade						
≥III vs ≤II	1.20	0.29–6.07	0.806			
Duration of hospital stay, d						
≥28 vs ≤27	0.82	0.28–2.41	0.716			
Oral intake at discharge kcal/IBW						
≥13 vs ≤12.9	0.37	0.12–1.09	0.073			
Albumin at discharge, g/dL						
≥3.5 vs ≤3.4	1.02	0.25–4.47	0.976			
PNI at discharge						
≥40 vs ≤39	0.54	0.07–2.68	0.469			
Cholinesterase at discharge, mg/dL						
≥201 vs ≤200	0.97	0.25–3.94	0.973			
Transthyletin at discharge, g/dL						
≥15.0 vs ≤14.9 g/dL	1.99	0.46–9.57	0.354			
Body weight at discharge, kg						
≥60 vs ≤59.9	0.18	0.03–0.84	**0.029**	0.63	0.63–0.97	**0.042**
Not receiving home enteral nutrition	3.24	1.26–7.56	**0.003**	3.86	1.81–15.2	**0.025**
Adjuvant chemotherapy	2.40	0.83–7.18	0.105			
Pathologic findings						
Malignancy vs benign	2.49	0.27–2.13	0.565			

ASA, American Society of Anesthesiologists; CI, confidence interval; HbA1c, glycated hemoglobin; IBW, ideal body weight; OR, odds ratio; PNI, prognostic nutritional index
Values marked in **bold** indicate statistically significant risk factors

we can conclude that HEN is a relatively safe procedure after PD. However, after preliminary introduction of HEN from March 2015, 6 of 30 patients (20%) could not receive HEN because of postoperative diarrhea, medical condition, or ability to administer HEN. Thus, we may conclude that, to receive HEN, patients still need to be in good condition especially regarding bowel function; moreover, significant knowledge and family support were also factors important in the decision to receive HEN.

Several studies reported on the efficacy of HEN after other GI surgery [10–12,21]. Bowrey et al. reported that compared with the postdischarge outcomes noted in 21 patients only with oral intake after esophagectomy or total gastrectomy, the outcomes noted in 20 patients who received HEN were significantly better in terms of maintaining body weight at 6 wk (mean difference, 3.9 kg; 95% CI, 1.6–6.2 kg) and 6 mo (mean difference, 2.5 kg; 95% CI, 1.2–6.1 kg), as well as in terms of muscle strength, showing higher mid-arm circumference, mid-arm muscle circumference, triceps skin fold thickness, and right handgrip [21]. The present study demonstrated that HEN is not only safe but also effective in improving postoperative morbidity (16.7%, 4 of 24 versus 43.6%, 17 of 39; $P = 0.032$) in

addition to facilitating beneficial changes in nutritional status after discharge, including improved rate of increase in body weight, serum albumin levels, and PNI on POD 90. In addition, on multivariate logistic analysis, not receiving HEN was one of the independent prognostic factors (OR, 3.86; 95% CI, 1.81–15.2; $P = 0.025$) for morbidity after discharge, the other factor being body weight at discharge (OR, 0.63; 95% CI, 0.63–0.97; $P = 0.042$). Unlike in-hospital morbidity such as postoperative pancreatic fistula and pancreatic hemorrhage, postdischarge morbidity mainly consisted of infectious complications and intestinal problems (e.g., anorexia resulting from delayed gastric emptying and diarrhea), which depend on immune and nutritional status. Given the unusually high morbidity rates after PD (up to 30% to 40%, which is higher than the morbidity rates associated with other GI surgery procedures) [22], the benefits of HEN are expected to be clinically relevant because HEN may contribute not only to improvement of nutritional status but also to the reduction of morbidity after discharge.

The limitations of the present study included its retrospective design and the low number of patients. Moreover, although our surgical procedure and postoperative protocol did not change significantly over the course of the study period (i.e., 2013 to 2016), the effect of historical and selection bias cannot be excluded because HEN was introduced from March 2015. The ratio of pancreatic adenocarcinoma and Roux-en-Y reconstruction was significantly higher in the non-HEN groups. Although the ratio of the plexus dissection was comparable in both groups, the patients with adenocarcinoma usually needs the wide range of plexus dissection, which may lead to decreases in the nutritional condition after surgery. The difference in the reconstruction of PD may also be one of the causes of the decreased nutritional condition. In addition, although the procedure associated with HEN may affect the patients' quality of life, we did not assess this aspect in the present study because no such data were included in the clinical records we reviewed. Further analyses using a strictly designed prospective study recruiting a large number of patients are needed to clarify the efficacy of HEN after PD.

Despite its limitations, this retrospective study found evidence that HEN is a safe and feasible procedure and moreover may improve postdischarge morbidity and nutritional status in malnourished patients.

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