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ORIGINAL ARTICLE

Early oral feeding after pancreatoduodenectomy enhances recovery without increasing morbidity

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Abstract

Objective: The aim of this study was to evaluate whether a change in the routine feeding strategy applied after pancreatoduodenectomy (PD) from nasojejunal tube (NJT) feeding to early oral feeding improved clinical outcomes.

Methods: An observational cohort study was performed in 102 consecutive patients undergoing PD. In period 1 ($n = 51$, historical controls), the routine postoperative feeding strategy was NJT feeding. This was changed to a protocol of early oral feeding with on-demand NJT feeding in period 2 ($n = 51$, consecutive prospective cohort). The primary outcome was time to resumption of adequate oral intake.

Results: The baseline characteristics of study subjects in both periods were comparable. In period 1, 98% ($n = 50$) of patients received NJT feeding, whereas in period 2, 53% ($n = 27$) of patients did so [for delayed gastric empting (DGE) ($n = 20$) or preoperative malnutrition ($n = 7$)]. The time to resumption of adequate oral intake significantly decreased from 12 days in period 1 to 9 days in period 2 ($P = 0.015$), and the length of hospital stay shortened from 18 days in period 1 to 13 days in period 2 ($P = 0.015$). Overall, there were no differences in the incidences of complications of Clavien–Dindo Grade III or higher, DGE, pancreatic fistula, postoperative haemorrhage and mortality between the two periods.

Conclusions: The introduction of an early oral feeding strategy after PD reduced the time to resumption of adequate oral intake and length of hospital stay without negatively impacting postoperative morbidity.

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Introduction

Pancreatoduodenectomy (PD) is the treatment of choice for resectable (pre-)malignant neoplasms in the pancreatic head or periampullary region.[1] Although postoperative mortality rates have decreased over recent decades,[2] PD is still associated with significant morbidity, including a 33–45% incidence of delayed gastric emptying (DGE),[3–5] which interferes with the resumption of a normal diet after surgery and frequently results in the need for nutritional support and a prolonged hospital stay.[6]

Some studies have suggested that enteral nutrition after PD reduces hospital length of stay (LoS), readmission rates and complication rates.[7–9] The guidelines of the European Society for Parenteral and Enteral Nutrition (ESPEN) recommend the routine use of early enteral nutrition in all patients undergoing major gastrointestinal resections for cancer.[10] By contrast, the current American Society of Parenteral and Enteral Nutrition (ASPEN) guidelines recommend the use of on-demand postoperative nutritional support.[11] In addition, a recent systematic review suggested that oral feeding, with on-demand nasojejunal tube (NJT)

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feeding, is the most appropriate routine feeding strategy after PD because it is at least non-inferior to enteral and parenteral nutrition in terms of hospital LoS and risk for complications.[12] Furthermore, nasoenteral and parenteral feeding strategies are associated with specific complications, including the dislodgement of NJTs in a third of patients, bowel strangulation and perforation following percutaneous jejunostomy (albeit rarely) and, in cases of parenteral nutrition, an up to twice as high risk for infectious complications.[13–17] However, studies directly comparing early oral feeding with routine NJT feeding after PD are lacking.

The discrepancy in views on the optimal routine feeding strategy after PD (routine versus on-demand nasoenteral feeding) and the lack of evidence to support routine (par)enteral nutrition after PD led the study institution to change its feeding protocol from routine NJT feeding to an early oral feeding strategy with on-demand NJT feeding. The aim of this study was to evaluate whether this change in the routine postoperative feeding strategy improved outcomes.

Materials and methods

Patients

An observational, non-randomized, prospective cohort study with historical controls was performed in 111 consecutive patients undergoing PD at the University Medical Centre Utrecht from June 2010 to December 2012. A subset of these patients ($n = 20$) has been described in a previous study.[13] Included were adult patients undergoing any of classic Whipple PD, pylorus-preserving PD or total pancreatectomy for any indication. Excluded were all patients who underwent PD in the transition period (October–December 2011), during which the new early oral feeding strategy was introduced on the ward ($n = 9$). In this transition period, all nurses and treating physicians attended a training session conducted by the study coordinator and the department's dietician to explain the standardized early oral feeding protocol. To further improve adherence, the protocol was made available to all nurses and physicians on a plastic card on the ward. No other changes in surgical or medical treatment strategy (e.g. surgical technique, erythromycin use) that might influence outcomes were introduced during the entire study period. Patients were categorized into two groups based on the period in which they underwent surgery and thereby the routine feeding protocol to which they were subjected.

Period 1: Routine NJT feeding

In period 1 (June 2010 to September 2011), the routine postoperative feeding strategy was NJT feeding. Enteral nutrition was delivered via a NJT (Freka Trelumina tube; Fresenius Kabi Ltd, Runcorn, UK), which was placed in the jejunum during PD. The tube was introduced by the anaesthesiologist through the nose, into the stomach and advanced for ≥30 cm through the duodeno- or gastrojejunostomy into the efferent limb after the creation of the dorsal part of this anastomosis. The tube was secured to the nostrils with tape. The patency of the tube was tested before the abdomen was closed. Enteral nutrition (NV Nutricia, Zoetermeer, the Netherlands) was started on the first postoperative morning at a rate of 25 ml/h and increased by 25 ml per 6 h to the amount advised by the consulting dietician according to national guidelines.[18] In the event of dislodgement of the NJT, the tube was replaced only when oral intake in the following days was expected to be inadequate.

Oral intake was started depending on digestive symptoms. When oral intake was adequate, enteral nutrition was discontinued. The NJT was removed at this stage.

Period 2: Early oral feeding strategy

The early oral feeding strategy implemented in period 2 (January–December 2012) involved the resumption of oral intake as per the feeding protocol. Patients were started on oral feeding immediately after surgery and were given liquid drinks from day 0 (day of surgery), solid food from day 2 and a regular diet from day 3. Oral nutritional supplements given twice per day (200 ml Nutridrink Protein; NV Nutricia) were initiated on day 2 and discontinued at discharge.

Oral intake was recorded daily and evaluated on days 4 and 7 by the consulting dietician. When oral intake was insufficient on postoperative day 7 (<50% of the required daily calorie/protein intake as calculated by the dietician), a NJT was endoscopically placed (on demand) and enteral nutrition was administered until oral intake was adequate.

In patients who were found to suffer from malnutrition at preoperative screening, a NJT was placed during PD to enable the provision of postoperative enteral nutrition according to the protocol followed in period 1. According to the intention-to-treat principle, these patients were included in the early oral feeding strategy group (period 2). Oral feeding was initiated simultaneously according to the early oral feeding protocol, but no oral nutritional supplements were given.

Preoperative management

In both periods, all patients were preoperatively screened for malnutrition in the outpatient department by trained nurses using the Malnutrition Universal Screening Tool (MUST)[19] and were informed about the postoperative feeding strategy. In the event of malnutrition [defined by a MUST score of ≥2, a body mass index (BMI) of <18.5 kg/m^2 and/or severe preoperative weight loss], patients were referred to a dietician and started on preoperative nutritional support, including oral nutritional supplements or enteral nutrition, if possible, at least 14 days before surgery.

Surgical approach

The surgical approach was identical in both periods. Pancreaticoduodenectomy was performed by a team specializing in hepatobiliary and pancreatic surgery. Reconstruction was performed with an end-to-side, duct-to-mucosa pancreatojejunostomy [International Study Group of Pancreatic Surgery (ISGPS) type IAS0[20]] over a 6-cm, 6-Fr stent, end-to-side

hepaticojejunostomy and antecolic end-to-side duodenojejunostomy (pylorus-preserving PD) or antecolic gastrojejunostomy combined with a Roux-en-Y reconstruction (Whipple procedure).

Postoperative management

Postoperative management was similar in both periods. Early postoperative analgesia was achieved epidurally or, when contraindicated or when epidural placement was not successful, by i.v. patient-controlled analgesia. Nasogastric tubes were removed on day 1 unless the drainage amount per 24 h was >300 ml. In such cases, the tube was removed when the drainage amount per 24 h dropped to <300 ml. Patients were mobilized out of bed from day 1 under the guidance of a physiotherapist or nurse. Peripancreatic drains were removed when the drainage amount per 24 h was <50 ml and amylase content was less than three times the upper normal serum value (measured on days 1, 3 and 5). Total parenteral nutrition (TPN) was started only when enteral feeding was unsuccessful or contraindicated. Patients were discharged when they were fully mobile (i.e. they had achieved autonomous activity or returned to their preoperative level of activity), oral intake was adequate and there was no evidence of local or systemic complications.

Definitions

All postoperative complications were graded according to the Clavien–Dindo system of classification.[21] The postoperative course was defined as complicated if a complication occurred that required any form of intervention (Clavien–Dindo Grade III or higher). Both postoperative NJT placement and NJT replacement after dislodgement were graded as representing a Clavien–Dindo Grade III incident. Postoperative pancreatic fistula, DGE and post-pancreatectomy haemorrhage were defined according to ISGPS definitions.[22–24] Cancer stage was defined according to the 7th edition of the American Joint Committee on Cancer (AJCC) staging system.[25] Severe preoperative weight loss was defined as unintentional weight loss of ≥10% of body weight within 6 months or ≥5% of body weight within 1 month prior to presentation at the outpatient department. Oral intake was defined as adequate when it exceeded 50% of the daily required caloric intake with an upward trend, or when it was reported as adequate by the treating physician or dietician. Tube dislodgement was defined as the displacement of the tip of the feeding tube into D2 or more proximally in the gastrointestinal tract, making the continuation of tube feeding unsafe or impossible.

Data collection

From 1 January 2012 (period 2), data were prospectively collected and entered into an electronic database. Prior to this date (period 1), data were retrospectively collected from computerized clinical records and daily notes. Baseline characteristics collected were patient age, sex, American Society of Anesthesiologists (ASA) physical status, BMI, MUST score, severe preoperative weight loss, preoperative dietary intervention, histopathological diagnosis, cancer stage and type of procedure.

Outcomes

The primary outcome was time to resumption of adequate oral intake. Secondary outcomes were time to start of oral and solid food intake, TPN use, duration of (par)enteral nutrition, use of prokinetic agents, weight loss during admission, postoperative surgical, general and tube-related complications (in-hospital and during readmission), incidence of postoperative pancreatic fistula, DGE, post-pancreatectomy haemorrhage, length of hospital and intensive care unit (ICU) stays, readmission within 30 days after discharge and in-hospital mortality.

Statistical analysis

Sample size was based on the number of eligible patients treated according to the early oral feeding strategy in a 1-year period (2012, period 2). These patients were compared with a control group, which included an equal number of eligible patients who were treated before the implementation of the new feeding strategy (period 1).

Analyses were performed according to intention to treat, meaning that there were no crossovers between groups. Values are expressed as the median and interquartile range (IQR), unless specified otherwise. Data were analysed using IBM SPSS Statistics for Windows Version 20 (IBM Corp., Armonk, NY, USA). Continuous non-normally distributed variables were compared using the Mann–Whitney *U*-test. Categorical variables were compared using the chi-squared test or Fisher's exact test as appropriate. For multivariable analysis, a binary logistic regression model was used. A two-tailed *P*-value of <0.05 was considered to indicate statistical significance. To assess the presence of any potential negative effects of early oral feeding in patients with a complicated postoperative course, subgroup analyses for the main nutritional and hospitalization parameters were performed in patients with (and without) a complicated postoperative course, DGE and pancreatic fistulae. An additional subgroup analysis was performed in period 2 based on the placement of a NJT in order to assess whether patients who eventually required NJT feeding in period 2 were disadvantaged by the early oral feeding strategy.

Results

Patients

Between January and December 2012 (period 2), 51 patients underwent PD with routine postoperative early oral feeding including on-demand NJT feeding. Another 51 consecutive patients who underwent PD with routine postoperative NJT feeding between June 2010 and September 2011 (period 1) served as historical controls. Baseline characteristics of patients did not differ between the periods (Table 1).

Table 1 Baseline characteristics of the study cohort

	Period 1 Routine NJT feeding (*n* = 51)	Period 2 Early oral feeding with on-demand NJT feeding (*n* = 51)	*P*-value
Male, *n* (%)	36 (71%)	29 (57%)	0.149
Age, years, median (IQR)	65 (58–74)	67 (63–74)	0.223
Body mass index, kg/m^2, median (IQR)	24.7 (21.9–26.9)	25.8 (23.3–28.4)	0.061
MUST score ≥2, *n* (%)	7 (17%)	12 (26%)	0.308
Severe weight loss, *n* (%)	21 (41%)	18 (36%)	0.539
Preoperative dietary intervention, *n* (%)	17 (33%)	25 (49%)	0.108
Preoperative enteral nutrition, *n* (%)	6 (12%)	5 (10%)	0.750
ASA class, *n* (%)			0.103
1	12 (24%)	16 (31%)	
2	34 (67%)	24 (47%)	
3	5 (10%)	11 (22%)	
AJCC cancer stage ≥IIa, *n* (%)	38 (75%)	43 (84%)	0.221
Histopathological diagnosis, *n* (%)			0.844
Pancreatic adenocarcinoma	20 (39%)	25 (49%)	
Ampullary adenocarcinoma	9 (18%)	9 (18%)	
Cholangiocarcinoma	8 (16%)	5 (10%)	
Duodenal adenocarcinoma	1 (2%)	2 (4%)	
Neuroendocrine tumour	4 (8%)	4 (8%)	
Pancreatitis	5 (10%)	2 (4%)	
Other	4 (8%)	4 (8%)	
Procedure, *n* (%)			0.621
Pylorus-preserving PD	37 (73%)	33 (65%)	
Whipple PD	2 (4%)	5 (10%)	
Total pancreatectomy	1 (2%)	2 (4%)	
PD with additional resection	11 (22%)	11 (32%)	

NJT, nasojejunal tube; IQR, interquartile range; MUST, Malnutrition Universal Screening Tool; ASA, American Society of Anesthesiologists; AJCC, American Joint Committee on Cancer; PD, pancreatoduodenectomy.

Efficacy

In period 2, postoperative time to the resumption of adequate oral intake decreased by 3 days and hospital LoS decreased by 5 days (Table 2).

Reasons for NJT feeding in period 2 (n = 27) were DGE in 20 patients and preoperative malnutrition in seven patients. In patients with DGE, NJT feeding was initiated after a median of 7 days (IQR: 4–8 days). Seven patients in whom additional postoperative nutrition was indicated by signs of preoperative malnutrition (see definition in Materials and methods) did not receive a NJT during PD for logistical reasons (e.g. the correct feeding tube was not available). Three of these patients received NJT feeding secondarily after 1, 2 and 5 days, respectively, and were discharged after a median of 15 days (IQR: 11–31 days). The other four patients were discharged without ever having received enteral nutrition after a median of 8 days (IQR: 6–11 days).

Complications

Morbidity and mortality rates are shown in Table 3. Overall morbidity requiring intervention (Clavien–Dindo Grade III or higher) and mortality did not differ between the periods.

The incidence of dislodgement of a primarily placed NJT significantly decreased from 43% of patients in period 1 to 20% in period 2. As only 27 patients in period 2 received a NJT, the rates of dislodgement of primarily placed tubes were similar in both periods [22 of 50 tubes (44%) in period 1 and 10 of 27 tubes (37%) in period 2; $P = 0.554$].

Subgroup analyses

Results of subgroup analyses in patients with and without an uncomplicated postoperative course, DGE and pancreatic fistulae are shown in Table 4.

Table 2 Nutritional and hospitalization parameters

	Period 1 Routine NJT feeding (*n* = 51)	Period 2 Early oral feeding with on-demand NJT feeding (*n* = 51)	*P*-value
Postoperative nutritional parameters			
Time to adequate oral intake, days, median (IQR)	12 (10–18)	9 (6–20)	**0.013**
Enteral nutrition use, *n* (%)	50 (98%)	27 (53%)	**<0.001**
Duration of enteral nutrition, days, median (IQR)	8 (6–13)	10 (5–20)	0.638
Parenteral nutrition use, *n* (%)	21 (41%)	13 (26%)	0.093
Duration of parenteral nutrition, days, median (IQR)	13 (7–23)	16 (7–25)	0.972
Use of prokinetics, *n* (%)	22 (43%)	27 (53%)	0.322
Postoperative weight/preoperative weight, %, median (IQR)	103 (97–106)	98 (96–103)	0.092
Hospitalization parameters			
Length of stay, days, median (IQR)	18 (12–28)	13 (9–24)	**0.015**
Intensive and medium care unit stay, days, median (IQR)	1 (1–4)	1 (1–3)	0.574
Readmission within 30 days, *n* (%)	4 (8%)	7 (14%)	0.338

P-values shown in bold indicate statistical significance ($P < 0.05$).
NJT, nasojejunal tube; IQR, interquartile range.

Results of subgroup analyses regarding NJT feeding are shown in Table 5. There was no significant difference in hospital LoS between patients in period 1 [median LoS: 18 days (IQR: 12–30 days)] and the 20 patients (39%) in period 2 who eventually required NJT feeding [median LoS: 22 days (IQR: 14–42 days)] ($P = 0.303$). In patients who did not require NJT feeding in period 2, hospital LoS was significantly reduced by 9 days [median LoS: 9 days (IQR: 7–11 days)] in comparison with patients in period 1 [median LoS: 18 days (IQR: 12–30 days)] ($P \leq 0.001$).

Multivariable analysis

A multivariable logistic regression analysis that adjusted for differences in age, gender, BMI, MUST score of ≥2, ASA class of ≥3 and cancer stage of ≥II found no difference between the two periods in rates of morbidity [Clavien–Dindo Grade III or higher: odds ratio (OR) 0.96, 95% confidence interval (CI) 0.38–2.44] or mortality (OR 0.13, 95% CI 0.00–9.44). Male patients had a greater risk for developing morbidity than female patients (OR: 2.81, 95% CI 1.04–7.59; $P = 0.041$). No independent factors for mortality were found.

Discussion

In the present study, the introduction of an early oral feeding strategy after PD was found to have significantly reduced the time to resumption of adequate oral intake and hospital LoS, without increasing morbidity or readmission rates. Early oral feeding was not associated with noticeable downturns in patients who eventually required NJT feeding or in patients with a complicated postoperative course (e.g. DGE).

This study focused on the impact of introducing a single facet of a fast-track or enhanced recovery after surgery (ERAS) protocol after PD, namely, early oral feeding. Although previous studies have supported early oral feeding after PD, these studies assessed the impact of introducing a wide range of new measures in ERAS programmes, rather than just the impact of early oral feeding and thus do not make clear the actual impact of early oral feeding.[26–29] Table 6 shows the postoperative oral feeding protocol applied in the present study in comparison with the protocols applied in previous studies. All previous studies reported a reduction in LoS without an increase in complications. The traditional feeding protocols used in the control groups in these previous studies were, however, either ill defined or included both oral and enteral feeding.[27–29] Only one of these studies, an observational single-surgeon study, compared the clinical outcomes of patients in whom an enhanced recovery programme including early oral feeding after PD was implemented ($n = 20$) with outcomes in a control group subjected to routine NJT feeding ($n = 24$).[26] The The enhanced recovery programme was associated with an earlier return to a liquid and solid diet, reduced hospital LoS and a decreased readmission rate, without any increase in the incidence of morbidity in comparison with the control group. When these results are compared with those of the present study, it seems that early oral feeding is especially responsible for these improvements.

Notably, one retrospective cohort study, which compared 152 patients who received routine NJT feeding with 123 controls who received non-protocolized oral feeding between 2000 and 2009, suggested that routine NJT feeding is superior in terms of time to resumption of oral intake, and incidences of DGE and postoperative haemorrhage, but not in terms of LoS.[9] However, in this study, the routine feeding strategy changed from one of oral feeding to one of routine enteral nutrition, which represents an opposite change to that implemented in the present study. Moreover, oral feeding was non-protocolized and thus is likely to have carried a

Table 3 Morbidity and mortality

	Period 1 Routine NJT feeding (*n* = 51)	Period 2 Early oral feeding with on-demand NJT feeding (*n* = 51)	*P*-value
Overall morbidity, *n* (%)			
Clavien–Dindo Grades I–V	46 (90%)	35 (69%)	**0.007**
Clavien–Dindo Grade III or higher	24 (47%)	23 (45%)	0.843
Surgical morbidity, *n* (%)	45 (88%)	32 (63%)	**0.003**
Delayed gastric emptying (grade B/C)	16 (31%)	18 (35%)	0.674
Pancreatic fistula (grade B/C)	6 (12%)	6 (12%)	0.999
Postoperative haemorrhage (grade B/C)	6 (12%)	5 (10%)	0.750
Surgical site infection	21 (41%)	12 (24%)	0.090
Intra-abdominal abscess	4 (8%)	6 (12%)	0.505
Anastomotic bowel leak	4 (8%)	5 (10%)	0.999
Chyle leak	8 (16%)	5 (10%)	0.539
Fascial dehiscence	6 (12%)	6 (12%)	0.999
Other surgical complications	7 (14%)	4 (8%)	0.338
General morbidity, *n* (%)	22 (43%)	22 (43%)	0.999
Infections			
Cholangitis	4 (8%)	0	0.118
Line infection	3 (6%)	3 (6%)	0.999
Urinary tract infection	6 (12%)	1 (2%)	0.112
Pneumonia	10 (20%)	6 (12%)	0.276
Other general complications	13 (26%)	17 (33%)	0.385
Tube-related morbidity	24 (47%)	13 (26%)	**0.023**
Dislodgement of primary placed tube, *n* (%)	22 (43%)	10 (20%)	**0.010**
Day of dislodgement, median (IQR)	8 (5–12)	6 (3–7)	0.077
Requiring replacement, *n* (%)	8 (16%)	7 (14%)	0.780
Disabling blockage, *n* (%)	3 (6%)	4 (8%)	0.999
Other tube-related complications[a], *n* (%)	0	1 (2%)	0.999
Mortality, *n* (%)	3 (6%)	1 (2%)	0.617

[a]Nasal pressure ulcer.
P-values shown in bold indicate statistical significance ($P < 0.05$).
NJT, nasojejunal tube; IQR, interquartile range.

risk for suboptimal and uncoordinated treatment, whereas the feeding strategy in the present study was protocolized and was supervised by dieticians in both periods.

The overall hospital LoS in the present study was relatively long in comparison with the 10–13 days generally reported.[30–32] This may be explained by the fact that the present study group had not yet implemented a formal ERAS strategy in this study population because the protocol involved a change in the feeding strategy specifically, rather than a change in the entire postoperative management strategy.

The conventional reluctance to initiate early oral feeding probably arises from the fear of an increased risk for postoperative complications; for example, the stimulation of pancreatic secretion may increase the risk for pancreatic fistula and gastric stasis due to DGE leading to aspiration. However, these concerns are not substantiated by the findings of the present study, nor of those of a recent systematic review of five feeding strategies after PD, which found no relevant differences in the incidence of pancreatic fistula between oral and (par)enteral feeding groups.[12] By contrast, complications related to (par)enteral nutrition, such as the frequent dislodgement of NJTs, are well known.[13–17] In the present study, 44% of NJTs placed during PD (period 1) became dislodged after a median of only 8 days. The fact that only a third of dislodged tubes required replacement can be seen to represent a further argument in favour of the 'on-demand' strategy for NJT feeding after PD. An early oral feeding strategy might therefore prevent unnecessary tube placement. This study also demonstrated that an early oral feeding strategy does not lead to unfavourable outcomes

Table 4 Subgroup analyses: nutritional and hospitalization parameters in patients with and without complications, delayed gastric emptying or pancreatic fistula

	Complication not present			Complication present		
	Period 1 Routine NJT feeding	Period 2 Early oral feeding with on-demand NJT feeding	*P*-value	Period 1 Routine NJT feeding	Period 2 Early oral feeding with on-demand NJT feeding	*P*-value
Overall morbidity (Clavien–Dindo Grades III and higher)	(*n* = 27)	(*n* = 28)		(*n* = 24)	(*n* = 23)	
Time to adequate oral intake, days, median (IQR)	11 (9–14)	6 (4–8)	**<0.001**	14 (11–37)	21 (14–33)	0.412
Length of stay, days, median (IQR)	15 (11–20)	9 (8–13)	**<0.001**	22 (17–48)	26 (14–46)	0.774
Delayed gastric emptying (grade B/C)	(*n* = 35)	(*n* = 33)		(*n* = 16)	(*n* = 18)	
Time to adequate oral intake, days, median (IQR)	11 (9–14)	7 (5–9)	**<0.001**	19 (14–53)	25 (14–44)	0.798
Length of stay, days, median (IQR)	17 (11–26)	9 (8–14)	**<0.001**	24 (16–53)	30 (22–54)	0.721
Pancreatic fistula (grade B/C)	(*n* = 45)	(*n* = 45)		(*n* = 6)	(*n* = 6)	
Time to adequate oral intake, days, median (IQR)	12 (10–16)	8 (6–14)	**0.002**	32 (13–70)	37 (19–81)	0.699
Length of stay, days, median (IQR)	18 (11–26)	11 (9–18)	**0.007**	50 (24–70)	49 (22–85)	0.999

P-values shown in bold indicate statistical significance ($P < 0.05$).
NJT, nasojejunal tube; IQR, interquartile range.

Table 5 Subgroup analysis: nutritional and hospitalization parameters based on timing of nasojejunal tube (NJT) placement

	Period 1	Period 2			*P*-value
	Routine intraoperative NJT	Intraoperative NJT	Postoperative NJT	No NJT	
	(*n* = 51)	(*n* = 7)	(*n* = 20)	(*n* = 24)	
Time to adequate oral intake, days, median (IQR)	12 (10–18)	17 (10–30)	18 (12–30)	6 (4–8)	**<0.001**
Length of stay, days, median (IQR)	18 (12–28)	24 (17–35)	22 (14–42)	9 (7–11)	**<0.001**

P-values shown in bold indicate statistical significance ($P < 0.05$).
IQR, interquartile range.

in patients who eventually do require NJT feeding. The present authors found no significant difference in hospital LoS between patients who received routine NJT feeding in period 1 and the 39% of patients in period 2 who eventually required the insertion of a NJT (18 days versus 22 days).

In patients who received routine early oral feeding, there was a trend towards less TPN use, which is favourable as TPN is associated with an increased risk for infection.[33] By contrast, other studies comparing enteral nutrition [via a (gastro)jejunostomy tube] with oral feeding after PD have reported an increase in TPN in the latter group.[7,8] In these patients, however, TPN was started directly if oral intake was insufficient without using enteral nutrition first.

The main limitation of the present study concerns the comparison of retrospective and prospective data. Selection bias may not have played a relevant role as patients in both periods represent consecutive cohorts. This assumption is supported by the absence of differences in baseline patient characteristics such as age, ASA physical status and cancer stage. There is, however, a clear risk for information bias in period 1 (with retrospective data collection), but such a bias would normally lead to the under-reporting of complications and thus a better outcome in period 1. Interestingly, as the rate of complications is actually slightly lower in period 2, information bias is unlikely to have had a relevant impact on the outcomes of this study. In addition, discharge criteria were not changed during the study period. Whether or not the study carries a high risk for performance bias is arguable because postoperative instructions to patients, regarding the resumption of oral intake, differed between the two periods. These instructions (e.g. encouraging the early introduction and increase of oral intake in period 2) are, however, an important element of the intervention under investigation and thus one of the positive aspects of the early oral feeding strategy.

In addition, although its cohort was larger than that in the only previous study to have compared early oral feeding with routine NJT feeding,[26] this study included a relatively small sample and therefore lacks the necessary power to prove true superiority of early oral feeding. Future research should ideally include a high-quality, randomized controlled trial to confirm the positive impact of an early oral feeding strategy, with on-demand NJT

Table 6 Oral feeding protocols in studies on early oral feeding after pancreatoduodenectomy

	Current study (2013)	Abu Hilal *et al* (2013)[26]	Nikfarjam *et al* (2013)[28]	Balzano *et al* (2008)[27]	Kennedy *et al* (2007)[29]
Day 0	Liquid diet	Sips of water			
Day 1	Liquid diet	60–100 ml/h to include energy drinks			Start sips of water and ice chips ≤30 ml/h
Day 2	Solid food and oral nutritional supplements	Clear fluids	Liquid diet		Clear liquid diet
Day 3	Regular diet as tolerated and oral nutritional supplements	Soup and jelly/ soft diet	Progression to a soft diet as tolerated in the next few days	Clear fluid intake (free amount)	Regular diet
Day 4		Diet as tolerated		Solid food intake	
Day 5				Diet increase on daily basis (given as five or six small meals) until reaching a calorie intake of 1000 kcal on day 8	
Nasogastric tube removal	Day 1 or when drainage amount is <300 ml/24 h	Day 4 unless high output	Day 1 or when drainage amount is <300 ml/6 h	Day 1 if drainage amount is <300 ml	Day 1

feeding, on outcomes after PD in comparison with routine NJT feeding.

In conclusion, this observational cohort study demonstrated that the introduction of an early oral feeding strategy, with on-demand NJT feeding, reduced the time to resumption of adequate oral intake and hospital LoS after PD, without having a negative impact on postoperative morbidity.

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Conflicts of interest

None declared.

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