ORIGINAL ARTICLE

Early versus On-Demand Nasoenteric Tube Feeding in Acute Pancreatitis

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ABSTRACT

BACKGROUND

Early enteral feeding through a nasoenteric feeding tube is often used in patients with severe acute pancreatitis to prevent gut-derived infections, but evidence to support this strategy is limited. We conducted a multicenter, randomized trial comparing early nasoenteric tube feeding with an oral diet at 72 hours after presentation to the emergency department in patients with acute pancreatitis.

METHODS

We enrolled patients with acute pancreatitis who were at high risk for complications on the basis of an Acute Physiology and Chronic Health Evaluation II score of 8 or higher (on a scale of 0 to 71, with higher scores indicating more severe disease), an Imrie or modified Glasgow score of 3 or higher (on a scale of 0 to 8, with higher scores indicating more severe disease), or a serum C-reactive protein level of more than 150 mg per liter. Patients were randomly assigned to nasoenteric tube feeding within 24 hours after randomization (early group) or to an oral diet initiated 72 hours after presentation (on-demand group), with tube feeding provided if the oral diet was not tolerated. The primary end point was a composite of major infection (infected pancreatic necrosis, bacteremia, or pneumonia) or death during 6 months of follow-up.

RESULTS

A total of 208 patients were enrolled at 19 Dutch hospitals. The primary end point occurred in 30 of 101 patients (30%) in the early group and in 28 of 104 (27%) in the on-demand group (risk ratio, 1.07; 95% confidence interval, 0.79 to 1.44; P=0.76). There were no significant differences between the early group and the on-demand group in the rate of major infection (25% and 26%, respectively; P=0.87) or death (11% and 7%, respectively; P=0.33). In the on-demand group, 72 patients (69%) tolerated an oral diet and did not require tube feeding.

CONCLUSIONS

This trial did not show the superiority of early nasoenteric tube feeding, as compared with an oral diet after 72 hours, in reducing the rate of infection or death in patients with acute pancreatitis at high risk for complications. (Funded by the Netherlands Organization for Health Research and Development and others; PYTHON Current Controlled Trials number, ISRCTN18170985.)

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N Engl J Med 2014;371:1983-93.
DOI: 10.1056/NEJMoa1404393
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Acute pancreatitis is the most common gastrointestinal disease leading to hospital admission, and its incidence continues to rise.[1-4] Most patients with acute pancreatitis recover uneventfully and are discharged after a few days.[5,6] In 20% of patients, the disease course is complicated by major infection, such as infected pancreatic necrosis, which is associated with a mortality of 15%.[7-11]

A meta-analysis of eight randomized trials involving 348 patients showed that nasoenteric tube feeding, as compared with total parenteral nutrition, reduced the rate of infections and mortality among patients with severe pancreatitis.[12] These infections are thought to be mediated by bacterial translocation from the gut, provoked by disturbed intestinal motility, bacterial overgrowth, and increased mucosal permeability.[13-18] Nasoenteric tube feeding is believed to stimulate intestinal motility — thus reducing bacterial overgrowth — and may increase splanchnic blood flow, which helps to preserve the integrity of the gut mucosa.[19,20] Total parenteral nutrition lacks the trophic effect of enteric feeding and is associated with central venous catheter–related infections as well as metabolic complications.[21]

A meta-analysis of randomized trials involving acutely ill patients admitted to the hospital for indications other than pancreatitis showed a 22% reduction in the rate of major infection when nasoenteric tube feeding was started very early (≤36 hours after admission or surgery) as compared with a later start.[22] Similarly, nonrandomized studies of acute pancreatitis have shown that nasoenteric tube feeding started within 48 hours after admission, as compared with a start after 48 hours, significantly reduced the rate of major infection and in some studies even reduced mortality.[23-26]

On the basis of these potential benefits, American and European nutritional societies recommend routine early nasoenteric tube feeding in all patients with severe pancreatitis.[27-29] Guidelines from gastroenterologic and pancreatic societies, however, state that, regardless of disease severity, tube feeding is indicated when patients are not able to tolerate an oral diet for up to 7 days.[30,31] Unfortunately, it takes 3 to 4 days after admission to make this assessment,[32] and by that time the window of opportunity for effective prevention of infection with early tube feeding has passed.[7] To address this problem in the management of acute pancreatitis, we compared the effects of early nasoenteric tube feeding with those of an oral diet started at 72 hours, with a switch to nasoenteric tube feeding only in the case of insufficient oral intake.

Methods

Study Participants

The protocol of the Pancreatitis, Very Early Compared with Selective Delayed Start of Enteral Feeding (PYTHON) trial has been published previously[33] and is available with the full text of this article at NEJM.org. The study was conducted according to the protocol. Adults with a first episode of acute pancreatitis who were at high risk for complications (i.e., patients predicted to have severe pancreatitis) were eligible to undergo randomization. Patients were considered to be at high risk for complications if, within 24 hours after presentation to the emergency department, the Acute Physiology and Chronic Health Evaluation (APACHE) II[34] score was 8 or higher (on a scale of 0 to 71, with higher scores indicating more severe disease), if the Imrie or modified Glasgow score[35] was 3 or higher (on a scale of 0 to 8, with higher scores indicating more severe disease), or if the serum C-reactive protein level was more than 150 mg per liter.[36] These assessments predict the development of complications during the course of the disease. Pancreatitis was diagnosed if at least two of the three following features were present: typical abdominal pain, a serum lipase or amylase level that was more than 3 times the upper limit of the normal range, or characteristic findings on cross-sectional imaging of the abdomen. The exclusion criteria are given in the Supplementary Appendix, available at NEJM.org.

Study Design and Oversight

The PYTHON trial was a multicenter, randomized, controlled superiority trial performed in six university medical centers and 13 large teaching hospitals of the Dutch Pancreatitis Study Group. Patients were randomly assigned in a 1:1 ratio either to nasoenteric tube feeding initiated within 24 hours after randomization (the early group) or to an oral diet starting at 72 hours (the on-

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demand group). Randomization was performed centrally by the study coordinator with the use of a Web-based system that used permuted-block randomization with a concealed, varying block size. Randomization was stratified according to treatment center and a dichotomized APACHE II score (<13 vs. ≥13); the latter stratification factor was used because patients with an APACHE II score of 13 or higher are at increased risk for major infection.

All the patients or their legal representatives provided written informed consent. The study protocol was approved by the institutional review board of the University Medical Center Utrecht and by all the participating centers. All the authors vouch for the veracity and completeness of the data and data analyses. The sponsors were not involved in the design or conduct of the study or in the preparation of the manuscript or the decision to submit it for publication.

STUDY PROCEDURES

Patients underwent randomization within 24 hours after presentation to the emergency department. Those assigned to early nasoenteric feeding received a nasojejunal feeding tube as soon as possible but not later than 24 hours after randomization. Feeding tubes were placed endoscopically or radiologically, according to local practice. Nasoenteric feeding was administered as Nutrison Protein Plus (Nutricia). After tube placement, feeding was started at 20 ml per hour during the first 24 hours and was gradually increased (see the Supplementary Appendix). In the two study groups, full nutrition was defined as an energy target of 25 kcal per kilogram of body weight per day for patients in the intensive care unit (ICU) and 30 kcal per kilogram per day for patients in the ward.[28,37,38]

Patients assigned to an oral diet did not receive nutrition by any means other than that provided by standard intravenous fluids during the first 72 hours after presentation to the emergency department. Exceptions were made for patients who requested oral food during this 72-hour period. At 72 hours, all the patients in the on-demand group were given an oral diet. If an oral diet was not tolerated, it was offered again after 24 hours. If an oral diet still was not tolerated after 96 hours from the time of presentation, nasoenteric feeding was started after the placement of a nasojejunal tube, and the same procedure was followed as in the early group.

END POINTS

The primary end point was a composite of major infection or death within 6 months after randomization. Major infection was defined as infected pancreatic necrosis, bacteremia, or pneumonia (for definitions, see Box S1 in the Supplementary Appendix). Predefined secondary end points included the development of necrotizing pancreatitis as diagnosed on the basis of computed tomography (CT) performed 5 to 7 days after admission (because pancreatic parenchymal necrosis may take up to 72 hours to develop) and the development of organ failure after randomization.

DATA COLLECTION AND END-POINT ASSESSMENT

Dieticians registered the caloric intake and calculated energy-intake targets during the first week after admission on the basis of actual body weight. All CT studies were interpreted by an author who is an experienced radiologist and who was unaware of the treatment assignments. An adjudication committee, consisting of four pancreatic surgeons and a gastroenterologist who were unaware of the treatment assignments, individually evaluated each patient for the occurrence of the primary end point before interim and final analyses. Disagreements with respect to major infection were resolved during a plenary consensus meeting.

PATIENT SAFETY

An independent data and safety monitoring committee evaluated the progress of the trial and examined safety end points after the completion of follow-up in each consecutive group of 25 patients. Adverse events were listed and presented to the data and safety monitoring committee in an unblinded fashion.

STATISTICAL ANALYSIS

The expected incidence of the primary end point in the on-demand group was based on data from individual patients in the placebo group of a previous randomized trial.[39] For the early group, data from randomized trials comparing nasoenteric with parenteral nutrition were used to estimate the incidence.[33,40-42] The sample-size calcu-

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lation was based on an expected reduction in the primary composite end point associated with early tube feeding from 40 to 22%.[33] We estimated that a sample of 208 patients would provide the study with at least 80% power, at a two-sided alpha level of 5% and assuming a 1% loss to follow-up. Analysis was based on the intention-to-treat method, with the exclusion only of patients for whom the adjudication committee, whose members were unaware of the treatment assignments, decided before any analysis that the diagnosis of acute pancreatitis was incorrect.

Predefined subgroups included patients with an APACHE II score below 13 and those with a score of 13 or higher at randomization. Two post hoc subgroup analyses were performed: one for patients with the systemic inflammatory response syndrome (SIRS, as defined by the Consensus Conference criteria of the American College of Chest Physicians–Society of Critical Care Medicine) at randomization, because such patients are at high risk for complications,[43] and one for a low or high body-mass index (BMI; the weight in kilograms divided by the square of the height in meters), since the BMI differed significantly between the two treatment groups at baseline.

An interim analysis of the primary end point was performed after 50% of the patients had completed 6 months of follow-up. The interim analysis was performed by an independent statistician, who was unaware of the treatment assignments, applying the Peto approach with symmetric stopping boundaries at a P value of less than 0.001.[33,44]

For the final analyses, a two-sided P value of less than 0.05 was considered to indicate statistical significance. P values were not adjusted for multiple testing.

RESULTS

ENROLLMENT AND RANDOMIZATION

From August 2008 through June 2012, a total of 867 patients were assessed for eligibility (Fig. S1 in the Supplementary Appendix). A total of 208 patients (24%) were enrolled and randomly assigned to early nasoenteric tube feeding (102 patients) or an oral diet with tube feeding if required (106). The adjudication committee excluded 3 patients who had undergone randomization and had been incorrectly diagnosed with acute pancreatitis (2 patients had gastric carcinoma and 1 had intestinal volvulus). A total of 101 patients in the early group and 104 in the on-demand group were included in the intention-to-treat analysis. Baseline characteristics, presented in Table 1, were equally distributed between the groups except for the mean (±SD) BMI (29±5 in the early group vs. 27±5 in the on-demand group, P=0.01).

Details regarding the number of calories delivered during the first week after admission and the timing of feeding are shown in Figure 1, and in Table S1 in the Supplementary Appendix. As specified by the protocol, patients in the early group received feeding earlier than those in the on-demand group. Nasoenteric tube feeding in the early group was started a median of 8 hours after randomization and a median of 23 hours after presentation to the emergency department, as compared with initiation of an oral diet 64 hours after randomization and 72 hours after presentation in the on-demand group (P<0.001) (Table S1 in the Supplementary Appendix). A total of 5 of 104 patients (5%) assigned to on-demand feeding requested and received food within the first 72 hours after presentation.

OUTCOMES

Primary End Point

The primary composite end point of major infection or death occurred in 30 patients (30%) in the early group, as compared with 28 (27%) in the on-demand group (risk ratio, 1.07; 95% confidence interval [CI], 0.79 to 1.44; absolute risk difference, 3 percentage points; 95% CI, −9 to 15; P=0.76). Major infections occurred in 25% of the patients in the early group and in 26% of those in the on-demand group (P=0.87) (Table 2). Mortality was 11% in the early group, as compared with 7% in the on-demand group (P=0.33), and most of the deaths were related to persistent multiple organ failure (defined as failure of two or more organs on ≥3 consecutive days).

Secondary End Points

Necrotizing pancreatitis developed in 63% of the patients in the early group and in 62% of those in the on-demand group. A total of 18% of the patients in the early group and 19% of those in the on-demand group required ICU admission (Table 2).

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Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Early Tube Feeding (N=101)	On-Demand Tube Feeding (N=104)
Female sex — no. (%)	46 (46)	45 (43)
Age — yr	65±16	65±15
Cause of pancreatitis — no. (%)		
Gallstones	59 (58)	56 (54)
Alcohol abuse	14 (14)	23 (22)
Other	28 (28)	25 (24)
Body-mass index — no./total no. (%)†		
<25	20/99 (20)	33/103 (32)
25 to <35	69/99 (70)	67/103 (65)
≥35	10/99 (10)	3/103 (3)
Disease severity		
APACHE II score‡		
Mean	11±4	11±5
≥13§	32 (32)	29 (28)
Imrie or modified Glasgow score¶		
Median	2	2
Range	0–6	0–5
C-reactive protein — mg/liter		
Median	70	75
Interquartile range	21–179	11–189
SIRS — no. (%)‖	63 (62)	70 (67)
Respiratory failure — no. (%)	30 (30)	27 (26)
Multiple organ failure — no. (%)**	6 (6)	5 (5)
Duration — hr		
Onset of symptoms to presentation at the emergency department		
Median	12	13
Interquartile range	5–28	4–33
Presentation at the emergency department to randomization		
Median	13	11
Interquartile range	5–19	4–19

* Plus–minus values are means ±SD. There were no significant between-group differences at baseline, except for body-mass index (P=0.01).
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Scores on the Acute Physiology and Chronic Health Evaluation (APACHE) II range from 0 to 71, with higher scores indicating more severe disease.[34]
§ Patients with an APACHE II score of 13 or higher constituted a predefined subgroup.
¶ Imrie or modified Glasgow[35] scores range from 0 to 8, with higher scores indicating more severe disease.
‖ The systemic inflammatory response syndrome (SIRS) was diagnosed with the use of the Consensus Conference criteria of the American College of Chest Physicians–Society of Critical Care Medicine.
** Organ failure was defined as a modified Marshall score of 2 or more (on a scale of 0 to 12, with higher scores indicating more severe disease), as proposed in the revised Atlanta classification of acute pancreatitis.[45] Multiple organ failure was defined as failure of two or more organs on the same day.

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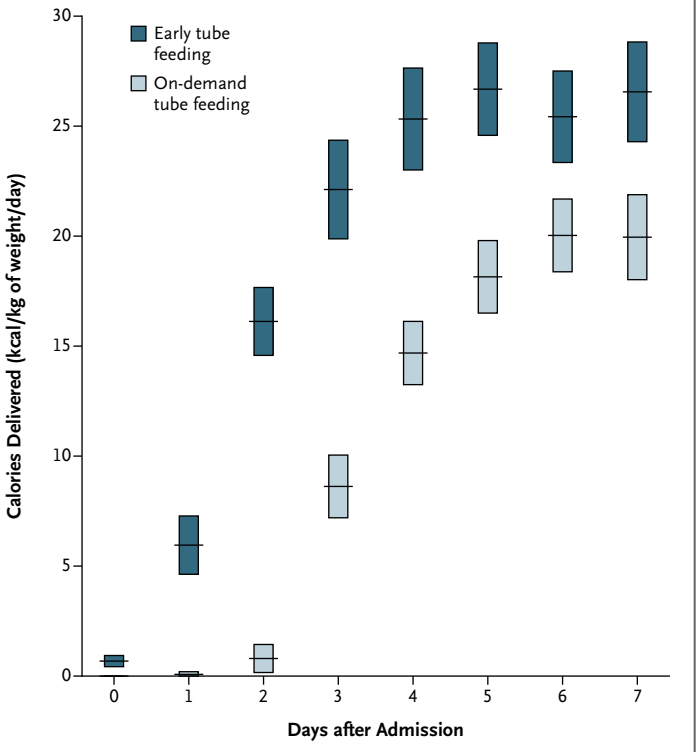

Figure 1. Calories Delivered with the Use of Early versus On-Demand Nasoenteric Tube Feeding.

Each rectangle shows the mean value (horizontal line) and 95% confidence interval (top and bottom of the rectangle).

In the on-demand group, 32 patients (31%) required nasoenteric tube feeding; 72 patients (69%) tolerated an oral diet and did not require tube feeding (Table 3). In 9 of these 32 patients (28%), tube feeding was prompted by the use of mechanical ventilation. The on-demand tube-feeding strategy reduced the number of days to full tolerance of an oral diet (9 days with the early strategy vs. 6 days with the on-demand strategy, P=0.001). Gastrointestinal events occurred frequently, but the frequency did not differ significantly between the groups.

Attenuation of the acute inflammatory response was hypothesized to be part of the beneficial effect of early feeding. However, such an effect did not occur (Fig. S3 in the Supplementary Appendix).

In a predefined subgroup analysis restricted to patients with an APACHE II score of 13 or higher at randomization, the occurrence of the primary end point did not differ significantly between the two treatment groups (Table S3 in the Supplementary Appendix). Post hoc subgroup analyses also did not show a significant between-group difference in the primary end point for patients with SIRS at randomization or those with a BMI of less than 25 or 35 or more (Table S3 in the Supplementary Appendix). No significant differences were observed in health care utilization except for the number of tube placements (145 tube placements in the early group vs. 57 in the on-demand group, P<0.001) (Table S4 in the Supplementary Appendix).

DISCUSSION

This multicenter, randomized trial involving patients with acute pancreatitis who were at high risk for complications did not show that an early start of nasoenteric tube feeding was superior to the introduction of an oral diet after 72 hours, with tube feeding only if required, in reducing the composite end point of major infection or death. With the oral diet and on-demand tube-feeding strategy, only approximately one third of patients required a nasojejunal feeding tube.

The absolute between-group difference in the primary end point was 3 percentage points, with the 95% confidence interval ranging from 9 percentage points lower to 15 percentage points higher. These findings do not support clinical guidelines recommending the early start of nasoenteric tube feeding in all patients with severe acute pancreatitis in order to reduce the risks of infection and death. However, this trial was not powered to exclude a substantial benefit of early feeding.

The results of our trial differ from those of previous trials and observational studies.[12,23-26] Previous trials showed an improved outcome after early nasoenteric tube feeding as compared with total parenteral nutrition. This may be explained in part by complications associated with providing total parenteral nutrition, such as catheter-related infections.[21] The negative outcome of our study, as compared with the outcomes in these previous trials, is not explained by differences in the timing of early tube feeding or the severity of pancreatitis in the study participants. The timing of early nasoenteric tube feeding in our study was similar to the timing

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Table 2. Primary and Secondary End Points, According to the Intention-to-Treat Analysis.*

Outcome	Early Tube Feeding (N=101)	On-Demand Tube Feeding (N=104)	Risk Ratio (95% CI)	P Value
Primary composite end point: infection or death — no. (%)	30 (30)	28 (27)	1.07 (0.79–1.44)	0.76
Secondary end points				
Infection — no. (%)†	25 (25)	27 (26)	0.97 (0.70–1.34)	0.87
Infected pancreatic necrosis	9 (9)	15 (14)	0.74 (0.43–1.26)	0.28
Bacteremia	17 (17)	18 (17)	0.98 (0.68–1.43)	1.00
Pneumonia	12 (12)	13 (12)	0.97 (0.63–1.50)	1.00
Death — no. (%)	11 (11)	7 (7)	1.27 (0.85–1.89)	0.33
Necrotizing pancreatitis — no. (%)‡	64 (63)	65 (62)	1.06 (0.77–1.47)	0.76
CT severity index§	4±2	4±3	—	0.29
ICU admission after randomization — no. (%)	18 (18)	20 (19)	0.95 (0.66–1.38)	0.86
Mechanical ventilation — no. (%)	12 (12)	14 (13)	0.93 (0.60–1.44)	0.84
New-onset organ failure — no./total no. at risk (%)¶				
Single organ failure	26/67 (39)	31/73 (42)	0.92 (0.65–1.32)	0.73
Persistent single organ failure	10/67 (15)	10/73 (14)	1.05 (0.65–1.70)	1.00
Multiple organ failure	7/67 (10)	6/73 (8)	1.14 (0.67–1.95)	0.77
Persistent multiple organ failure	4/67 (6)	4/73 (5)	1.05 (0.51–2.14)	1.00

* Plus-minus values are means ±SD. Risk ratios are for early tube feeding as compared with on-demand tube feeding. ICU denotes intensive care unit.
† Patients may have had more than one type of infection.
‡ Necrotizing pancreatitis was defined as pancreatic parenchymal necrosis or extrapancreatic necrosis.[45,46] In nine patients (9%) in the early group and seven (7%) in the on-demand group, no CT was performed.
§ Scores on the CT severity index range from 0 to 10, with higher scores indicating more extensive pancreatic or extrapancreatic necrosis.
¶ New-onset organ failure was defined as organ failure that was not present at randomization. Persistent organ failure was defined as organ failure present on 3 or more consecutive days (>48 hours). Multiple organ failure was defined as failure of two or more organs on the same day.

in the previous studies. In addition, we used similar criteria for enrolling patients at high risk for complications, and we observed similar rates of major infection and death.

Previous observational studies investigating the initiation of nasoenteric tube feeding within 48 hours after admission, as compared with initiation more than 48 hours after admission, cannot differentiate between cause and effect (i.e., less severely ill patients may have been fed earlier). This is in line with a recently revived debate on the presumed benefit of early enteral feeding in critically ill patients in general. Early enteral feeding is recommended in most current ICU guidelines.[38,47] However, the methodologic quality of the trials that form the basis for these general ICU recommendations has been criticized.[48] Thus, for critically ill patients in general and for those with acute pancreatitis specifically, large, high-quality, randomized, controlled trials that show an improved outcome with early enteral feeding are lacking.[49]

There are several possible explanations for the negative result of our study. First, early enteral feeding may not be as effective as we anticipated. Our hypothesis was that the trophic effect of early enteral feeding would stabilize the integrity of the gut mucosa, reducing inflammation and improving the outcome. Early enteral feeding was not associated with a reduction in any

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Table 3. Nutrition Tolerance and Gastrointestinal Events.*

Outcome	Early Tube Feeding (N=101)	On-Demand Tube Feeding (N=104)	Risk Ratio (95% CI)	P Value
Nutrition variable				
Need for nasoenteric feeding tube — no. (%)	NA	32 (31)	—	—
Dislodging of nasoenteric feeding tube — no./total no. (%)†	38/99 (38)	14/32 (44)	0.95 (0.77–1.16)	0.68
Obstruction of nasoenteric feeding tube — no./total no. (%)†	11/99 (11)	4/32 (12)	0.97 (0.70–1.33)	0.76
Need for insertion of nasogastric tube for decompression — no. (%)‡	19 (19)	23 (22)	0.90 (0.62–1.30)	0.61
Need for parenteral nutrition — no. (%)‡	5 (5)	10 (10)	0.66 (0.32–1.37)	0.28
Days from admission to full tolerance of oral diet§			—	0.001
Median	9	6		
Interquartile range	6–12	5–10		
Gastrointestinal event — no. (%)¶				
Nausea	32 (32)	37 (36)	0.91 (0.68–1.24)	0.66
Vomiting	19 (19)	26 (25)	0.82 (0.57–1.20)	0.31
Aspiration‖	0	4 (4)	—	0.12
Ileus**	10 (10)	11 (11)	0.96 (0.60–1.54)	1.00
Diarrhea	21 (21)	29 (28)	0.81 (0.57–1.17)	0.26

* NA denotes not applicable.
† Dislodging or obstruction of the nasogastric tube was noted in case-record forms by the attending physician or nurse. The denominator is the number of patients who had a feeding tube inserted. Two patients in the early group declined tube feeding.
‡ The need for a nasogastric tube to be inserted for decompression or the need for parenteral nutrition was indicated by the attending physician.
§ Full tolerance of an oral diet was defined as tolerance of the oral diet without receipt of any other type of nasoenteric or parenteral nutrition.
¶ Gastrointestinal events were assessed during each day of the hospital stay.
‖ Data are for suspected aspiration as noted by a physician or nurse in the case-record forms.
** Ileus was diagnosed by the attending physician and noted in the case-record forms.

of the variables indicating inflammation (Fig. S3 in the Supplementary Appendix). We did not evaluate gut permeability and bacterial translocation on the basis of the serum intestinal fatty acid–binding protein level or endotoxin exposure.[17,50] Therefore, we cannot determine whether gut permeability was influenced by early feeding in a subset of our patients. Increased gut permeability and bacterial translocation may be restricted to patients with acute pancreatitis who have multiple organ failure,[14] a subgroup that accounted for only a small fraction of the patients in this trial. However, a study of acute pancreatitis in which the rates of multiple organ failure and death were similar to the rates in our study did show an increase in gut permeability and endotoxin exposure in most patients with severe acute pancreatitis.[51]

Another possibility is that tube feeding in the early group in our trial should have been started even earlier. In a trial involving a small number of patients at one center, it would be possible to start nasogastric tube feeding some hours earlier by using a feeding tube that could be placed at the bedside. In daily practice, however, we believe that an earlier start of tube feeding would not be feasible. Starting an oral diet later in the on-demand group in order to increase the difference in timing between the two study groups would not be ethical because it would put patients at risk for malnutrition.

A third explanation for the negative result may be that the study was too small to detect a difference between the two groups. To our knowledge, this is the largest trial of nutrition in patients with acute pancreatitis that has been performed so far, but the wide confidence interval for the primary end point may indicate that an even larger trial is needed.

Fourth, the widely accepted scoring systems

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for prediction of severity in acute pancreatitis are only moderately accurate.[52] In early-intervention studies in acute pancreatitis, it is therefore unavoidable that mild or moderate disease will develop in a proportion of patients who were classified at presentation as having severe pancreatitis. Nevertheless, at randomization, approximately one third of our patients had organ failure and two thirds had SIRS. Organ failure is one of the determinants of severe pancreatitis, and SIRS is increasingly recognized as an early indicator of severe pancreatitis.[30,45]

A feeding tube frequently causes discomfort, excessive gagging, or esophagitis and is often dislodged or becomes obstructed, which necessitates the replacement of the feeding tube.[53,54] If tube feeding were restricted to patients who could not tolerate an oral diet, this would result in substantial avoidance of discomfort and costs.

In conclusion, our trial did not show the hypothesized benefit of early nasoenteric tube feeding in patients with acute pancreatitis who were at high risk for complications. The observation that the clinical outcomes of early tube feeding were similar to those of an oral diet initiated at 72 hours, with tube feeding only if required, challenges the concept of the gut mucosa–preserving effect of early enteral feeding during acute pancreatitis.

Supported by grants from the Netherlands Organization for Health Research and Development, the ZonMw Health Care Efficiency Research Program (170992902), and Nutricia (08/KR/AB/002).

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Vera Zeguers for assistance as a study research nurse, all the medical and nursing staff at the participating centers for assistance in the enrollment and care of the patients in this study, and the patients and their families for contributions to the study.

APPENDIX

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