

2018

Early oral refeeding in acute pancreatitis reduces length of hospital stay

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Recommended Citation

POLSKY SB. Early oral refeeding in acute pancreatitis reduces length of hospital stay. Clin. Res. Prac. 2018 Aug 21;4(1):eP1566. doi: 10.22237/crp/1534464060

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Erratum

In the initial publication, the author's first name was incorrectly listed as Sophie on the PDF of this critical analysis. It is Sylvie, corrected here (as of 2018.08.28), with the editors' sincere apologies to the author.

Early oral refeeding in acute pancreatitis reduces length of hospital stay

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ABSTRACT A critical appraisal and clinical application of Lariño-Noia J, Lindkvist B, Iglesias-García J, Seijo-Ríos S, Iglesias-Canle J, Domínguez-Muñoz J. Early and/or immediately full caloric diet versus standard refeeding in mild acute pancreatitis: A randomized open-label trial. *Pancreatology*. 2014;14(3):167-173. doi: [10.1016/j.pan.2014.02.008](https://doi.org/10.1016/j.pan.2014.02.008).

Keywords: *pancreatitis, oral feeding, hospital length of stay*

Clinical Context

A 57 year-old woman presented to the emergency department with sharp epigastric pain radiating to her back associated with nausea and vomiting. Laboratory studies revealed elevated serum lipase (368 IU/L) and leukocytosis (13.3 K/ul). No acute inflammatory changes or peripancreatic fluid collection were identified on CT scan. The patient was admitted for management of acute pancreatitis. She was initially treated with intravenous fluids, analgesics, and antiemetics. Shortly after initiation of treatment the patient's nausea, vomiting, and pain were controlled. At this point the question arose of when to resume an oral diet and which type of diet would be best. The patient was anxious about starting oral intake as she feared it could increase her pain and worsen her clinical condition.

Clinical Question

Is there a difference in clinical outcomes between patients with acute pancreatitis receiving early or delayed refeeding?

Research Article

Lariño-Noia J, Lindkvist B, Iglesias-García J, Seijo-Ríos S, Iglesias-Canle J, Domínguez-Muñoz J. Early and/or immediately full caloric diet versus standard refeeding in mild acute pancreatitis: A randomized open-label trial. *Pancreatology*. 2014;14(3):167-173. doi: [10.1016/j.pan.2014.02.008](https://doi.org/10.1016/j.pan.2014.02.008)

Related Literature

Literature review began with a PubMed search using keywords "feeding" AND "acute pancreatitis". The search was limited to humans, English language, and systematic reviews. This resulted in 38 papers, all of which were reviewed for relevance to our patient. There were eight systematic reviews or guidelines. The most recent review, published by Vaughn et al.¹ asked the most relevant question for my patient: early versus delayed enteral nutrition in acute pancreatitis. This review was well done with a comprehensive search strategy, relevant study selection criteria, good inter-rater reliability, and risk of bias assessment using the Cochrane Collaboration tool. The systematic review suggested that early feeding in patients with acute pancreatitis does not

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ISSN: 2379-4550

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increase adverse events and may reduce length of hospital stay, however the strength of conclusions were limited by the variability of trials included in the review.

Since the patient was capable of intake of food by mouth, only studies limited to oral feeding for both early and delayed groups were considered and studies which evaluated enteral tube feeding were excluded. This yielded four randomized trials: Eckerwall et al.², Karabulut et al.³, Lariño-Noia et al.⁴, and Teich et al.⁵. Of these, only Eckerwall et al. and Lariño-Noia et al. were deemed as low-risk for bias by the authors of the systematic review.

In both of these studies, early feeding was associated with a reduced length of hospital stay when compared with delayed feeding with no difference in feeding intolerance. The more recent study with a larger sample size by Lariño-Noia et al. was selected for critical appraisal.

Critical Appraisal

The selected study is a randomized controlled open-label trial evaluating early refeeding versus standard refeeding in acute pancreatitis. The study also assessed the effect of initial resumption of full caloric diet versus a stepwise increase in caloric intake in these patients. Patients were eligible for inclusion in the study if they were admitted to the hospital for acute pancreatitis. The diagnosis was based on presence of acute upper abdominal pain and serum amylase or lipase levels greater than three times the upper limit of normal. Exclusion criteria included inability or unwillingness to give informed consent, decreased capability for oral intake due to reasons other than acute pancreatitis, factors affecting normal pancreatic exocrine function such as history of chronic pancreatitis or pancreatic surgery, pregnancy, and lactation.

Upon admission to the hospital, patients were assigned to one of four groups below in an even ratio. Randomization was performed in blocks of four and the sequence was open to the investigator. There were no statistically significant differences in age, sex, etiology of acute pancreatitis, or lipase level at admission between the groups. The patients included in the study were similar to the 57 year-old woman described here. In the study, 54.2% of the patients were female and the mean age was 60. One difference was that the average serum lipase at admission in the study was 4390 IU/L (range 1020 – 17200 IU/L) while the patient described here had a lipase of 368 IU/L. While still meeting the criteria for an acute pancreatitis diagnosis as defined in the study (lipase greater than 3 times the upper limit of normal), this patient's low lipase level compared to the patients included in the trial might suggest less severe illness and even lower risk of refeeding.

Patients in the study were randomly assigned to: 1. stepwise increase in caloric intake started at standard time, 2. stepwise increase in caloric intake started early, 3. immediate full caloric intake started at standard time, 4. immediate full caloric intake started early.

Early refeeding was initiated as soon as bowel sounds were determined to be present. Standard refeeding was also started after bowel sounds were present but also required resolution of abdominal pain, fever, and decreasing lipase and leukocyte levels. All diets included normal solid foods. The main outcomes measured were length of hospital stay and tolerance to food intake. Criteria for hospital discharge were tolerance of a full caloric meal followed by an observation of at least 24 hours. Intolerance to oral refeeding was defined as any of the following within 24 hours: severe abdominal pain requiring analgesics, nausea and vomiting that could not be alleviated by metoclopramide, relapse of acute pancreatitis, or inability to ingest at least 50% of meals.

The study showed that length of hospital stay was significantly shorter in subjects receiving early refeeding compared to refeeding at a standard time (median 5 vs. 7 days, $p=0.001$). There was no statistically significant difference in length of hospital stay when comparing stepwise increase of calories to full caloric initial intake. There was no difference related to tolerance of oral intake between any of the groups. The results of the study considered both statistical and clinical significance. Early refeeding showed no increased adverse outcomes and shorter length of hospital stay.

One limitation of this study was that neither patients nor physicians were blinded to the treatment. This could potentially have influenced patients' assessment of their symptoms after refeeding. This potential bias was limited by use of a standardized questionnaire and predefined criteria for outcomes. In addition, a potential flaw in this study design is that physicians could have been influenced when making decisions about discharge for patients in different groups. However, predefined criteria were used in order to determine discharge in an attempt to minimize this bias.



In this study 8 of the 80 patients (10%) initially randomized to the groups were eventually excluded due to missing inclusion criteria or presence of exclusion criteria that were not initially noted. The patients who dropped out of the study were not included in the analysis. This use of a per-protocol analysis is not considered optimal statistical analysis. An intention-to-treat analysis including those 8 patients would have provided stronger evidence if it were to show statistical significance.

The strength of this recommendation to employ early refeeding in acute pancreatitis is B based on inconsistent or limited-quality patient-oriented evidence, according to the SORT taxonomy described by Ebell et al.⁶.

The paper discloses that there were no sources of funding or conflicts of interest. In addition, the authors of a systematic review article rated this study as low-risk of bias using the Cochrane Collaboration tool.

Clinical Application

Early feeding in acute pancreatitis is something that can be easily implemented in clinical practice without additional cost. It provides potential benefit without any increased risk of negative outcomes. Two additional days of hospitalization is clinically significant result as 2 days in the hospital can carry a significant cost burden as well as unnecessary risk to the patient for exposure to pathogens and medical errors.

This study demonstrated decreased length of hospital stay with early refeeding in acute pancreatitis with no change in tolerance of oral intake. It is important to convey to patients that evidence shows that early refeeding can decrease time spent in the hospital without increasing the risk of additional symptoms. In addition it may be beneficial to discuss some of the risks of lengthier hospital stays if patients do not feel motivated to return home. The benefit of full caloric intake immediately was not statistically significant so if patients, like the one described, have a concern about resuming oral intake, starting with smaller meals and increasing their calories incrementally should provide similar benefit for decreased length of stay. Based on the literature review, shortly after her admission, the patient was encouraged to eat as tolerated.

Take home points:

1. Evidence supports early oral refeeding of patient with acute pancreatitis as reducing length of hospital stay.
2. Early oral refeeding is well tolerated with no difference between initiation with full caloric intake vs. stepwise intake.

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