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Research Article

Clinical Outcomes of Immediate Oral Refeeding in Acute Pancreatitis: A Randomized Trial in Mild and Moderate Cases

JA Jayalal, Angeline Vincent, Velmurugan*, MR Vivek and Aravinthan S

Department of Surgery, Kanyakumari Government Medical College and Hospital, Tamil Nadu, India

***Corresponding Author:** Velmurugan, Department of General Surgery, Kanyakumari Government Medical College and Hospital, Asaripallam, Kanyakumari, Tamil Nadu, India.

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Abstract

Background: Oral nutrition plays a crucial role in managing mild and moderate acute pancreatitis (AP). Early refeeding has shown significant benefits, yet the precise timing for initiating oral intake remains debated. This study aims to determine the optimal timing for oral refeeding in mild and moderate AP to minimize hospital length of stay (LOS) and complications.

Methods: A single-center, randomized controlled trial was conducted involving patients diagnosed with mild or moderate AP, admitted between February and October 2024. Participants were randomized into two groups: the immediate oral refeeding (IORF) group, where a low-fat solid diet was initiated immediately upon admission, and the conventional oral refeeding (CORF) group, where a gradual oral diet was resumed after clinical and laboratory improvements. The primary outcome was LOS, with secondary outcomes including pain relapse, diet intolerance, and complications.

Results: Eighty patients were randomized. The mean LOS was significantly shorter in the IORF group compared to the CORF group (3.4 ± 1.7 days vs. 8.8 ± 7.9 days, $p < 0.001$). Pain relapse occurred in 16% of the CORF group. Additionally, complications were less frequent in the IORF group (8%) compared to the CORF group (26%).

Conclusion: Immediate oral refeeding is a safe and effective approach for mild and moderate AP. It substantially reduces LOS without increasing adverse effects or complications.

Keywords: Acute Pancreatitis; Immediate Oral; Ref-Feeding

Introduction

Acute pancreatitis (AP) poses a significant threat to public health, with rising incidence rates globally [1,2]. Nutritional support plays a vital role in the early management of AP, aiding in the prevention of malnutrition and reducing complications and mortality [3]. Studies have consistently demonstrated that enteral nutrition (EN) is superior to parenteral nutrition (PN) for AP patients, and current guidelines recommend EN over PN for those unable to feed orally [4,5].

Historically, "pancreatic rest" through fasting was a standard initial treatment strategy for AP, aimed at avoiding disease relapse and pain. However, recent research highlights that mitochondrial damage and ATP depletion are pivotal during the early phase of AP, leading to a substantial energy deficit [6-8]. Consequently, early energy intake—via oral or tube feeding—has been shown to benefit AP recovery [2,9,10].

Oral feeding, a form of EN, is preferable to tube feeding due to its higher acceptability, reduced discomfort, and fewer associated complications [11,12]. The timing of oral refeeding significantly impacts recovery and length of hospital stay (LOS) in AP patients [13]. Current clinical guidelines [14,15] suggest that oral refeeding (ORF) may begin early under specific conditions, such as the absence of pain and improvement in laboratory parameters. However, a consensus on the precise definition of "early" remains lacking [16,17]. This ambiguity may explain why conventional oral refeeding (CORF), which involves fasting for the initial 24–48 hours followed by a gradual increase in oral intake over 5–7 days, continues to be widely used for managing mild AP [18].

To address these gaps, this study aims to compare the outcomes of immediate oral refeeding (IORF) versus CORF in patients with mild and moderate AP. The hypothesis is that IORF would reduce LOS and hospital costs without increasing the risk of complications.

Materials and Methods

This single-center, randomized, controlled clinical trial was conducted at Kanyakumari Medical College and Hospital, Asaripallam, Tamil Nadu, India, from February to October 2024. Eligible participants included patients admitted to the emergency department who met at least two of three diagnostic criteria for acute pancreatitis (AP): acute abdominal pain, elevated serum amylase and/or lipase levels (≥three times the upper reference limit), and imaging evidence of AP on ultrasound or computed tomography. The severity of AP was classified using the Modified International Multidisciplinary Classification [19-21], while systemic inflammatory response syndrome (SIRS) and organ failure (OF) were assessed using established criteria [14,22].

Inclusion and exclusion criteria

Patients aged >18 years with mild or moderate AP were included. Exclusion criteria encompassed pancreatic neoplasm, surgery, trauma or endoscopic retrograde cholangiopancreatography as the etiology, chronic pancreatitis, short bowel syndrome, and severe or critical AP on admission.

Randomization and interventions

A total of 80 participants were enrolled through consecutive sampling and randomized into two groups: immediate oral refeeding (IORF) and conventional oral refeeding (CORF). Due to the nature of the intervention, allocation was unblinded for patients and physicians, but outcome assessors were blinded to reduce bias. Informed consent was obtained prior to enrollment.

- **IORF Group**: Patients initiated a low-fat solid diet immediately upon hospital admission, irrespective of symptoms or lab parameters.
- **CORF Group**: Patients transitioned from fasting to a low-fat solid diet through clear liquids, reintroduced only upon meeting criteria such as absence of abdominal pain, restoration of peristalsis, normalized pancreatic enzymes (< 2× the upper reference limit), leukocyte count < 15,000/mm^3, and reduced C-reactive protein levels.

Patient management followed International Association of Pancreatology (IAP)/American Pancreatic Association (APA) evidence-based guidelines [14], including intravenous fluids, correction of electrolyte imbalances, analgesia, and monitoring for complications.

Definitions and measurements

- **Diet Tolerance**: Ingesting >50% of each meal during admission.
- **Diet Intolerance**: Inability to ingest >50% due to uncontrolled abdominal pain, nausea/vomiting, AP relapse, or abdominal pain relapse.
- **Length of Stay (LOS)**: Calculated as the total number of nights in the hospital.
- **Discharge Criteria**: Diet tolerance ≥75%, absence of nausea/vomiting, and pain control (VAS ≤2).

Clinical follow-ups occurred 1-3 months post-discharge.

Study Endpoints

- **Primary Endpoint**: LOS.
- **Secondary Endpoints**: Complications, abdominal pain relapse, laboratory findings, and diet intolerance.

Data analysis

Data were analyzed using SPSS Version 21.0. Fisher's exact test and ANOVA were applied for categorical and quantitative variables, respectively, with non-parametric tests for non-normal distributions. Linear regression with logarithmic transformation was used for LOS, with Lasso selection for predictor variables. Statistical significance was considered as $p < 0.05$.

Results and Discussion

In table 1, the demographic characteristics and baseline clinical features of the study participants are presented, with comparisons between the Immediate Oral Refeeding (IORF) and Conventional Oral Refeeding (CORF) groups. The mean age was slightly higher in the IORF group (70.2 years) compared to the CORF group (64.9 years), though this difference was not statistically significant ($p = 0.15$). Both groups had a similar proportion of males (IORF: 52.1%, CORF: 50.0%; $p = 1.0$). The distribution of ASA scores was comparable across groups, with most participants falling under ASA II (IORF: 50.0%, CORF: 55%). The mean weight and BMI were also similar between the two groups, with no significant differences observed (weight $p = 1.0$, BMI $p = 0.56$). Etiology of acute pancreatitis was predominantly biliary (IORF: 30%, CORF: 17.5%) and alcoholic (IORF: 22.5%, CORF: 15%), with no significant differences in distribution ($p = 0.18$). Clinical symptoms, including abdominal pain

Outcomes	Total (n = 80)	IORF Group (n = 40)	CORF Group (n = 40)	p-value
Age - years, mean (SD)	67.8 (17.2)	70.2 (14.2)	64.9 (15.5)	0.15
Sex - male, n (%)	67 (51.1%)	21 (52.1%)	20 (50.0%)	1.0
ASA				
I, n (%)	26(32.5%	15 (37.5%)	11(27.5%)	0.3
II, n (%)	42(52.5%)	20 (50.0%)	22(55%)	
III, n (%)	9(11.25%)	4 (10.0%)	5(12.5%)	
IV, n (%)	3(3.75%)	1 (2.5%)	2(5%)	
Weight - kg (SD)	74.8 (14.5)	75.7 (13.3)	73.7 (12.7)	1.0
BMI - kg/m^2 (SD)	28.06 (4.9)	28.5 (4.1)	27.5 (4.5)	0.56
Etiology				
Biliary, n (%)	19(23.75%)	12(30%)	7(17.5%)	
Alcoholic, n (%)	15((18.75%)	9(22.5%)	6(15%)	0.18
Miscellaneous, n (%)	6(7.5%)	4(10%)	2(5%)	
Days from onset of symptoms to admission - days (SD)	1 (1.25)	1 (2.5%)	1 (2.5%)	1.0
Signs and Symptoms				
Abdominal pain, VAS (SD)**	8(10%)	6(15%)	2(5%)	0.12
Pain and vomits, n (%)	32(40%)	20(50%)	12(30%)	0.47
Peristalsis, n (%)	40(50%)	22(55%)	18(45%)	0.17
Glasgow scale < 15	0	0	0	-
Serum amylase, U/L, mean (SD)	1421.6 (402.3)	4182.5 (209.5)	5259.7 (1062.5)	0.16
Leukocytes, 10^9/L, mean (SD)	9.3 (0.4)	9.4 (0.25)	9.2 (0.3)	0.06
CRP, mg/dl, mean (SD)	10.0 (22.0)	10.5 (21.1)	9.4 (15.6)	1.0
Pre-Albumin, g/L, mean (SD)	0.22 (0.06)	0.20 (0.05)	0.24 (0.05)	0.02
Albumin, g/L, mean (SD)	34.7 (5.6)	34.2 (4.7)	35.5 (4.9)	0.94
Triglycerides, mg/dl, mean (SD)	153.1 (267.1)	167.7 (294.4)	133.6 (91.9)	1.00
Cholesterol, mg/dl, mean (SD)	168.5 (56.8)	169.7 (54.5)	166.9 (40.4)	0.69
Glycemia, mg/dl, mean (SD)	135.7 (51.5)	138.9 (49.6)	131.6 (36.6)	0.46
SIRS, n (%)	10 (7.6%)	3 (4.2%)	7 (11.7%)	0.10

Table 1: Demographic Characteristics of Study Participants.

IORF: Immediate Oral Refeeding; CORF: Conventional Oral Refeeding; ASA: "American Society of Anesthesiologists" Physical Status Classification System; BMI: Body Mass Index; VAS: Visual Analog Pain Scale; SIRS: Systemic Inflammatory Response Syndrome; CRP: C-Reactive Protein; SD: Standard Deviation. aNormal: 20-104; bNormal20 Breaths Per Minute or a PaCO290lpm; Leukocytes: >12 109 /L

severity (VAS), peristalsis, and the presence of pain with vomiting, showed no statistically significant differences between groups. All participants had a Glasgow Coma Scale score of 15, indicating no impairment of consciousness. Regarding laboratory parameters, there were no significant differences in serum amylase, leukocyte count, CRP, triglycerides, cholesterol, or glycemia levels between the groups. However, pre-albumin levels were significantly lower in the IORF group (0.20g/L) compared to the CORF group (0.24g/L, p = 0.02), indicating a slight nutritional difference. Systemic Inflammatory Response Syndrome (SIRS) was present in 7.6% of participants, with a higher occurrence in the CORF group (11.7%) than in the IORF group (4.2%), though this was not statistically significant (p = 0.10).

In table 2, the clinical outcomes comparing the Immediate Oral Refeeding (IORF) group and the Conventional Oral Refeeding (CORF) group highlight significant differences in multiple mea-

Outcomes	IORF Group	CORF Group	p-value
Length of hospital stay, days, mean (SD)	3.4 (1.7)	8.8 (7.9)	< 0.001
Days from admission to refeeding, days, mean (SD)	0	2.8 (1.7)	< 0.001
Days from refeeding to discharge, days, mean (SD)	3.4 (1.7)	5.4 (4.8)	< 0.001
Need for opioids or analgesia infusion, n (%)	0 (0%)	3 (7.5%)	< 0.001
Intolerance diet, n (%)	1 (2.5%)	9 (22.5%)	< 0.001
Reasons for intolerance			
Relapse of pain, n (%)	0 (0%)	6 (15.0%)	< 0.001
Nausea and vomiting, n (%)	1 (2.5%)	2 (5.0%)	0.37
Anorexia, n (%)	0 (0%)	1 (2.5%)	0.44
Progression of acute pancreatitis, n (%)	0 (0%)	4 (10.0%)	< 0.006
Complications, n (%)	2 (5.0%)	7 (17.5%)	< 0.009
Interventions			
Radiology, n (%)	0 (0%)	1 (2.5%)	0.19
Surgery, n (%)	0 (0%)	1 (2.5%)	0.44
ICU admission, n (%)	0 (0%)	2 (5.0%)	0.03
Mortality, n (%)	0 (0%)	1 (2.5%)	0.44
Hospital readmission, n (%)	1 (2.5%)	4 (10.0%)	0.15

Table 2: Outcomes comparing groups.

IORF: Immediate Oral Refeeding; CORF: Conventional Oral Refeeding; SD: Standard Deviation; ICU: Intensive Care Unit

sures. The length of hospital stay was significantly shorter in the IORF group (mean 3.4 days) compared to the CORF group (mean 8.8 days; $p < 0.001$). Additionally, the time from admission to refeeding was immediate (0 days) in the IORF group, whereas it averaged 2.8 days in the CORF group ($p < 0.001$). The duration from refeeding to discharge was also significantly shorter in the IORF group (mean 3.4 days vs. 5.4 days; $p < 0.001$). The need for opioids or analgesic infusions was entirely absent in the IORF group but required in 7.5% of the CORF group ($p < 0.001$). Diet intolerance was significantly lower in the IORF group (2.5%) compared to the CORF group (22.5%; $p < 0.001$). Among the reasons for intolerance, relapse of pain was noted in 15% of the CORF group but none in the IORF group ($p < 0.001$). Complications such as progression of acute pancreatitis (10% in the CORF group, $p = 0.006$) and general complications (17.5% in the CORF group vs. 5.0% in the IORF group; $p = 0.009$) were also significantly higher in the CORF group. ICU admission occurred only in the CORF group (5.0%; $p = 0.03$). Mortality was minimal, with one case in the CORF group (2.5%, $p = 0.44$). Hospital readmissions were higher in the CORF group (10.0%) than the IORF group (2.5%), though the difference was not statistically significant ($p = 0.15$). Overall, the IORF strategy demonstrated superior outcomes, with shorter hospital stays, lower complication rates, fewer readmissions, and better tolerance to refeeding. These findings strongly support the clinical efficacy and safety of immediate oral refeeding in the studied population.

In table 3, the clinical situation on the refeeding day is compared between the Immediate Oral Refeeding (IORF) and Conventional Oral Refeeding (CORF) groups. The IORF group had a significantly shorter duration from admission to refeeding (0 days) compared to the CORF group (mean 2.8 days, $p < 0.001$). On the refeeding day, the IORF group reported significantly higher abdominal pain (VAS score of 6.2 vs. 2.0 in CORF, $p < 0.001$). Additionally, serum amylase and lipase levels were significantly higher in the IORF group (1339.9 U/L vs. 298.6 U/L for amylase and 4182.5 IU/L vs. 1388.8 IU/L for lipase, both $p < 0.001$), indicating more severe pancreatic enzyme elevations. Leukocyte levels were slightly elevated in the IORF group (mean 9.4 vs. 9.09 in CORF, $p = 0.04$), suggesting a mild inflammatory response. The albumin level was significantly higher in the IORF group (34.2g/L vs. 31.3g/L in CORF, $p = 0.03$), indicating better nutritional status in the IORF group. Cholesterol levels were also significantly higher in the IORF group (169.7 mg/dl vs. 151.4 mg/dl in CORF, $p = 0.007$), and glycemia was higher in the IORF group (138.9 mg/dl vs. 112.8 mg/dl in CORF, $p = 0.002$). There were no significant differences between the two groups in terms of weight, BMI, CRP, pre-albumin, triglycerides, and cholesterol levels, though there was a trend towards lower cholesterol in the CORF group. These findings suggest that the IORF group had more severe acute pancreatitis indicators on the refeeding day but also displayed better nutritional status as reflected by albumin levels.

Outcomes	IORF Group	CORF Group	p-value
Days from admission to refeeding, days, mean (SD)	0	2.8 (1.7)	< 0.001
Abdominal pain, VAS (SD)	6.2 (2.6)	2.0 (0.3)	< 0.001
Weight, kg (SD)	75.7 (15.1)	73.2 (13.8)	0.28
BMI, kg/m^2 (SD)	28.5 (4.7)	27.3 (5.2)	0.16
Serum amylase, U/L, mean (SD)	1339.9 (1341.1)	298.6 (13.8)	< 0.001
Serum lipase, IU/L, mean (SD)	4182.5 (4075.3)	1388.8 (2080.7)	< 0.001
Leukocytes, 10^9/L (SD)	9.4 (0.3)	9.09 (0.4)	0.04
CRP, mg/dl (SD)	10.9 (24.7)	14.6 (24.2)	0.65
Pre-Albumin, g/L (SD)	0.20 (0.06)	0.18 (0.12)	0.33
Albumin, g/L (SD)	34.2 (5.7)	31.3 (8.2)	0.03
Triglycerides, mg/dl (SD)	167.7 (341.6)	136.2 (80.9)	0.69
Cholesterol, mg/dl (SD)	169.7 (63.6)	151.4 (41.4)	0.007
Glycemia, mg/dl (SD)	138.9 (57.6)	112.8 (49.1)	0.002

Table 3: Clinical Situation on the Refeeding Day.

**Refeeding day = admission day for IORF group. See table 1, values of admission day. IORF: Immediate oral refeeding; CORF: Conventional oral refeeding; VAS: Visual analog pain scale; BMI: Body mass index; CRP: C-reactive protein; SD: Standard deviation; a Normal:20-104; b Normal

Discussion

The optimal timing for refeeding in acute pancreatitis (AP) was investigated in this single-center randomized study. It demonstrated that administering an immediate oral low-fat solid diet to patients with mild or moderate AP significantly reduced the length of hospital stay (LOS) without increasing the risk of complications, compared to the conventional oral refeeding (CORF) strategy. Given the variability in timing of refeeding and the persistent use of CORF in many hospitals, this study provides high-quality evidence to support decision-making in managing AP patients.

The most recent clinical guidelines vary in their recommendations for refeeding in AP. The International Association of Pancreatology/American Pancreatic Association (IPA/APA) guidelines recommend restarting a diet in mild AP once abdominal pain decreases and inflammatory markers improve [14]. The American College of Gastroenterology (ACG) guidelines suggest starting a diet immediately if there is no nausea or vomiting and abdominal pain has resolved [23]. Meanwhile, the American Gastroenterological Association (AGA) guidelines advocate for early (within 24 hours) oral feeding as tolerated [23]. These differences in recommendations partly explain why the outdated practice of "pancreatic rest" persists in clinical practice. Pancreatic rest involves fasting until pancreatic enzyme levels drop, peristalsis returns, and patients are pain-free. This conventional approach unnecessarily prolongs LOS for most patients with mild AP.

A 2015 Canadian study found that hospital compliance with guidelines for AP was poor, with 80.6% of patients unnecessarily subjected to fasting, contributing significantly to disease costs [18]. This study aimed to address the timing of refeeding in AP, in line with recent reviews highlighting the lack of solid evidence on the optimal onset of diet in mild AP [24-28,29].

In the present study, the CORF group followed the conventional fasting strategy before gradually reintroducing diet, progressing from clear liquids to solids, which remains common practice despite updated guidelines. Conversely, the IORF group started a low-fat solid diet upon admission, achieving a significant 51% reduction in LOS compared to the CORF group [23-27,33-35]. This result was achieved without waiting for reductions in abdominal pain, peristalsis, or appetite recovery and without imposing analytical restrictions, such as monitoring amylase or leukocyte levels (Table 1 and 3). Similar findings have been reported in other studies, suggesting that early oral feeding is feasible and safe for patients with mild or moderate AP [31,32,36].

Abdominal pain relapse, traditionally considered a risk of early refeeding, was notably absent in the IORF group and occurred in only 16% of the CORF group. This lower relapse rate in the IORF group contributed to the reduced LOS and fewer requirements for opioids or continuous analgesic infusion. Diet intolerance, another

concern, was minimal in the IORF group, affecting only 1% of patients compared to over 20% in the CORF group. These findings align with prior studies, which report no significant differences in adverse effects between early oral feeding and conventional strategies [23,29-32,36-39].

Notably, this study adopted a low-fat solid diet for the IORF group to minimize potential confounders like biliary colic, a common concern with normal-fat diets. Moraes., *et al*. [34] demonstrated that a normal-fat diet caused no adverse effects but acknowledged no differences in LOS or pain relapse across different diets. The present study's decision to use a low-fat solid diet ensured no additional complications while yielding significant benefits, including reduced abdominal pain relapse and better symptom control with conventional analgesia in the IORF group.

This study evaluated all potential adverse effects, including complications, intensive care unit admissions, progression to severe or critical AP, and hospital readmissions. Although not all differences were statistically significant, the IORF group showed better outcomes across all parameters [23,29-32,36]. The study thus confirms that immediate refeeding with a low-fat solid diet is safe, effective, and feasible in mild or moderate AP patients.

The unblinded design may be a limitation, as both patients and physicians were aware of the assigned treatment groups. However, clear criteria for refeeding and discharge reduced the risk of subjective bias. Additionally, although the findings align with other studies [27,33,35], future research comparing low-fat and normal-fat diets in sufficiently powered studies is necessary to evaluate differences in complications or adverse effects.

Conclusion

The administration of an immediate oral low-fat solid diet to patients with mild or moderate AP significantly reduced LOS and hospital costs without increasing the risk of complications. These findings provide robust evidence to support greater adherence to clinical guidelines, replacing outdated fasting strategies with early oral feeding. Future studies may explore comparisons between low-fat and normal-fat diets to refine nutritional management further.

Conflict of Interest

None Declared.

Bibliography

1. MS Petrov and D Yadav. "Global epidemiology and holistic prevention of pancreatitis". *Nature Reviews Gastroenterology and Hepatology* 16.3 (2019): 175-184.

2. Jayalal JA., *et al.* "Role of Fluid Resuscitation in Acute Pancreatitis: A Randomised Control Trial". *Int International Journal of Science and Research (IJSR)* 7.942 (2022).

3. MA Mederos., *et al.* "Acute pancreatitis: a review". *JAMA* 325 (2021): 382-390.

4. SS Vege., *et al.* "Initial medical treatment of acute pancreatitis: American gastroenterological association institute technical review". *Gastroenterology* 154.4 (2018): 1103-1139.

5. M Arvanitakis., *et al.* "ESPEN guideline on clinical nutrition in acute and chronic pancreatitis". *Clinical Nutrition (Edinb)* 39.3 (2020): 612-631.

6. J Maléth and P Hegyi. "Ca2+ toxicity and mitochondrial damage in acute pancreatitis: translational overview". *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 1700 (2016): 371.

7. J Maléth., *et al.* "Breakdown of bioenergetics evoked by mitochondrial damage in acute pancreatitis: mechanisms and consequences". *Pancreatology* 15.4 (2015): S18-S22.

8. L Judák., *et al.* "Ethanol and its non-oxidative metabolites profoundly inhibit CFTR function in pancreatic epithelial cells which is prevented by ATP supplementation". *Pflügers Archiv - European Journal of Physiology* 466.3 (2014): 549-562.

9. Jayalal JA., *et al.* "A comparative study of early versus delayed enteral feeding after Gastrointestinal surgeries". *International Journal of Science and Research (IJSR)* 13.04 (2024).

10. Sathik and Jayalal JA. "Prophylactic antibiotics compliance and its impact on SSI -a prospective study". *International Journal of Academic Medicine and Pharmacy* 5.3 (2023): 884-888.

11. PJ Lodewijkx., *et al.* "Nutrition in acute pancreatitis: a critical review". *Expert Review of Gastroenterology and Hepatology* 10 (2016): 571-580.

12. KM Roberts., *et al.* "Nutritional aspects of acute pancreatitis". *Gastroenterology Clinics of North America* 47 (2018): 77-94.

13. U Karabulut., *et al.* "Early oral refeeding and selection of initial diet in mild acute pancreatitis". *Japanese Journal of Gastroenterology and Hepatology* 1.2 (2019): 1-5.

14. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis". *Pancreatology* 13.4-2 (2013): e1-e15.

15. Párnicsky A., *et al.* "EPC/HPSG evidence-based guidelines for the management of pediatric pancreatitis". *Pancreatology* 18.2 (2018): 146-160.

16. Li X., *et al.* "Early enteral nutrition within 24 hours or between 24 and 72 hours for acute pancreatitis: evidence based on 12 RCTs". *Medical Science Monitor* 20 (2014): 2327-2335.

17. Horibe M., *et al.* "Timing of oral refeeding in acute pancreatitis: a systematic review and meta-analysis". *United European Gastroenterology Journal* 4.6 (2016): 725-732.

18. Greenberg JA., *et al.* "Compliance with evidence-based guidelines in acute pancreatitis: an audit of practices in university of Toronto hospitals". *Journal of Gastrointestinal Surgery* 20.2 (2016): 392-400.

19. Dellinger EP., *et al.* "Determinant-based classification of acute pancreatitis severity: an international multidisciplinary consultation". *Annals of Surgery* 256.6 (2012): 875-880.

20. Banks PA., *et al.* "Classification of acute pancreatitis - 2012: revision or the Atlanta classification and definitions by international consensus". *Gut* 62 (2013): 102-111.

21. Zubia-Olaskoaga F., *et al.* "Comparison between revised Atlanta classification and determinant-based classification for acute pancreatitis in intensive care medicine. Why do not use a modified determinant-based classification?" *Critical Care Medicine* 44.5 (2016): 910-917.

22. Boadas J., *et al.* "Valoración y tratamiento de la pancreatitis aguda. Documento de posicionamiento de la Societat Catalana de Digestologia, Societat Catalana de Cirurgia y Societat Catalana de Pàncreas". *Gastroenterology Hepatology* 38.2 (2015): 82-96.

23. Khan S., *et al.* "Efficacy of early oral refeeding in patients of mild acute pancreatitis". *Pakistan Journal of Medical Sciences* 33.4 (2017): 899-902.

24. Nelly DM., *et al.* "Systematic review with Meta-analysis. Nasogastric nutrition is efficacious in severe acute pancreatitis: a systematic review and meta-analysis". *British Journal of Nutrition* 112.11 (2014): 1769-1778.

25. Li X., *et al.* "Early enteral nutrition within 24 hours or between 24 and 72 hours for acute pancreatitis: evidence based on 12 RCTs". *Medical Science Monitor* 2 (2014): 2327-2335.

26. Horibe M., *et al.* "Timing of oral refeeding in acute pancreatitis: a systematic review and meta-analysis". *United European Gastroenterology Journal* 4.6 (2016): 725-732.

27. Sathiaraj E., *et al.* "Clinical trial: oral feeding with a soft diet compared with celar liquid diet as initial meal in mild acute pancreatitis". *Alimentary Pharmacology and Therapeutics* 15.2 (2008): 777-781.

28. Moher D., *et al.* "CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomized trials". *International Journal of Surgery* 10.1 (2012): 28-55.

29. Lariño-Noia J., *et al.* "Early and/or immediately full caloric diet versus standard refeeding in mild acute pancreatitis: a randomized open-label trial". *Pancreatology* 14.3 (2014): 167-173.

30. Teich N., *et al.* "Optimal timing of oral refeeding in mild acute pancreatitis: results of an open randomized multicenter trial". *Pancreas* 39.7 (2010): 1088-1092.

31. Li J., *et al.* "Early oral refeeding wisdom in patients with mild acute pancreatitis". *Pancreas* 42.1 (2013): 88-91.

32. Zhao XL., *et al.* "Early oral refeeding based on hunger in moderate and severe acute pancreatitis: a prospective controlled, randomized clinical trial". *Nutrition* 31.1 (2015): 171-175.

33. Jacobson BC., *et al.* "A prospective, randomized trial of clear liquids vs. low-fat solid diet as the initial meal in mild acute pancreatitis". *Clinical Gastroenterology and Hepatology* 5.8 (2007): 946-951.

34. Moraes JM., *et al.* "A full solid diet as the initial meal in mild acute pancreatitis is sabe and result in a shorter length of hospitalization: results from a prospective, randomized, controlled, double-blind clinical trial". *Journal of Clinical Gastroenterology* 44.7 (2010): 517-522.

35. Rajkumar N., *et al.* "Clear liquid diet vs soft diet as the initial meal in patients with mild acute pancreatitis: a randomized interventional trial". *Nutrition in Clinical Practice* 28.3 (2013): 365-370.

36. Eckerwall GE., *et al.* "Immediate oral feeding in patients with mild acute pancreatitis is safe and may accelerate recovery—a randomized clinical study". *Clinical Nutrition*26.6 (2007): 758-763

37. Meng WB., *et al.* "Three initial diets for management of mild acute pancreatitis: a meta-analysis". *World Journal of Gastroenterology* 17.37 (2011): 4235-4241.

38. Petrov MS., *et al.* "Oral refeeding after onset of acute pancreatitis: a review of literature". *American Journal of Gastroenterology* 102.9 (2007): 2079-2084.

39. Valverde-López F., *et al.* "Evaluation and management of acute pancreatitis in Spain". *Gastroenterology and Hepatology* 41.10 (2018): 618-628.