ESIC2024 Posted: 22/11/2024

Early Enteral Feeding Versus Delayed Feeding in Acute Pancreatitis Patients

Naji Hamed Hajid Alharbi[1], Ibrahim Abdulaziz Almohsen[1], Faisal Saleh Lafi Alharbi[1], Bader Abdullah Hadi Alharbi[1], Khalid Saud Khalid Alharbi[1], Saad Hameed Hamdan Almutairi[1], Mujib Sinhat Olayan Alharbi[1], Hani Ijl Fahim Almutairi[1], Mohammad Ali Alharbi[2]

[1]Nutritional Therapist
[2]Specialist Food and Nutrition

Abstracts

In clinical practice within intensive care units (ICUs) in Saudi Arabia, physicians often delay the initiation of feeding for critically ill patients until after the first 48 hours. This cautious approach primarily aims to mitigate the risk of refeeding syndrome, which is recognized as a significant barrier to the administration of early nutrition in such patients (Zaher, 2022). In this review I want to investigate the effects of early nutrition (within the first 48 hours of admission) versus delayed nutrition (after 48 hours of admission) in patients with acute pancreatitis receiving enteral feeding only.

1. Introduction

Acute pancreatitis (AP) is marked by the release of pancreatic enzymes within the pancreas triggered by various factors like hypertriglyceridemia and cholelithiasis. This release leads to localized inflammatory responses such as autodigestion, edema, hemorrhage, and necrosis within pancreatic tissue, constituting the primary pathological alterations. These changes may occur independently or alongside other conditions affecting the organ function (IAP, W.G. and Guidelines, 2013). And it stands as the primary gastrointestinal cause for hospital admissions in the United States (Peery et al, 2012). Gallstones and alcohol are the primary causes of AP, while medications, metabolic disturbances such as hypercalcemia and hypertriglyceridemia, and infections are less common causes (Tenner et al, 2013). Over the past decade, the management of acute pancreatitis has significantly evolved. This includes adopting a customized, multidisciplinary strategy that incorporates less invasive techniques such as endoscopic, radiological, and surgical interventions for treating infected pancreatic and peripancreatic necrosis. Additionally, advancements in critical care have led to a decrease in both morbidity and mortality (Van Brunschot et al, 2018). Providing optimal nutrition for patients with acute pancreatitis is crucial for maintaining intestinal barrier integrity, preventing bacterial translocation, and minimizing the systemic inflammatory response syndrome (Capurso et al, 2012). Fostier et al. (2022) showed that recent research supports that early oral feeding in patients

with acute pancreatitis results in shorter hospital stays, fewer complications, and reduced costs. Additionally, early enteral nutrition (within 48 hours) has been shown to lower hospital mortality in cases of both mild and severe acute pancreatitis. Therefore, if there is intolerance to oral feeding or in cases of severe disease, nutritional therapy should be initiated within 24 to 72 hours. When oral feeding is not possible due to feeding intolerance, both the European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Society of Gastrointestinal Endoscopy recommend using a nasogastric tube rather than a naso-jejunal tube. However, in situations of gastric feeding intolerance, In approximately 15% of cases, where issues such as delayed gastric emptying or gastric outlet obstruction syndrome occur, often secondary to significant perivisceritis, a naso-jejunal tube is recommended (Arvanitakis et al, 2020) (Arvanitakis et al, 2021). Additionally, enteral nutrition is preferred over parenteral nutrition because it is associated with a shorter hospital stay and fewer complications (Fostier et al, 2022). In a recent systematic review by Yao et al. (2022), investigates whether immediate or early oral refeeding can influence the recovery outcomes in patients with mild to moderate acute pancreatitis compared to delayed oral refeeding with a focus on recovery markers such as length of stay in hospital and overall healthcare costs. The writers conclude that immediate or early oral refeeding can reduce hospital stay and costs with no significant differences in adverse events such as mortality, pain relapse, or other complications in patients with mild to moderate acute pancreatitis. In this review the focus will be on three markers which are pancreatic necrosis which can be defined as the diffuse or localized regions of nonviable pancreatic parenchyma typically accompany peripancreatic fat necrosis (Bradley et al, 1993). The second marker is systematic inflammatory response syndrome (SIRS), it is frequently encountered in critically ill patients and characterizes a variety of systemic inflammatory reactions to factors such as trauma, surgery, and infections (Toliver-Kinsky et al, 2018). And the last marker to be assessed is mortality rate which is how many deaths during the intervention.

2. Methods

The search strategy was used on two databases: PubMed and Midline. The following keywords were used in the search: (early feeding) OR (early nutrition) AND (acute pancreatitis). The studies included were selected in accordance with the Preferred Reporting Items for Systematic Reviews guidelines (PRISMA, 2020), as shown in Figure 1.

The PICO model was followed in this review:

- Population: acute pancreatitis patients.
- Intervention: early feeding.
- Comparison: delayed feeding.
- Outcome: occurrence of pancreatic necrosis.

- Inclusion Criteria

1. RCTs.
2. Published between 2013 and 2024.
3. Adult patients.
4. Acute pancreatitis patients on enteral feeding only.
5. Studies feeding patients within 48 hours of admission.
6. Studies written and published in English.

- Exclusion Criteria:

1. Non-RCT studies.
2. Published before 2013.
3. Studies on children.
4. Studies that are not in English.
5. Patients receiving oral feed.

Primary Outcome

Pancreatic necrosis.

Secondary Outcomes

Mortality rate and systemic inflammatory response syndrome.

3. Results and Discussion:

The quality assessment was conducted using the modified Cochrane Collaboration tool to evaluate the risk of bias of RCTs (high, low, or unclear) on five domains (randomization process, intended intervention, missing outcome, outcome measurement and selection of results). (Sterne et al., 2019). See table1.

Table1.

Biases / Authors	Randomization process	Intended intervention	Missing outcome	Outcome measurement	Selection of results	Overall risk of bias
Bakket et al, 2014	High risk	Low risk	Low risk	Low risk	Low risk	High risk

Jin et al, 2020	High risk	Low risk	Some concerns	Low risk	Some concerns	High risk
Wereszczynska et al, 2013	High risk	High risk	Some concerns	Low risk	Some concerns	High risk
Stimac et al, 2016	High risk	Some concerns	Low risk	Some concerns	Low risk	High risk

From 4 RCTs reviewed in this paper published between 2013-2024 in different countries that compared the effect of early nutrition with delayed nutrition in acute pancreatitis patients.

All the studies measured the incidence of pancreatic necrosis, mortality rates and 3 of the studies measured the systematic inflammatory response syndrome, with a total number of 978 patients as shown in table2.

Table2:

Author's	Location	N of participants	Intervention	Outcomes
Bakker et al, 2014	The Netherlands	208	EN (within 24 hours) vs DN (after 72 hours).	PN in 63% of EN vs 64% in DN. Mortality rates were 11% in EN and 7% in DN. 62% EN had SIRS vs 67% in DN.
Jin et al, 2020	China	287	EN (within 24 hours) vs DN (after 72 hours).	PN incidences were 27.27% in DN and 14.29% in EN (both VFO patients). Mortality rates were 5.68% in DN and 4.40% in EN (both VFO).
Wereszczynska et al, 2013	Poland	197	EN (within 24 hours) vs DN (after 72 hours).	PN incidence were 4.1% in EN and 18% in DN. Persistent SIRS in 46.4% EN patients and 53% DN patients. In the first 48 hours no deaths in EN while in DN 9% mortality rate.
Stimac et al, 2016	Croatia	214	EN (within 24 hours) vs DN (after 72 hours).	34.6% in the EN developed PN compared to 30.8% in EN. SIRS developed in 4 EN patients compared to 2 in DN. Mortality rates were 9.4% in EN and 15.9% in DN.

Abbreviations: N= number, EN= early nutrition, DN= delayed nutrition, PN= pancreatic necrosis, SIRS= systematic inflammatory response syndrome, VFO= visceral fat obesity.

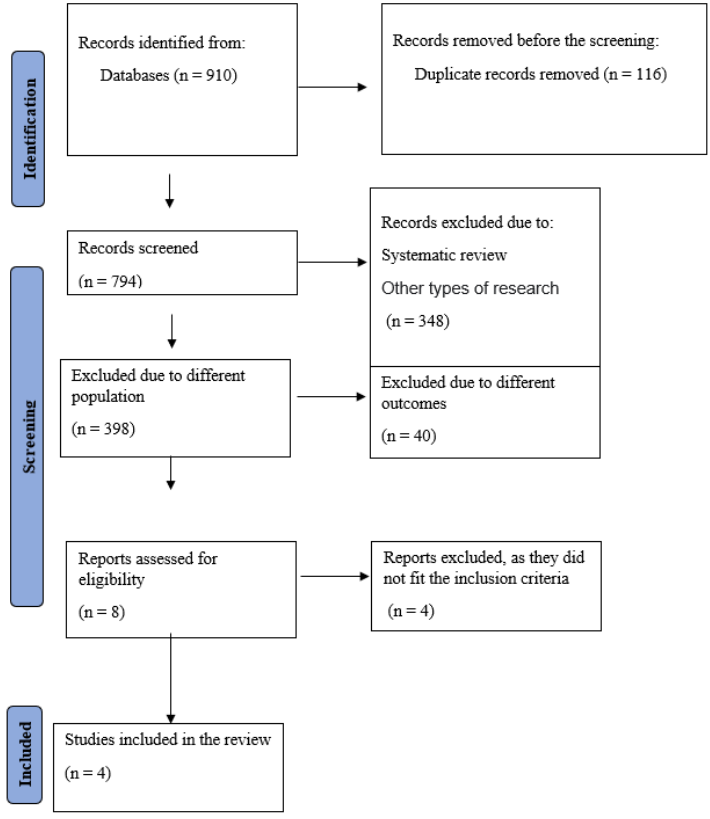

Figure 1: PRISMA flowchart demonstrating the selection of articles included in the review

Primary Outcome:

Pancreatic necrosis was measured in all of the RCTs and the results were different in terms of incidence and significance, in Bakker et al. (2014) the occurrence of pancreatic necrosis was notably high across both groups, affecting 63% of patients in the early nutrition group and 64% in the delayed nutrition group. This high prevalence shows the severity and commonality of necrosis among patients experiencing severe cases of pancreatitis, p= 0.28.

Jin et al. (2020) divided patients based on their visceral fat obesity (VFO) status and were either assigned to early enteral nutrition (EEN) or delayed enteral nutrition (DEN). Group A consisted of 108 non-VFO patients receiving DEN, Group B included 88 VFO patients also on DEN, and Group C comprised 91 VFO patients on EEN. All groups had a similar mean age range of 46-48 years and displayed a balanced gender distribution. However, Groups B and C, both VFO, had significantly higher visceral fat areas compared to Group A. In terms of pancreatic necrosis outcomes, 40.7% of Group A experienced pancreatic necrotic collections. Group B showed a higher incidence, with 63.6% having pancreatic necrotic collections, indicating a pronounced

effect of VFO on the severity of the condition under delayed nutritional support. In contrast, Group C had a markedly lower incidence of pancreatic infected necrosis at 14.3%, suggesting that early enteral nutrition might mitigate the severity of necrotic complications in VFO patients. High levels of visceral fat, as seen in Groups B and C, are associated with increased inflammation. This pro-inflammatory condition in patients with substantial visceral fat can worsen acute pancreatitis, potentially resulting in severe complications such as pancreatic necrosis. The findings from the study emphasize the significance of visceral fat obesity as a crucial risk factor that can lead to poorer outcomes in pancreatic necrosis, p= 0.028.

While in Wereszczynska et al. (2013) trial, in group A, where early enteral nutrition was initiated within 48 hours of admission, pancreatic necrosis occurred in 4 out of 97 patients, accounting for 4.1% of the group. Conversely, in Group B, where enteral nutrition was delayed beyond 48 hours, pancreatic necrosis or fluid collection was observed in 18 out of 100 patients, which corresponds to 18.0% of the group. These results highlight a significantly higher incidence of pancreatic necrosis in the group receiving delayed enteral nutrition compared to those receiving it early., p=0.028.

Lastly, in Stimac et al. (2016) trial, among 107 participants in the early nutrition group, 37 (34.6%) suffered from pancreatic necrosis, while in the delayed nutrition group, also with 107 participants, 33 (30.8%) experienced the same condition. Although the Early Nutrition group had a marginally higher rate of pancreatic necrosis, the difference between the two groups was not statistically significant, p=0.275.

The findings illustrate that the effects of enteral nutrition timing on pancreatic necrosis outcomes are not consistent across all cases. For example, Bakker et al. (2014) found no significant difference in necrosis rates between early and delayed nutrition groups, indicating that timing alone may not influence the severity of outcomes universally. However, under specific circumstances, such as in patients with visceral fat obesity (VFO), early nutrition significantly reduces the incidence of necrosis, as shown by Jin et al. (2020) and Wereszczynska et al. (2013). These findings suggest that early enteral nutrition can be particularly beneficial for higher-risk patients, highlighting its importance in such subgroups. On the other hand, Stimac et al. (2016) reported no significant differences in outcomes between early and delayed groups in a broader pancreatitis cohort, suggesting that the timing of nutritional support may be less crucial in populations without particular risk factors. This variation in results underscores the need to plan nutritional intervention strategies based on individual patient risk profiles in managing pancreatic necrosis.

Secondary Outcomes:

In terms of mortality rate Bakker et al. (2014) reported mortality rates of 11% for early nutrition and 7% for delayed nutrition. Jin et al. (2020) found mortality rates of 4.40% for early nutrition and 5.68% for delayed nutrition, both having visceral fat obesity. Wereszczynska et al. (2013) observed no deaths in early nutrition while delayed nutrition had a 9% mortality rate within the first 48 hours, and Stimac et al., 2016 noted mortality rates of 9.4% for early nutrition and 15.9% for delayed nutrition.

Regarding Systematic Inflammatory Response Syndrome (SIRS), in the study conducted by Bakker et al. (2014), 62% of patients receiving early nutrition exhibited symptoms of SIRS compared to 67% in those with delayed nutrition. Also Wereszczynska et al. (2013) found that SIRS persisted in 46.4% of patients on early nutrition and in 53% of those on delayed nutrition. Additionally, Stimac et al. (2016) reported that SIRS developed in four patients receiving early nutrition, whereas only two patients experienced SIRS under delayed nutrition conditions.

ESPEN guidelines recommended in their latest review that enteral nutrition should be initiated early, between 24 to 72 hours after admission, if oral feeding is not tolerated (Arvanitakis et al, 2024). In addition, NICE guidelines also recommends administering enteral nutrition to patients with severe or moderately severe acute pancreatitis, and begin within 72 hours of their admission and aim to quickly meet their dietary requirements (NICE, 2018). he recommendations from both ESPEN and NICE highlight the importance of early initiation of enteral nutrition in managing patients with acute pancreatitis, particularly when oral feeding isn't possible. Starting enteral nutrition within 24 to 72 hours after admission ensures that patients receive necessary nutrients to support their recovery. This approach not only aligns with best practices for promoting healing and preventing complications but also underscores the critical nature of nutritional management in severe cases of pancreatitis. It's clear that both guidelines prioritize rapid nutritional intervention as a key component of patient care in these situations.

The fact that the four studies were conducted in different countries adds a valuable dimension to the generalizability of their results in the context of managing acute pancreatitis through nutritional interventions. Overall, the international nature of these studies strengthens their generalizability, suggesting that the findings could be relevant to a wide array of clinical settings globally. Moreover, blinding in clinical trials is a crucial methodological technique used to mitigate bias by preventing participants, caregivers, and sometimes those analyzing the results from knowing the interventions being administered. However, blinding critically ill patients, such as those with severe acute pancreatitis, presents a clear challenge because of the nature of the intervention. For instance, interventions involving enteral nutrition versus standard care or nil by mouth approaches inherently differ in their administration patients will likely be aware if they are receiving nutrition via a tube compared to not receiving any food at all. This awareness can influence patient-reported outcomes and potentially their physiological responses due to psychological factors.

4. Conclusion:

The investigation into the timing of enteral nutrition in patients with acute pancreatitis has emphasized the complexity and variability in clinical outcomes related to early versus delayed nutritional interventions especially reducing the risk of pancreatic necrosis. This research highlights the importance of individualizing nutritional strategies to enhance clinical outcomes and mitigate the risks associated with acute pancreatitis. Moreover, the findings suggest that early enteral nutrition may contribute to reduced mortality rates and a decrease in systemic inflammatory response syndrome (SIRS), reinforcing the recommendations of both ESPEN and NICE guidelines.

In summary, although further research is necessary to fully understand the impact of early versus delayed enteral nutrition in acute pancreatitis, existing data advocate for a proactive approach to nutrition in certain patient groups. This approach is in line with best clinical practices and highlights the importance of customized nutritional strategies in enhancing outcomes for patients with acute pancreatitis.

Future Implications:

The insights from this review on the timing of enteral nutrition for acute pancreatitis patients could lead to significant changes in both clinical practice and medical research. There's a growing push for global clinical guidelines to not only promote early nutritional intervention but also to ensure these guidelines are adaptable based on individual patient factors like obesity and other conditions. This approach could lead to more customized nutritional strategies that are more effective for diverse patient needs.

Innovations may also arise in the types of nutritional formulations tailored specifically for acute pancreatitis, alongside technological advancements in how these nutrients are delivered—making the process smoother and safer. From an economic perspective, initiating nutrition earlier could mean shorter hospital stays and reduced healthcare costs, which begs for further investigation into the long-term financial benefits of such practices.

Moreover, the results underscore the importance of integrating personalized medicine into nutritional care plans, which would require updates to healthcare policies and enhanced training for providers. This shift towards personalized nutrition care also brings up the need for new ethical guidelines in clinical research, ensuring that trials are designed to effectively address the unique challenges of delivering nutritional interventions to critically ill patients. This approach not only aims to improve immediate clinical outcomes but also enhances the overall healthcare journey for patients with acute pancreatitis.

WORKS CITED

Arvanitakis, M., Gkolfakis, P., Despott, E.J., Ballarin, A., Beyna, T., Boeykens, K., Elbe, P., Gisbertz, I., Hoyois, A., Mosteanu, O. and Sanders, D.S., 2021. Endoscopic management of enteral tubes in adult patients–Part 1: Definitions and indications. European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy, 53(01), pp.81-92.

Arvanitakis, M., Ockenga, J., Bezmarevic, M., Gianotti, L., Krznarić, Ž., Lobo, D.N., Löser, C., Madl, C., Meier, R., Phillips, M. and Rasmussen, H.H., 2020. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. Clinical Nutrition, 39(3), pp.612-631.

Arvanitakis, M., Ockenga, J., Bezmarevic, M., Gianotti, L., Krznarić, Ž., Lobo, D.N., Löser, C., Madl, C., Meier, R., Phillips, M. and Rasmussen, H.H., 2024. ESPEN practical guideline on clinical nutrition in acute and chronic pancreatitis. Clinical Nutrition, 43(2), pp.395-412.

Bakker, O.J., van Brunschot, S., van Santvoort, H.C., Besselink, M.G., Bollen, T.L., Boermeester, M.A., Dejong, C.H., van Goor, H., Bosscha, K., Ali, U.A. and Bouwense, S., 2014. Early versus on-demand nasoenteric tube feeding in acute pancreatitis. New England Journal of Medicine, 371(21), pp.1983-1993.

Bradley, E.L., 1993. A clinically based classification system for acute pancreatitis: summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. Archives of surgery, 128(5), pp.586-590.

Capurso, G., Zerboni, G., Signoretti, M., Valente, R., Stigliano, S., Piciucchi, M. and Delle Fave, G., 2012. Role of the gut barrier in acute pancreatitis. Journal of clinical gastroenterology, 46, pp.S46-S51.

Fostier, R., Arvanitakis, M. and Gkolfakis, P., 2022. Nutrition in acute pancreatitis: when, what and how. Current Opinion in Clinical Nutrition & Metabolic Care, 25(5), pp.325-328.

IAP, W.G. and Guidelines, A.A.P., 2013. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology, 13(4), pp.e1-e15.

Jin, Z., Wang, Z. and Wang, J., 2020. Early enteral nutrition prevent acute pancreatitis from deteriorating in obese patients. Journal of clinical gastroenterology, 54(2), pp.184-191.

Nice guidelines, <https://www.nice.org.uk/guidance/ng104> [accessed on 26\4\2024].

Peery, A.F., Dellon, E.S., Lund, J., Crockett, S.D., McGowan, C.E., Bulsiewicz, W.J., Gangarosa, L.M., Thiny, M.T., Stizenberg, K., Morgan, D.R. and Ringel, Y., 2012. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology, 143(5), pp.1179-1187.

Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., . . . Higgins, J. P. T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. BMJ :

Stimac, D., Poropat, G., Hauser, G., Licul, V., Franjic, N., Zujic, P.V. and Milic, S., 2016. Early nasojejunal tube feeding versus nil-by-mouth in acute pancreatitis: a randomized clinical trial. Pancreatology, 16(4), pp.523-528.

Tenner, S., Baillie, J., DeWitt, J. and Vege, S.S., 2013. American College of Gastroenterology guideline: management of acute pancreatitis. Official journal of the American College of Gastroenterology| ACG, 108(9), pp.1400-1415.

Toliver-Kinsky, T., Kobayashi, M., Suzuki, F. and Sherwood, E.R., 2018. The systemic inflammatory response syndrome. Total burn care, pp.205-220.

Van Brunschot, S., Hollemans, R.A., Bakker, O.J., Besselink, M.G., Baron, T.H., Beger, H.G., Boermeester, M.A., Bollen, T.L., Bruno, M.J., Carter, R. and French, J.J., 2018. Minimally invasive and endoscopic versus open necrosectomy for necrotising pancreatitis: a pooled analysis of individual data for 1980 patients. Gut, 67(4), pp.697-706.

Wereszczynska-Siemiatkowska, U., Swidnicka-Siergiejko, A., Siemiatkowski, A. and Dabrowski, A., 2013. Early enteral nutrition is superior to delayed enteral nutrition for the prevention of infected necrosis and mortality in acute pancreatitis. Pancreas, 42(4), pp.640-646.

Yao, Q., Liu, P., Peng, S., Xu, X. and Wu, Y., 2022. Effects of immediate or early oral feeding on acute pancreatitis: a systematic review and meta-analysis. Pancreatology, 22(2), pp.175-184.

Zaher, S., 2022. Barriers to delivery of enteral nutrition in intensive care settings in Saudi Arabia: A comparative study of the perceptions of health care providers working in adult and paediatric ICUs. Risk Management and Healthcare Policy, pp.2357-2370.