Relationship between Early Enteral Nutrition and BISAP Score with Duration of Hospitalization in Patients with Acute Edematous Pancreatitis

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ABSTRACT: Objective: This study aimed to examine and demonstrate the contribution of early enteral nutrition support to the disease prognosis and duration of hospitalization in appropriate patients with well-defined acute pancreatitis. **Materials and Methods:** This cross-sectional study included 84 patients admitted to the Internal Medicine Clinic with a diagnosis of acute edematous pancreatitis. To reveal the statistical relationship of early enteral nutrition support with hospitalization and mortality during the treatment process, patients who received the same infusion protocol and the same intravenous fluid were included in the study. The number of hours after each patient was started on enteral nutrition support was determined. **Results:** The effect of the BISAP score on the initiation of enteral nutrition was evaluated via binary logistic regression analysis. A BISAP score of 3 or above significantly increased the duration of enteral nutrition initiation to more than 72 hours (OR=29.167; CI: 4.634-183.576). **Discussion**: No studies regarding the relationships between early enteral nutrition and the BISAP score and the duration of hospitalization have been reported. As the BISAP score is calculated according to the clinical evaluation in the first 24 hours and its statistical relationship with mortality has been demonstrated in previous reports, we aimed to reveal the relationship between early enteral nutrition support and hospitalization duration in the evaluation of the course, severity, and prognosis of acute pancreatitis. **Conclusions:** We believe that early enteral nutrition (≤72 hours) in patients with acute pancreatitis significantly reduces hospitalization time and complications.

Keywords: acute pancreatitis, early enteral feeding, BISAP score, hospitalization

Main Points

- Early initiation of enteral nutrition in patients diagnosed with acute pancreatitis is associated with a shorter hospitalization duration.
- Early initiation of enteral nutrition in patients diagnosed with acute pancreatitis is associated with a reduction in disease complications.
- A BISAP score >3 in patients diagnosed with acute pancreatitis is associated with failure to provide early enteral nutrition.

Introduction

Acute pancreatitis is the most common gastroenterological disease requiring hospitalization. Most patients present with mild acute pancreatitis that is self-limiting and typically resolves within 1 week. Approximately 20% of patients develop moderate to severe acute pancreatitis with pancreatic or peripancreatic tissue necrosis or organ failure or a combination of both, which has a mortality rate of 20–40% (1, 2).

The most common presentation of acute pancreatitis is severe upper abdominal pain, and two of the following three criteria must be met for a diagnosis: 1.) upper abdominal pain, 2.) serum amylase or lipase (or both) at least three times the upper normal limit, or 3.) findings consistent with acute pancreatitis on contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), or abdominal ultrasound (3). Typically, necrotizing pancreatitis is detected by imaging 72–96 hours after the findings (3).

According to current guidelines, etiological evaluation should be performed at an early stage (3). In terms of etiology, gallstones (40–70%) and alcohol consumption (25–35%) are among the most common causes of acute pancreatitis (4). Less common causes include medications, endoscopic retrograde cholangiopancreatography (ERCP), hypercalcemia, hypertriglyceridemia, infections, genetic factors, autoimmune diseases, surgery, and trauma, particularly trauma that damages the pancreatic duct (5). In hypertriglyceridemia, triglyceride levels >1000 mg/dL trigger acute pancreatitis attacks, though lower triglyceride levels can also trigger attacks (6).

The Acute Physiology and Chronic Health Evaluation II (APACHE II), Ranson score, Acute Pancreatitis Bedside Severity Index (BISAP) score and biochemistry tests such as C-reactive protein (CRP) and blood urea nitrogen (BUN) are used in routine practice to determine the severity of acute pancreatitis (7). In line with current recommendations, systemic inflammatory response syndrome (SIRS) or end-organ damage should be assessed for at least 48 hours from the time of presentation to predict the course of the disease (8).

The severity classification of acute pancreatitis is defined as mild, moderate, or severe according to the revised Atlanta classification (9). When evaluated via the revised Atlanta classification criteria, the severity of acute pancreatitis is categorized into three groups on the basis of the presence of organ dysfunction and local (pancreatic or peripancreatic fluid accumulation or portal vein thrombosis) or systemic (exacerbation of comorbidities) complications. When no local or systemic complications or organ failure are present, acute pancreatitis is classified as “mild” (9). Conservative treatment is typically sufficient in patients with mild acute pancreatitis. The absence of local or systemic complications and permanent organ failure in patients with acute pancreatitis is categorized as “moderate” (9). The development of permanent single- or multiple-organ failure in the clinical presentation of acute pancreatitis is classified as “severe” and is associated with a mortality rate of 20–40% (1).

In interstitial edema of the pancreas, homogeneous fluid-containing accumulations that develop during the first 4 weeks of disease are referred to as acute pancreatic or peripancreatic fluid accumulations. These accumulations typically regress without requiring intervention. If these accumulations persist for more than 4 weeks from the onset of the disease, pancreatic pseudocysts may develop. In necrotizing pancreatitis, accumulations that form within the first 4 weeks of disease onset are referred to as “acute necrotic accumulations.” Acute necrotic collections are usually called "walled-off" necrosis when they mature and encapsulate after the first 4 weeks (9).

The cornerstones of acute pancreatitis treatment are fluid resuscitation, pain palliation, and nutrition. In acute pancreatitis, hypovolemia and end-organ failure may occur with fluid extravasation into the third space accompanied by a systemic immune response. Therefore, appropriate and adequate fluid resuscitation maintains intravascular volume and increases microperfusion and organ perfusion. Favorable effects of optimal fluid resuscitation on clinical outcomes have been demonstrated in the early clinical course of the disease (10). Although there are various publications in the literature regarding optimal fluid resuscitation, current guidelines recommend a heart rate <120/min, mean arterial pressure (MAP) of 65–85 mm Hg, and urine output >0.5–1.0 mL/kg/hour (3). However, a multicenter randomized multicenter study by Enrique de-Madaria et al. comparing aggressive (20 mL/kg loading followed by 3 mL/kg maintenance) and moderate (10 mL/kg loading followed by 1.5 mL/kg maintenance) fluid resuscitation with Ringer's lactate solution in patients with acute pancreatitis concluded that early aggressive fluid resuscitation was associated with fluid overload without clinical improvement (11). Compared with fluid resuscitation with normal saline, fluid resuscitation with Ringer's lactate solution was associated with less SIRS development and lower CRP levels (12).

Nutritional support is a cornerstone treatment for pancreatitis. Optimal nutritional support maintains intestinal barrier function, prevents bacterial translocation and reduces SIRS (13). Parenteral nutrition is not recommended over enteral nutrition due to increased risk of complications, atrophy of the intestinal mucosa, increased permeability of the intestinal mucosal barrier, and mortality (14). Although the role of the activation of inflammatory and proteolytic cascades in the underlying mechanism of acute pancreatitis is known, studies have suggested that cell signaling is triggered by bacterial infections. As a result of bacterial translocation, macrophages, circulating neutrophils, and granulocytes are stimulated, and proinflammatory cytokines are released. As a result of this imbalance in the inflammatory response, SIRS, infectious pancreatic necrosis, and multiple organ failure may develop (15). According to meta-analyses by Marik and Zaloga and McClave et al., early enteral nutrition is associated with a reduction in hospitalization and infection-related complications (16, 17). If bacterial translocation can be prevented by maintaining the intestinal barrier with enteral nutrition, early initiation of enteral nutrition is recommended. In summary, early initiation of enteral nutrition in the clinical course of acute pancreatitis has been associated with a reduction in the length of hospitalization (18).

Although several studies have investigated acute pancreatitis, the majority of these studies focus on fluid management, pain palliation, and pancreatitis complications. Few studies have associated early enteral nutrition in acute pancreatitis with the course of pancreatitis and hospitalization. No studies have focused on the BISAP score, a frequently used acute pancreatitis severity scoring index, and its relationship with the duration of hospitalization and transition to early enteral nutrition. Therefore, the primary objective of our study was to investigate the contribution of early enteral nutritional support to disease prognosis and length of hospital stay in appropriate patients with a well-defined diagnosis of acute pancreatitis.

Materials and Methods

This cross-sectional study included data from 83 patients who were diagnosed with acute edematous pancreatitis and followed up at the Internal Medicine Clinic between July 1, 2022 and July 1, 2024.

Study Design: Patients included in our study met the following criteria:

i. Patients between 18–92 years of age who were admitted to the Internal Medicine Clinic with a diagnosis of acute edematous pancreatitis;
ii. Patients with no cause of illness other than acute edematous pancreatitis;
iii. Patients who did not require any treatment other than that for acute edematous pancreatitis;
iv. Patients who received the same intravenous fluid protocol,
v. Patients who were cooperative, had no mental or psychiatric defects, and had no diagnosis of psychiatric illness;
vi. Patients without illicit drug use;
vii. Patients with enteral nutrition adherence,
viii. Patients who did not require intensive care at any time during the hospitalization and who were followed up only by the ward team at the Internal Medicine Clinic, where treatments prepared according to the protocol in accordance with the algorithm were administered.

The following patients were excluded from our study:

i. Patients under 18 years of age and patients over 92 years of age;
ii. Patients with active infection requiring prolonged hospitalization for other etiologies,
iii. Patients who could not tolerate active enteral nutrition;
iv. Patients with necrotizing and severe pancreatitis;
v. Patients with biliary acute pancreatitis,
vi. Patients with cognitive dysfunction;
vii. Patients with a history of nonpancreatitis hospitalization,
viii. Patients with autoimmune and chronic pancreatitis;
ix. Patients with pancreatic malignancy,
x. Patients with cholangitis and cholecystitis;
xi. Patients on parenteral nutrition,
xii. Patients with acute renal failure at and before hospitalization;
xiii. Patients diagnosed with chronic renal failure;
xiv. Patients receiving medical treatment that caused hyperuricemia;
xv. Patients who developed acute respiratory distress syndrome (ARDS) at the time of diagnosis or during ward follow-up;
xvi. Patients with active lung infection;
xvii. Patients receiving antibiotherapy.

Patients with imaging findings suggestive of acute edematous pancreatitis were included in the study. According to the American Gastroenterological Association (AGA) and the revised Atlanta classification (2012) (19), the diagnosis of acute pancreatitis is based on abdominal pain consistent with acute pancreatitis, at least a threefold increase in serum lipase or amylase, and radiological findings suggestive of acute pancreatitis on ultrasound, magnetic resonance imaging, or computed tomography. Patients with acute edematous pancreatitis who developed necrotizing and severe pancreatitis at diagnosis or follow-up were excluded from the study. The patient age, admission date, and discharge dates of the 84 patients included in this study were recorded. The vital signs of the patients were analyzed after hospitalization. Ringer's lactate fluid resuscitation protocol was administered at 5 ml/kg loading, followed by a 1.5 ml/kg maintenance protocol. The comorbidities of the patients were subsequently evaluated for hypertriglyceridemia, which is the most common etiology of acute pancreatitis, and alcohol consumption. Patients with biliary pancreatitis were excluded as they could not be objectively evaluated due to late transition to enteral nutrition. To reveal the statistical relationship of early enteral nutrition support with hospitalization and mortality during the treatment process, patients who received the same infusion protocol and the same intravenous fluid were included in the study. The number of hours after the patients were started on enteral nutrition support was determined.

The parameters used in the evaluation of the BISAP score (20) include:

- Blood urea nitrogen (BUN) > 25 mg/dL
- Signs of impaired mental function
- ≥2 Systemic inflammatory response syndrome (SIRS) findings*
- Age>60 years
- Presence of pleural effusion

*: The presence of SIRS signs requires the presence of two of the following findings: body temperature <36° or >38°, heart rate >90/min, respiratory rate >20/min or $PaCO_2$<32 mm Hg, and leukocyte count >12,000 or <4,000/mm^3.

A BISAP score of <2 has been associated with 0–0.5% mortality, and a score of ≥3 has been associated with 5–20% mortality (20).

Statistical Analysis: Descriptive statistics (arithmetic mean, median, standard deviation, percentage, etc.) were evaluated using IBM SPSS 25v package program. Compliance with a normal distribution was checked via the Shapiro–Wilk test. The chi-square test was used to compare the qualitative variables between the groups. The Mann–Whitney U test was used to compare the quantitative variables without a normal distribution between the groups. The effect of the BISAP score on the transition to an early enteral nutrition regimen was evaluated via binary logistic regression analysis. P<0.05 was considered statistically significant.

Ethics Committee: The study was approved by the Afyonkarahisar Health Sciences University Clinical Research Ethics Committee on May 2, 2025 (Meeting number: 2025/6). Our investigation relies on open-source data, follows the guidance of ethics committees, and is free from ethical issues and other conflicts of interest. The study was conducted retrospectively and adhered to the data scheme outlined in the approved ethics committee application. Additionally, no changes were made to the study plan or content after the ethics committee approval. Informed consent was obtained from all individual participants included in the study. Clinical trial number: not applicable. All procedures involving human participants performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Results

The patients' characteristics are provided in Table 1. The mean age of the patients was 55±20.63 years. Seventy-three (88%) of the patients were hospitalized for 9 days or more, 20 (24.1%) had hypertriglyceridemia, 75 (90.4%) did not consume alcohol, and 56 (67.5%) did not have diabetes. Seventy-six (91.6%) of the patients had a BISAP score of 2 or less in the first 24 hours, and 72 (86.7%) had an enteral nutrition onset of 72 hours or less.

Table 1. Patient characteristics (n=83)

Variables	n (Number)	% (Percent)
Age (years)*	55±20.63	
Length of Stay		
>9 days	10	12
≤9 days	73	88
Hypertriglyceridemia		
No	63	75.9
Yes	20	24.1
Alcohol Consumption		
No	75	90.4
Yes	8	9.6
Diabetes		
No	56	67.5
Yes	27	32.5
BISAP Score		
≥3	7	8.4
≤2	76	91.6
Enteral Nutrition Initiation		
>72 hours	11	13.3
≤72 hours	72	86.7

(*) (mean±standard) (expressed as deviation)

When the characteristics of the patients were evaluated according to the start of enteral nutrition, there was a statistically significant difference in the first 24 hours of BISAP score (p<0.001). In 5 (71.4%) of the patients with a BISAP score of 3 or

above, the start of enteral nutrition was more than 72 hours. In 70 (92.1%) of those with a BISAP score of 2 or less, the onset of enteral nutrition was 72 hours or less (Table 2).

Table 2. Evaluation of the characteristics of the patients in the study according to the start of enteral nutrition (n=83)

Variables	Enteral Nutrition				p
	>72 hours		≤72 hours		
	n	%	n	%	
Age (years)*	78 (36-83)		55 (40.25-68.75)		0.104
Duration of Hospitalization					
>9 days	10	100	0	0	-
≤9 days	1	1.4	72	98.6	
Hypertriglyceridemia					
No	8	12.7	55	87.3	0.721
Yes	3	15	17	85	
Alcohol Consumption					
No	9	12	66	88	0.286
Yes	2	25	6	75	
Diabetes					
No	8	14.3	48	85.7	0.689
Yes	3	11.1	24	88.9	
BISAP Score					
≥3	5	71.4	2	28.6	**<0.001**
≤2	6	7.9	70	92.1	

(*expressed as the median (25th percentile–75th percentile)).

(The Mann-Whitney U test and chi-square test were used).

The effect of the BISAP score on enteral nutrition initiation was evaluated via binary logistic regression analysis. A BISAP score of 3 or above significantly increased the duration of enteral nutrition initiation longer than 72 hours in patients (OR=29.167; CI: 4.634-183.576) (Table 3).

Table 3. Effect of the BISAP score on enteral nutrition initiation (binary logistic regression)

Variables	B	Standard Error	Wald	sd	p	OR (exp(B))	OR 95% Confidence Interval	
							Alt	Top
BISAP Score	3.373	0.939	12.915	1	**<0.001**	29.167	4.634	183.576

(OR:) (odds ratio)

Discussion

In this study, a BISAP score of 3 or above significantly increased the duration of enteral nutrition initiation longer than 72 hours in patients (OR=29.167; CI: 4.634-183.576). It has been reported that a BISAP score ≥3 is significantly associated with increased mortality (21). Compared with other scoring systems used in the evaluation of acute pancreatitis, such as the Ranson criteria and APACHE II, the BISAP scoring system requires easy calculations, contains fewer parameters, and can only be applied based on clinical information within the first 24 hours after evaluation. The requirement of a 48-hour evaluation to meet the Ranson criteria may result in missing data during the early treatment period. In addition, the fact that some parameters in the APACHE II system are unrelated to the diagnosis and treatment of acute pancreatitis and some parameters are difficult to obtain outside of intensive care conditions makes it difficult to use the APACHE II scoring system in the setting of acute

pancreatitis (22). Gao et al. reported that the BISAP score has higher specificity and lower sensitivity for mortality and the development of severe acute pancreatitis than the Ranson and APACHE II scores do (21).

Although previous studies have examined the relationship between early enteral nutrition and the length of hospital stay in patients with acute pancreatitis, there are no studies examining the relationship between early enteral nutrition and the BISAP score or duration of hospitalization. As the BISAP score is calculated via clinical evaluation in the first 24 hours and its statistical relationship with mortality has been demonstrated in the literature, we aimed to reveal the relationship between early enteral nutrition support and the duration of hospitalization and its role in evaluating the course, severity, and prognosis of acute pancreatitis. In a meta-analysis by Pascal et al., 496 of 707 patients with acute pancreatitis received early enteral nutrition support within the first 24 hours, and patients who were administered early enteral nutrition had a significantly shorter duration of hospitalization than patients who were administered late enteral nutrition (18). In our study, in addition to the evaluation of the recommendations of the American Gastroenterology Association (AGA) (23), which associates the initiation of enteral nutrition support within the first 24 hours with fewer complications in patients with mild and moderate pancreatitis, the recommendations in the literature and the duration of enteral nutrition in patients diagnosed with acute pancreatitis were examined, and the concept of "early" enteral nutrition was established according to the average 72-hour limit. Ramanathan et al. reported that the initiation of early enteral nutrition support within the first 48–72 hours in patients diagnosed with acute pancreatitis had positive results in terms of hospitalization, complication rates, prognoses, mortality rates, and costs; however, larger randomized studies are needed (24). A meta-analysis by Capursa et al. examining the role of the intestinal barrier in acute pancreatitis demonstrated that fluid loss to the third space and ischemia–reperfusion injury in acute pancreatitis are the beginnings of conditions leading to serious systemic complications and that appropriate intravenous fluid resuscitation and early enteral nutrition support limit intestinal damage, leading to severe acute pancreatitis (13). In our study, a statistically significant correlation was found between early enteral nutrition support for ≤72 hours and duration of hospitalization for ≤9 days in patients with a BISAP score ≤2 who underwent the same intravenous fluid resuscitation protocol for mild to moderate acute edematous pancreatitis ($p<0.001$). Patients with acute pancreatitis with BISAP scores ≥3 experienced a 5–20% increase in mortality. Pancreatitis follows a severe course in these patients. The results of our study revealed that late enteral nutrition is administered in these patients due to the risk of possible complications.

Several studies have examined complications that may arise from enteral and parenteral nutrition in patients with acute pancreatitis. The development of sepsis and multiple organ dysfunction syndrome and the mortality rate of patients with acute pancreatitis are significantly lower in the enteral nutrition group than in the parenteral nutrition group (25). Kusanaga et al. demonstrated that switching to an enteral feeding regimen within 7 days in patients with acute pancreatitis was associated with a 56% reduction in in-hospital mortality rates (26). A meta-analysis evaluating the relationship between early and late enteral nutrition provision revealed that early enteral nutrition was associated with a significantly shorter duration of hospitalization, especially in patients with acute severe pancreatitis (27). In summary, our study revealed that early enteral nutrition support in patients with acute edematous pancreatitis did not cause any complications and significantly reduced the hospitalization period, especially in patients with mild to moderate acute pancreatitis (28).

Conclusions

Acute pancreatitis is a sudden-onset inflammatory disease with an overall mortality rate of 3–5%, depending on the severity of the disease (29). Generally, acute pancreatitis cases progress in a "mild" course during clinical follow-up and is self-limiting. We believe that the use of scoring methods that are easily applicable during clinical follow-up, have high prognostic value, and provide opportunities for early treatment is predictive in terms of follow-up and treatment, especially in patients with acute pancreatitis. In our study, mortality risk was increased in patients with a BISAP score ≥3, and enteral nutrition was administered after 72 hours in patients with this course. Our study had some limitations. In particular, the fact that the study was not conducted in multiple centers and the small number of patients limited the study and we believe that multicenter studies on similar topics are needed in the future.We believe that, especially in patients with acute pancreatitis for ≤ 72 hours, early enteral nutrition significantly reduces hospitalization time, costs, and complications.

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Conflicts of Interest: The authors declare that they have no competing financial interests or personal relationships that may have influenced the work reported in this study.

Ethics Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Afyonkarahisar Health Sciences University Clinical Research Ethics Committee Decisions of 02.05.2025 with meeting number 2025/6.

Consent Statement: Informed consent was obtained from all individual participants included in the study.

Written consent for publication: All authors have provided written consent for publication.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Code availability: Not applicable.

Author Contributions: M.A.: conceptualization, investigation, methodology, analysis, interpretation of data, writing-original draft preparation, and writing-review and editing; O.S.: contributed to the discussion, writing, review, and editing. A.S.: contributed to the discussion, writing, review, and editing. All the authors have read and agreed to the published version of the manuscript.

Data Availability Statement: Data is available upon reasonable request.

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