

# **PAKISTAN JOURNAL OF HEALTH SCIENCES**

https://thejas.com.pk/index.php/pjhs ISSN (P): 2790-9352, (E): 2790-9344 Volume 5, Issue 6 (June 2024)



#### **Original Article**

Length of Hospital Stay in Patients Related with Moderate Fluid Resuscitation and Aggressive Fluid Resuscitation in Acute Pancreatitis

Aafaq Ahmad<sup>1</sup>, Nowshad Khan<sup>2\*</sup>, Moeen-Ul- Haq<sup>3</sup>, Muhammad Siddique<sup>4</sup>, Muhammad Ayaz<sup>5</sup> and Fahad Shaheen<sup>4</sup>

ABSTRACT

<sup>1</sup>Department of Gastroenterology, Hayatabad Medical Complex, Peshawar, Pakistan

<sup>2</sup>Department of Medicine, Gomal Medical College, Dera Ismail Khan, Pakistan

<sup>3</sup>Department of Gastroenterology, Gomal Medical College, Dera Ismail Khan, Pakistan

<sup>4</sup>Department of Gastroenterology, Muhammad College of Medicine, Peshawar, Pakistan

<sup>5</sup>Department of Medicine, Muhammad College of Medicine, Peshawar, Pakistan

## ARTICLE INFO

#### Keywords:

Acute Pancreatitis, Fluid Resuscitation, Moderate Resuscitation, Aggressive Resuscitation, BISAP score, PAN-PROMISE score

#### How to Cite:

Ahmad, A., Khan, N., Haq, M. ul, Siddique, M., Ayaz, M., & Shaheen, F. (2024). Length of Hospital Stay in Patients Related with Moderate Fluid Resuscitation and Aggressive Fluid Resuscitation in Acute Pancreatitis: Hospital Stay Duration in Acute Pancreatitis. Pakistan Journal of Health Sciences, 5(06). https://doi.org/10.54393/pjhs.v5i06.1756

#### \*Corresponding Author:

Nowshad Khan

Department of Medicine, Gomal Medical College, Dera Ismail Khan, Pakistan knowshad70@yahoo.com

Received Date: 6<sup>th</sup> May, 2024 Acceptance Date: 26<sup>th</sup> June, 2024 Published Date: 30<sup>th</sup> June, 2024

# INTRODUCTION

The impulsive inflammation of the pancreas is known as acute pancreatitis. An organ situated beneath the stomach, the pancreas is essential to blood sugar management. Inflammation of the pancreas can result in symptoms such as excruciating stomach pain. Gallstones, one of the most frequent causes, can obstruct the pancreatic duct and cause inflammation. Pancreatitis can develop from long-term excessive alcohol consumption. Pancreatitis can be brought on by abdominal injuries, such as those sustained in falls or auto accidents [1]. The moderate fluid resuscitation strategy is to gradually restore fluid balance while avoiding the dangers of excessive resuscitation. usually entails giving out fluids at a rate of one to two liters every day. Continual fluid administration or smaller boluses (about 250–500 mL every 4-6 hours) may be used, contingent on the patient's state and therapeutic response. The aggressive fluid resuscitation method, which is frequently utilized in cases of shock or severe dehydration, is to quickly restore the volume of blood in circulation. usually entails giving fluids at a rate of more than two liters per day; depending on the severity of the condition, this can sometimes reach 4-6 liters or higher. Large boluses of fluid—typically 500–1000 mL spread over 30–60 minutes—are frequently

Due of the intricacy of their illness and the possibility of complications, patients with acute

pancreatitis may need to stay in the hospital longer or shorter, approach used. **Objective:** To compare the treatment of moderate fluid resuscitation with aggressive fluid resuscitation in

acute pancreatitis patients as well as duration of hospital stay. Methods: It was cross-sectional

study conducted in the Department of Medicine Muhammad Teaching Hospital Peshawar, with

duration of six months, from July 2023 to December 2023. A total number of participants was

(N=170) in this study. The age of patients was >16 years included both male and female. There

were two groups, first group was moderate fluid resuscitation and second group was aggressive

fluid resuscitation each group consists of patients n=85. Results: A total number of participants

was N=170 and age range was 16-60 years and mean age was 38.5±2.5 years. The frequency of

male and female patients was 105.8% and 94.1%. The results indicate that median hospital stay

length 4 to 8 days in the aggressive group and 3-5 days in the moderate-resuscitation group.

Conclusions: In response to treatment, and the emergence of complications were more

important to determine patient long stays in the hospital for pancreatitis, even though the

decision between aggressive and moderate fluid resuscitation may have a minor effect.

administered; these might be repeated as needed depending on the patient's response and continued losses [2]. Pancreatitis is an adverse effect of some drugs. Pancreatitis can result from blood triglyceride levels that are abnormally high. Pancreatitis can be brought on by bacterial or viral illnesses, such as the mumps or viral hepatitis. One of the main signs of acute pancreatitis is severe abdominal pain. Usually starting abruptly, the pain is felt in the upper abdomen and sometimes spreads to the back. Here is more information about acute pancreatitis and severe abdominal pain: many people describe the discomfort as gnawing and ongoing. It could be continuous or sporadic [3]. Some patients say it feels like they've been stabbed. Though it can also be felt on the left or right side, the pain typically starts in the middle of the belly, right below the sternum, or in the upper abdomen. It could spread between the shoulder blades and extend to the back. Eating or drinking, particularly during large or fatty meals, might make the pain worse. Patients can have increased pain [4]. Intravenous (IV) fluid replacement is a fundamental component of treatment for acute pancreatitis. Fluid loss may result from acute pancreatitis as a result of decreased oral intake and vomiting. IV fluids aid in the replacement of lost fluids and the maintenance of proper hydration, preventing dehydration a critical condition for the proper functioning and recuperation of all organs [5]. Hypotension, or low blood pressure, can result from dehydration and worsen tissue damage and organ perfusion. IV fluids assist in preserving normal blood pressure, which guarantees sufficient blood flow to essential organs [6]. Staying properly hydrated is essential for preserving kidney function, particularly in individuals suffering from acute pancreatitis, since kidney damage can arise as a consequence of the illness. IV fluids aid in maintaining renal perfusion and guard against acute kidney damage[7]. IV fluids are necessary in severe cases of acute pancreatitis, especially those that are compounded by fluid shifts and third-spacing. Hypovolemic shock is a potentially fatal situation in which there is insufficient blood volume to perfuse the tissues. Electrolyte abnormalities, such as hypokalemia or hypocalcaemia, can result from acute pancreatitis because of things like vomiting and fluid loss. Electrolyte-containing IV fluids can assist in reversing these imbalances and preserving appropriate electrolyte levels [8]. If a patient cannot take oral intake, dextrose solutions may be added to their IV fluids to avoid tissue breakdown and to provide them energy. This keeps the body's nutritional needs met while pancreatitis is in its acute stage. I/V fluid administration decisions are made by doctors based on a variety of parameters, including JVP, a useful tool for fluid status assessment. Fluid resuscitation can only be carried out safely and successfully with the help of comprehensive patient assessment, clinical judgment, sophisticated monitoring tools, and adherence to clinical guidelines [9]. Longer hospital stays are sometimes necessary for patients with moderate to severe pancreatitis, particularly if they experience consequences including pancreatic necrosis, contaminated pancreatic fluid collections, or organ failure. Depending on the severity of their ailment and well they respond to treatment, their hospital stay could last anywhere from a few weeks to several months or even longer. The length of hospital stay can be considerably increased in the event of difficulties [10]. The highlights the usefulness of the BISAP score in predicting severe acute pancreatitis and lays the groundwork for its validation across various centers. This work aims to explain how treatment affects creatinine, hematocrit, and urea levels by examining the effects of fluid resuscitation on biochemical markers and systemic inflammation. For example, patients who require surgery to address problems such as infected necrosis can require a longer hospital stay for recuperation and post-operative care. Patients may need nutritional support in certain situations, such as enteral or parenteral nutrition, which could lengthen their hospital stay until they are able to tolerate oral intake sufficiently. The duration of hospital stay is also affected by the underlying causes of pancreatitis. For example, if gallstones are the source of the pancreatitis, patients may need treatments like cholecystectomy (removal of the gallbladder) and have to stay longer in hospital [11]. The duration of hospital stay is mostly determined by how the patient responds to initial care and therapies. While patients with chronic symptoms or consequences may need a longer hospital stay for continued care, those who demonstrate improvement and stability of their condition may be home early [12].

The aim of this study was to compare the treatment of moderate fluid resuscitation with aggressive fluid resuscitation in acute pancreatitis patients as well as duration of hospital stay.

## METHODS

A cross-sectional study was conducted in the Department of Medicine Muhammad Teaching Hospital Peshawar. The duration of this study was 6 months, from July 2023 to December 2023. A total number of participants was (N=170) in this study. The age of patients was >16 years included both male and female. There were two groups, first group was moderate fluid resuscitation and second group was aggressive fluid resuscitation each group consists of patients n=85. The median hospital stay length was 5 days in the moderate fluid resuscitation group and 6 days in the aggressive resuscitation group. Inclusion criteria: diagnosed acute pancreatitis, organ failure, necrosis, hemodynamic instability. Exclusion criteria: heart failure, pregnant, breastfeeding, and pancreatic

cancer. Bedside Index for Severity in Acute Pancreatitis, or BISAP, is a straightforward clinical scoring system for determining the severity of acute pancreatitis. Higher scores denote greater severity. The score goes from 0 to 5. To measure the mental stress, SIRS,>60years, and pulmonary fluid buildup. Pancreatitis Outcome Model for Severity and Intrahospital Mortality is referred to as PAN-PROMISE. This is a more thorough scoring method to estimate the risk of mortality and severity in patients with acute pancreatitis. A combination of clinical and laboratory parameters, such as the following, determine the score: The levels of urea, creatinine, Hematocrit and SIRS. The ratio of participants in Group A to Group B, the expected effect size, and the standard deviation were taken into account, IRB was taken from the Ethical review committee (MTH/EC/76/2022). For comparing means between two independent groups, the sample size for each group can be calculated using the formula:  $n=(\Delta/\sigma Z\alpha/2+Z\beta)^2$ . Where:  $Z\alpha/2$  value for the significance level (e.g., 1.96 for a 5%) significance level with a two-tailed test).  $Z\beta$  value for the desired power (e.g., 0.84 for 80% power).  $\Delta$  is the effect size, the expected difference in means between the two groups.  $\sigma$  is the pooled standard deviation of the outcome measure. Medical records, standardized guestionnaires, and direct measurements were used in the data collection process. For normally distributed data, the means of Groups A and B were compared using the Mann-Whiteny Utest. Data were analyzed statically by SPSS. 26. P value <0.05 showed that the variables were very significant.

### RESULTS

A total number of patients N=170 with acute pancreatitis patients were evaluated in order to determine. Overall, N=170 patients were randomly assigned into two groups; first group was moderate fluid resuscitation n=85 and second group were aggressive fluid resuscitation n=85 patients. The demographic patient characteristics were split equally between the two experimental groups. The patient age range was 16-60 years and mean age was 38.5±2.5 years. The age range frequency of patient from 16-30 years was 32.3%. The frequency of age range from 31-45 years was 76.4%. The frequency of age range from 46-60 years was 58.8%. The frequency of male and female patients was 105.8% and 94.1%. After just 1st, 2nd and 3rd day in the hospital, some patients 41.1%, 68.2% and 24.7% were stay hospital with acute pancreatitis treatment. The patients of acute pancreatitis were conduct lab test such as Creatinine (80-83), Hematocrit (76-79) and Urea (70-74). Some patients were SIRs 17.6% which indicate severe illnesses including sepsis, septic shock, or multiple organ failure syndrome can develop from SIRs. A predictive tool for determining the severity of acute pancreatitis and forecasting patient outcomes is the Bedside Index for Severity in Acute Pancreatitis (BISAP) score was 40(43-47). The PAN-PROMISE score was used to estimate the probability of mortality in patients with acute pancreatitis was 15(18-21), see in table 1.

 Table 1: Demographic Characteristics of Study Participants (n=

 170)

Variables	IQR N (%)			
Tumor Grade				
16-30	55(32.3%)			
31-45	65(76.4%)			
46-60	50 (58.8%)			
Gender				
Male	90 (105.8%)			
Female	80 (94.1%)			
Medical Issue	e			
Acute Pancreatitis Disorder	170 (100%)			
Hospital Stay	s			
1 Day	70 (41.1%)			
2 Days	58(68.2%)			
3 Days	42(24.7%)			
Biochemical Varia	ables			
Creatinine mg/dL (IQR)	65(80-83)			
Hematocrit % (IQR)	61(76-79)			
Urea mg/dL (IQR)	68(70-74)			
SIRs	30(17.6%)			
Moderate Fluid Resuscitation	85(50%)			
Aggressive Fluid Resuscitation	85(50%)			
BISAP Score (IQR)	40 (43-47)			
PAN-PROMISE Score (IQR)	15 (18-21)			

According to our results to found that, there was no significant difference in the development of moderate and severe pancreatitis, which consists of 32 %, 41.1% and 41.1%, 49.9% in moderate and aggressive fluid resuscitation group, odd ratio relative risk [95% CI, 2.10 (0.67-4.15)] and [95% CI, 1.10 (0.33-2.12)]. The necrotizing pancreatitis was observed 3.5% of patients in the moderate-resuscitation group and 16.4% in the regressive fluid group The proportion of patients with renal failure was 2.3% and 22.3%, respectively, an odd ratio [95% CI, 1.43(0.14-3.33)]. The respiratory failure, kidney failure, invasive treatment was shown in table 2.

**Table 2:** Primary and Secondary Outcomes of Study Participants(n=85)

Variables	Moderate Fluid Resuscitation N (%)	Aggressive Fluid Resuscitation N (%)	Odd Ratio 95% Cl N (%)	
Moderate Pancreatitis	27(32%)	35(41.1%)	2.10 (0.67-4.15)	
Sever Pancreatitis	35(41.1%)	42(49.4%)	1.10 (0.33-2.12)	
Local Complications				
Necrotizing Pancreatitis	3(3.5%)	14 (16.4%)	1.43 (0.14-3.33)	
SIRS				
12 Hours	24(28.2%)	49(57.6%)	3.17 (1.2-4.65)	
24 Hours	10 (11.7%)	31(36.4%)	1.20 (1.99-3.11)	
48 Hours	6(7%)	12 (14.1%)	0.66 (0.12-1.95)	
72 Hours	2(2.3%)	21(24.7%)	2.76 (0.57-2.95)	
Other Outcomes				
Invasive Treatment	6(7%)	22(25.5%)	2.50 (0.85-4.14)	
Nutritional Support	5(5.8%)	18 (21.1%)	1.05 (0.15-3.60)	

ICU Admission	2(2.3%)	17(20%)	1.17 (0.27-4.14)
Respiratory Failure	3(3.5%)	16(18.8%)	1.70 (0.77-3.15)
Kidney Failure	2(2.3%)	19 (22.3%)	1.60 (2.15-6.10)

Our analysis revealed that the median hospital stay for the aggressive-resuscitation group was 6 days (interquartile range: 4 to 8) and the median hospital stay for the moderate-resuscitation group was 5 days (interquartile range: 3 to 7). The relative risk [95% CI 1.25 (0.55-2.85)] for the moderate fluid resuscitation group was 8 points (IQR, 6-10) and for the aggressive resuscitation group it was 21 points (IQR, 19-23) at 12 hours, according to the full case analysis. Higher scores indicated greater symptom intensity. The relative risk [95% CI 0.25 (0.25-2.45)] after 48 hours was 3 points (IQR, 1-5) in the moderate fluid resuscitation group, indicating more significantly reduced symptoms, as shown in table 3.

**Table 3:** Duration of Hospital Stay and Efficacy Outcomes of StudyParticipants

Variables	Moderate Fluid Resuscitation N (%)	Aggressive Fluid Resuscitation N (%)	Odd Ratio 95% Cl N (%)	P- Value	
Duration of Hospital Days (IQR)	5(3-7)	6(4-8)	2.55 (2.5-5.5)	0.001	
Number of Days in ICU (IQR)	0%	0%	-	-	
	PAN-Promise Score (IQR)				
12 Hours	8 (6-10)	21(19-23)	1.25(0.55-2.85)	0.001	
24 Hours	5(3-7)	27(24-30)	2.35 (1.35-5.15)	0.001	
48 Hours	3 (1-5)	22(20-24)	0.25(0.25-2.45)	0.001	
72 Hours	1(2-4)	19 (17-21)	1.15 (2.04-6.76)	0.000	
	Biochemical Variables				
C-Reactive Protein mg/mL (IQR)	1.5 (2.9-5.4)	6.46 (9.3-12.5)	4.11(2.11-5.76)	0.111	
48 Hours	7.5 (3.2-3.6)	15.2 (13.5-16.5)	3.10 (1.22-6.65)	0.121	
72 Hours	8.5(4.1-4.4)	18.5 (15.4-18.4)	1.22 (3.35-7.75)	0.008	

Mann-Whiteny U-test

Compared to moderate fluid resuscitation, which had an adjusted relative risk of 14.1%, aggressive fluid resuscitation (32.5%) was linked to a significantly greater incidence of fluid overload [95% Cl, 5.2(3.02-6.15)]. The management of volume overload was carried out in the following ways: diuretics were used in 90% of cases, inotropes were used in 9% of cases, and decreased hydration was used in none of the cases in the aggressiveresuscitation group. No patient in the aggressiveresuscitation group required hemofiltration, although one patient had an orotracheal intubation. The median time of fluid overload was 28 hours in the aggressive resuscitation and 35 hours in the moderate resuscitation. Fluid resuscitation was associated with symptoms of fluid overload included dyspnea 14.1% in the moderate resuscitation group then aggressive resuscitation group 25.5% relative risk adjust [95% CI, (1.75(3.5-7.8)]. The sign of fluid overload also included peripheral edema 35.2% and pulmonary edema 29.4% in the aggressive resuscitation group in the patients respectively, adjust relative risk, [95%Cl, 4.15(0.5-3.44), and 3.33(2.5-4.8)]. The study ended because the aggressive resuscitation group's safety outcomes were noticeably worse than those of the moderate resuscitation group, and there was no indication of a trend toward better outcomes. The data and safety monitoring board examined these results(Table 4).

Table 4: Safety	y Outcomes of Study	v Participants
	, outoonnooon otuu	y i ai cioipanico

Variables	Moderate Fluid Resuscitation N (%)	Aggressive Fluid Resuscitation N (%)	Odd Ratio 95% Cl N (%)
Fluid Overload	12 (14.1%)	28(32.5%)	5.2(3.02-6.15)
Moderate Fluid Overload	11(12.9%)	24(28.2%)	1.05 (0.15-2.15)
Sever Fluid Overload	2(2.3%)	25(29.4%)	3.6 (1-9-4.7)
Symptoms of Fluid Overload	-	-	-
Dyspnea	12 (14.1%)	22(25.5%)	1.75 (3.5-7.8)
Peripheral Edema	11(12.9%)	30(35.2%)	4.15(0.5-3.44)
Pulmonary Edema	10 (11.7%)	25(29.4%)	3.33 (2.5-4.8)
Imaginary Testing	-	-	-
Hemodynamic Testing	8(9.4%)	26(30.5%)	2.25 (1.50-4.75)
Heart Failure ECO Cardiogram	3(3.5%)	27(31.7%)	4.6(2.43-6.23)
Pulmonary Congestion by Radiographic Evidence	10 (11.7%)	30(35.2%)	1.55 (0.11-3.23)

Mann-Whiteny U-test

# DISCUSSION

Indeed, aggressive fluid resuscitation during acute pancreatitis might raise the risk of volume overload, which can result in consequences such abdominal compartment syndrome, pulmonary edema, and congestive heart failure [13]. Aggressive fluid resuscitation in pancreatitis attempts to preserve tissue perfusion and avoid squeal such as organ failure. Volume overload can occur, nevertheless, if an excessive amount of fluid is given to the body too soon, beyond its capacity to handle it. In order to prevent volume overload, healthcare professionals must closely monitor patients undergoing vigorous fluid resuscitation and make sure that fluid delivery is balanced and altered as necessary. In order to effectively manage fluid balance, this may entail closely monitoring fluid intake and output, evaluating clinical symptoms of fluid overload such as edema and shortness of breath, and, if necessary, adopting further measures like diuretics or renal replacement therapy. In the previous literature, the effectiveness of aggressive fluid resuscitation in pancreatitis attempts to preserve tissue perfusion [14]. There are a number of considerations when comparing aggressive versus moderate fluid resuscitation for pancreatitis, including the dangers involved and how well it improves outcomes. The moderate fluid resuscitation technique is to provide the patient enough fluids at a pace that keeps their tissue perfusion at a sufficient level without overloading them. Using a higher rate of fluid administration to guarantee good tissue perfusion and

avoid consequences like organ failure is known as the aggressive fluid resuscitation technique [15]. The degree of aggressiveness of the method and specific patient characteristics determine the risk of complications from fluid resuscitation in pancreatitis. Severe fluid resuscitation can upset the balance of electrolytes, resulting in consequences including hyponatremia (low sodium), hypernatremia (high sodium), hypokalemia (low potassium), or hyperkalemia (high potassium), which can impair heart and brain function [16]. Fluid resuscitation, especially in patients with acute pancreatitis or underlying coagulopathy, can dilute platelets and clotting factors, increasing the risk of bleeding problems or Disseminated Intravascular Coagulation (DIC). Over distribution of fluids can lead to metabolic acidosis, a disorder marked by an imbalance in the body's acid-base state that can deteriorate organ performance and patient outcomes. In the past study, the different fluid resuscitation disturbed physiological function [17]. The moderate fluid resuscitation less dangerous than aggressive fluid resuscitation. The moderate fluid resuscitation is to give the patient enough fluids at a pace that keeps their tissue perfusion intact without going overboard. Compared to intensive fluid resuscitation, moderate fluid delivery reduces the risk of abrupt changes in electrolyte balance. Aggressive fluid resuscitation often has a higher risk of gastrointestinal problems, even though moderate fluid resuscitation may still cause some fluid accumulation in the stomach. We were agreed from the previous study [18]. While aggressive resuscitation increases the risk of acute kidney injury, moderate fluid resuscitation still carries some risk, particularly for patients with pre-existing kidney problems. The severity of pancreatitis, the patient's reaction to treatment, the existence of comorbidities, and the fluid resuscitation method used are some of the variables that can affect how long a patient stayed in the hospital [19]. Let us examine the possible effects of aggressive versus moderate fluid resuscitation on the duration of hospital stay in patients with pancreatitis: Compared to patients undergoing intensive fluid resuscitation, patients receiving moderate fluid resuscitation may need to stay in the hospital for a little while longer. We used the concept of past experience (CBL workshop) also referred to as patient receive moderate fluide which was better results [20]. The moderate fluid resuscitation is to give the patient enough fluids at a rate that keeps their tissue perfusion intact without going over their fluid threshold. Although this method of treating pancreatitis might work, if complications arise or if the patient's condition does not improve as quickly, it could result in a lengthier hospital stay. Individuals undergoes vigorous fluid resuscitation might spend a little less time in the hospital than those having moderate resuscitation. The aggressive fluid resuscitation is to deliver fluids more quickly in order to maintain ideal tissue perfusion and avoid consequences like organ failure. This strategy can, in certain circumstances; result in shorter hospital stays since it efficiently manages the acute pancreatitis and decrease the risk of complications [21]. Regardless of the fluid resuscitation technique used, patients with severe pancreatitis may need to stay in the hospital longer because of the complexity of their illness and the possibility of consequences. The moderate fluid resuscitation patients were shown shorter duration of hospital as compared to aggressive fluid resuscitation. In the past study, inflammation or infected patients was stay longer [22]. The fluid resuscitation strategy, the emergence of complications such organ failure, infection, or gastrointestinal bleeding can extend hospital stays. The duration of hospital stayed and treatment response in cases of pancreatitis might be influenced by a patient's age, comorbidities, nutritional state, and other unique factors [23]. The length of hospital stay can also be influenced by individual patient characteristics, including age, comorbidities, nutritional state, and social support. Longer hospital stays may be necessary for patients with numerous comorbidities or little social support in order to receive complete care and discharge preparation. This study shows similar results previous studies [24, 25].

# CONCLUSIONS

Factors like the severity of the illness, response to treatment, and the emergence of complications are more important in determining how long a patient stayed in the hospital for pancreatitis, even though the decision between aggressive and moderate fluid resuscitation may have a minor effect.

## Authors Contribution

Conceptualization: AA Methodology: NK, MS, MA, FS Formal analysis: NK Writing, review and editing: NK, MUH, MA, FS

All authors have read and agreed to the published version of the manuscript.

### Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

### REFERENCES

- [1] Szatmary P, Grammatikopoulos T, Cai W, Huang W, Mukherjee R, Halloran C et al. Acute pancreatitis: diagnosis and treatment. Drugs. 2022 Aug; 82(12): 1251-76. doi: 10.1007/s40265-022-01766-4.
- [2] de-Madaria E, Buxbaum JL, Maisonneuve P, García García de Paredes A, Zapater P, Guilabert L et al.

Aggressive or moderate fluid resuscitation in acute pancreatitis. New England Journal of Medicine. 2022 Sep;387(11): 989-1000. doi: 10.1056/NEJMoa220288 4.

- [3] Mederos MA, Reber HA, Girgis MD. Acute pancreatitis: a review. Journal of the American Medical Association. 2021 Jan; 325(4): 382-90. doi: 10.1001/ja ma.2020.20317.
- [4] Walkowska J, Zielinska N, Karauda P, Tubbs RS, Kurtys K, Olewnik Ł. The pancreas and known factors of acute pancreatitis. Journal of Clinical Medicine. 2022 Sep; 11(19): 5565. doi: 10.3390/jcm11195565.
- [5] Ćeranić DB, Zorman M, Skok P. Interleukins and inflammatory markers are useful in predicting the severity of acute pancreatitis. Bosnian Journal of Basic Medical Sciences. 2020 Feb; 20(1): 99. doi: 10.17305/bjbms.2019.4253.
- [6] Yaowmaneerat T and Sirinawasatien A. Update on the strategy for intravenous fluid treatment in acute pancreatitis. World Journal of Gastrointestinal Pharmacology and Therapeutics. 2023 May; 14(3): 22. doi: 10.4292/wjgpt.v14.i3.22.
- [7] Crosignani A, Spina S, Marrazzo F, Cimbanassi S, Malbrain ML, Van Regenmortel N *et al.* Intravenous fluid therapy in patients with severe acute pancreatitis admitted to the intensive care unit: a narrative review. Annals of Intensive care. 2022 Oct; 12(1): 98. doi: 10.1186/s13613-022-01072-y.
- [8] Giakoumakis MI, Gkionis IG, Marinis AI, Flamourakis ME, Spiridakis KG, Tsagkataki ES et al. Management of Acute Pancreatitis: Conservative Treatment and Step-Up Invasive Approaches-Evidence-Based Guidance for Clinicians. GastroHep. 2022; 2022(1): 2527696. doi: 10.1155/2022/2527696.
- [9] Ding X, Chen B. Effect of Aggressive Intravenous Fluid Resuscitation Versus Nonaggressive Fluid Resuscitation in the Treatment of Acute Pancreatitis: A Systematic Review and Meta-Analysis. Pancreas. 2023 Feb 1;52(2):e89-100.
- [10] Kayhan S, Akyol BS, Ergul M, Baysan C. The effect of type of fluid on disease severity in acute pancreatitis treatment. European Review for Medical & Pharmacological Sciences. 2021 Dec 1;25(23).
- [11] Jaber S, Garnier M, Asehnoune K, Bounes F, Buscail L, Chevaux JB et al. Guidelines for the management of patients with severe acute pancreatitis, 2021. Anaesthesia Critical Care & Pain Medicine. 2022 Jun; 41(3): 101060. doi: 10.1016/j.accpm.2022.101060.
- [12] Di Martino M, Van Laarhoven S, Ielpo B, Ramia JM, Manuel-Vázquez A, Martínez-Pérez A, Pavel M, Miranda PB, Orti-Rodríguez R, de la Serna S, Rabbione GJ. Systematic review and meta-analysis of fluid therapy protocols in acute pancreatitis: type, rate

and route. Hpb. 2021 Nov 1;23(11):1629-38.

- [13] Crosignani A, Spina S, Marrazzo F, Cimbanassi S, Malbrain ML, Van Regenmortel N, Fumagalli R, Langer T. Intravenous fluid therapy in patients with severe acute pancreatitis admitted to the intensive care unit: a narrative review. Annals of Intensive care. 2022 Oct 17;12(1):98.
- [14] Lee PJ and Papachristou GI. Management of severe acute pancreatitis. Current Treatment Options in Gastroenterology. 2020 Dec; 18: 670-81. doi: 10.1007/s11938-020-00322-x.
- [15] Bolado F, Buxbaum JL, Vaillo-Rocamora A, Cárdenas-Jaén K, Maisonneuve P, De-Madaria E. Early weightbased aggressive vs. non-aggressive goal-directed fluid resuscitation in the early phase of acute pancreatitis: An open-label multicenter randomized controlled trial (The WATERFALL trial), design, and rationale. Frontiers in Medicine. 2020 Sep; 7: 440. doi:10.3389/fmed.2020.00440.
- [16] Choosakul S, Harinwan K, Chirapongsathorn S, Opuchar K, Sanpajit T, Piyanirun W et al. Comparison of normal saline versus Lactated Ringer's solution for fluid resuscitation in patients with mild acute pancreatitis, A randomized controlled trial. Pancreatology. 2018 Jul; 18(5): 507-12. doi: 10.1016/j.pan.2018.04.016.
- [17] Adrogué HJ, Tucker BM, Madias NE. Diagnosis and management of hyponatremia: a review. Journal of the American Medical Association. 2022 Jul; 328(3): 280-91. doi: 10.1001/jama.2022.11176.
- [18] Hogge J, Christensen E. For adult patients hospitalized with acute pancreatitis, does treatment with moderate intravenous fluids improve outcomes compared with treatment with aggressive intravenous fluids?. Evidence-Based Practice. 2024 Jul 1;27(7):23-5.
- [19] Gad MM and Simons-Linares CR. Is aggressive intravenous fluid resuscitation beneficial in acute pancreatitis? A meta-analysis of randomized control trials and cohort studies. World Journal of Gastroenterology. 2020 Mar; 26(10): 1098. doi: 10.3748/wjg.v26.i10.1098.
- [20] Martin GS and Bassett P. Crystalloids vs. colloids for fluid resuscitation in the Intensive Care Unit: A systematic review and meta-analysis. Journal of Critical Care. 2019 Apr; 50: 144-54. doi: 10.1016/j.jcrc. 2018.11.031.
- [21] Malbrain ML, Van Regenmortel N, Saugel B, De Tavernier B, Van Gaal PJ, Joannes-Boyau O et al. Principles of fluid management and stewardship in septic shock: it is time to consider the four D's and the four phases of fluid therapy. Annals of Intensive Care. 2018 Dec; 8: 1-6. doi: 10.1186/s13613-018-0402-x.

- [22] Ismail MT and Elbaih AH. Principles of intravenous fluids therapy. Emergency Medicine and Critical Care. 2020 May; 4(6): 24-46.
- [23] Marik PE, Byrne L, Van Haren F. Fluid resuscitation in sepsis: the great 30 mL per kg hoax. Journal of Thoracic Disease. 2020 Feb; 12(1): S37. doi: 10.21037/ jtd.2019.12.84.
- [24] Smart L and Hughes D. The effects of resuscitative fluid therapy on the endothelial surface layer. Frontiers in Veterinary Science. 2021 May; 8: 661660. doi: 10.3389/fvets.2021.661660.
- [25] Dawson A, Karunakaran M, Sharma ZD, Ullah S, Barreto SG. Fluid resuscitation in the early management of acute pancreatitis-evidence from a systematic review and meta-analysis. HPB. 2023 Aug 29.