

Clinical outcomes between aggressive versus moderate fluid resuscitation in the management of acute pancreatitis: a quasi-experimental study

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ABSTRACT

Introduction: Early intravenous fluid resuscitation is essential in acute pancreatitis (AP), but the optimal volume strategy remains uncertain. Aggressive hydration raises concerns about iatrogenic damage from excessive fluid intake.

Objectives: To compare the clinical outcomes of moderate versus aggressive fluids resuscitations in the management of acute pancreatitis.

Materials and Methods: A quasi-experimental, alternate-allocation comparison study was conducted between October 2023 to March 2025. About 260 adults with first-episode AP were enrolled and alternately assigned to aggressive (20 mL/kg bolus followed by 3 mL/kg/h) or moderate (10 mL/kg bolus if hypovolemic, followed by 1.5 mL/kg/h) lactated Ringer's (LR) protocols. The primary endpoints comprised hospital length of stay (LOS) and incidence of persistent organ failure. Secondary outcomes included ICU admissions, treatments, SIRS (Systemic Inflammatory Response Syndrome) at 24 and 48 hours, changes in hematocrit and blood urea nitrogen (BUN), pancreatic necrosis, and in-hospital mortality.

Results: Baseline characteristics were balanced across 260 patients. About 8.5% patients on aggressive LR and 6.2% on moderate LR experienced persistent organ failure ($p=0.43$). Median hospital LOS for aggressive LR was 6 days (IQR 4–8) and for moderate LR was 5 days (IQR 3–7) ($p=0.05$). ICU admission (15.4% vs 9.2%; $p=0.08$), any organ failure (8.5% vs 6.2%; $p=0.43$), invasive interventions (10.0% vs 7.7%; $p=0.49$), and mortality (2.3% vs 1.5%; $p=0.67$) were comparable. Despite no improvement in clinical outcomes, aggressive LR yielded greater 24-hour reductions in hematocrit and BUN ($p<0.05$).

Conclusions: Larger volumes of LR did not improve outcomes in this cohort. Adoption of customized, moderate-volume techniques with regular reassessment in early AP is supported by these data.

Keywords: Acute Pancreatitis; Fluid Therapy; Multiple Organ Failure; Ringer's Lactate.

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AK: Conceptualization, protocol design, manuscript drafting, manuscript writing, corresponding author.

RU: Study logistics coordination, data analysis, critical revision.

FW: Patient recruitment, data collection, manuscript drafting, critical review.

IU: Data analysis and data interpretation, manuscript drafting, response to reviewer.

IA: Data validation, clinical oversight, manuscript writing, critical review.

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INTRODUCTION

The incidence of acute pancreatitis (AP) is increasing by around 3% per year globally, making it a major cause of unscheduled gastrointestinal hospitalizations.^{1,2} The majority of deaths, intensive care unit admissions, and medical expenses are caused by necrosis or chronic organ failure, which occurs in 15–20% of patients even if the majority have a benign course.^{3,4} The updated Atlanta classification made it easier to compare research and guidelines by standardizing definitions of severity and problems.⁵ In actuality, prompt assessment of severity, supportive care, and avoiding iatrogenic injury have a significant impact on results.⁶

Fluid resuscitation becomes a first-hour priority when third-space losses and capillary leak cause early hypovolemia. To avoid hypoperfusion, vigorous hydration was advised by traditional guidelines.⁷ On the other hand, high quantities might cause consequences such as abdominal compartment syndrome and pulmonary edema. While meta-analyses indicate that moderate, goal-directed techniques with lactated Ringer's solution may be safer and as effective, recent trials, such as the 'Waterfall' research, have demonstrated that aggressive regimens increase fluid overload without improving organ failure or death.^{8–10}

There is still a dearth of evidence-based data directing fluid management in AP in South Asia, and Pakistan specifically. High caseloads, gallstone-related etiology, and resource limitations that prevent rigorous surveillance pose challenges to local practice.¹¹ In the present study aggressive versus moderate resuscitation procedures in first-episode AP were compared using a prospective cohort at two tertiary referral sites in Peshawar to close this gap. The goal was to find out if, in this situation, a moderate fluid approach reduces fluid-related problems while producing similar clinical results.

MATERIALS AND METHODS

This prospective quasi-experimental, alternate-allocation comparative study was conducted at the Department of Gastroenterology, Medical Teaching Institute-Hayatabad Medical Complex (MTI-HMC), Peshawar Pakistan from October 2023 to March 2025. The protocol was approved by the Ethical Review Board of the Hayatabad Medical Complex (Doc No: HMC-QAD-F Approval No: 1423 dated 10.7.2023). Written informed consent was obtained from all the study participants. The sample size was estimated using the WHO technique for comparing two proportions and a sample of 236 was required to detect a 10% absolute difference with 80% power at a two-sided α of 0.05, given robust resuscitation and a 15% risk of irreversible organ failure.⁴ To compensate for missing data, sequential sampling was used to recruit 260 patients in total (130 in each group). Consecutive adults (≥ 18 years) with a first episode of acute pancreatitis were screened. Serum lipase or amylase levels greater than three times the upper limit of normal, characteristic imaging abnormalities, or typical abdominal pain were necessary for diagnosis, according to the Revised Atlanta Classification. Patients with pre-existing end-stage renal or cardiac failure, chronic pancreatitis, pregnancy, or organ failure at admission were excluded to isolate the effects of early resuscitation.

Revised Atlanta criteria were used to classify the severity of persistent organ failure as mild, moderately severe, or severe. The modified Marshall score for cardiovascular, renal, or pulmonary dysfunction was used to identify persistent organ failure. Additionally, Bedside Index of Severity in Acute Pancreatitis (BISAP) scores and Systemic Inflammatory Response Syndrome (SIRS) criteria were calculated.

Patients were alternately allocated upon admission to one of the two lactated Ringer's regimens: an aggressive protocol with 20 mL/kg bolus (maximum 2 L) followed by 3 mL/kg/h for 24 hours or moderate protocol with 10 mL/kg bolus only if clinical hypovolemia was present, followed by 1.5 mL/kg/h for 24 hours. After the first 24 hours, fluids were titrated to maintain urine output ≥ 0.5 mL/kg/h and mean arterial pressure ≥ 65 mmHg. The study teams were aware of allocation and the nurses recorded the volume of fluids administered. All care, including analgesia and nutrition, were provided according to institutional standards. Baseline data included age, sex, body mass index, etiology, comorbidities, vital signs, hematocrit, and blood urea nitrogen (BUN).

The primary outcomes were the length of hospital stay and the occurrence of chronic organ failure. Secondary outcomes included ICU admission, the requirement for percutaneous or endoscopic procedures, the presence of ≥ 2 SIRS criteria at 24 and 48 hours, CT-proven pancreatic necrosis, in-hospital mortality, and 24-hour changes in hematocrit and BUN. Patients were observed after being admitted to the hospital until they were discharged.

Continuous variables, expressed as mean \pm standard deviation or median with interquartile range, were compared using the Mann-Whitney U test or the student's t-test. Chi-square or Fisher's exact tests were used to compare categorical variables, which were expressed as counts and percentages. Multivariable logistic regression was used to assess the independent influence of hydration strategy after controlling for age, etiology, BISAP score, body mass index, comorbidities, baseline hematocrit, and BUN. For all two-sided analyses, p -values < 0.05 were considered statistically significant. Since secondary outcomes were considered exploratory, multiple comparisons were not officially adjusted for them.

RESULTS

Adult Patients ($n=260$) with a first episode of acute pancreatitis were alternately assigned to aggressive ($n=130$) or moderate ($n=130$) LR fluid-resuscitation protocols. The initial demographic and clinical attributes were similar between groups (Table 1). The mean age of the study participants was 46 ± 12 years, 53% were male, and gallstones accounted for acute pancreatitis in 61% of cases. Seventeen to nineteen percent of patients had admission BISAP scores of three or above, and the mean baseline hematocrit and blood urea nitrogen (BUN) levels were similar in all groups.

Table 1: Baseline demographic and clinical characteristics of study participants

Variables	Aggressive (n=130)	Moderate (n=130)	p-value*
Age (years, mean \pm SD)	45.2 \pm 12.3	46.7 \pm 11.8	0.52
Male gender n (%)	70 (53.8%)	68 (52.3%)	0.75
Etiology/Risk Factors for AP n (%)			
Gallstones	78 (60.0%)	81 (62.3%)	0.70
Alcohol	15 (11.5%)	17 (13.1%)	0.78
Hypertriglyceridemia	13 (10.0%)	11 (8.5%)	0.68
Idiopathic/Other	24 (18.5%)	21 (16.1%)	0.63
Body mass index (kg/m ² , mean \pm SD)	27.4 \pm 4.8	26.9 \pm 5.2	0.45
BISAP score \geq 3 n (%)	22 (16.9%)	24 (18.5%)	0.74
Admission hematocrit (% mean \pm SD)	44.1 \pm 5.0	43.8 \pm 5.3	0.66
Admission BUN (mg/dL, mean \pm SD)	19.8 \pm 6.2	19.2 \pm 6.5	0.48

*p-value <0.05 was considered statistically significant

Table 2: Primary, secondary outcomes and laboratory markers at 24 hours between patients on aggressive and moderate LR protocol

Outcomes	Variables	Aggressive (n=130)	Moderate (n=130)	p-value*
Primary	Hospital LOS – days (IQR)	6 (4–8)	5 (3–7)	0.05*
Secondary	ICU admission – n (%)	20 (15.4%)	12 (9.2%)	0.08
	Any organ failure – n (%)	11 (8.5%)	8 (6.2%)	0.43
	Persistent organ failure – n (%)	7 (5.4%)	5 (3.8%)	0.56
	Pancreatic necrosis on CT – n (%)	17 (13.1%)	13 (10.0%)	0.44
	Invasive interventions (drainage/surgery) – n (%)	13 (10.0%)	10 (7.7%)	0.49
	SIRS \geq 2 at 24 h – n (%)	39 (30.0%)	30 (23.1%)	0.18
	SIRS \geq 2 at 48 h – n (%)	16 (12.3%)	10 (7.7%)	0.21
	In-hospital mortality – n (%)	3 (2.3%)	2 (1.5%)	0.67
Laboratory Markers	Hematocrit change (% from baseline, mean \pm SD)	-6.1 \pm 2.9	-1.7 \pm 2.4	<0.01*
	BUN change (mg/dL, mean \pm SD)	-8.2 \pm 4.1	-3.8 \pm 3.6	0.02*

*p-value <0.05 was considered statistically significant; LR-Lactated Ringer

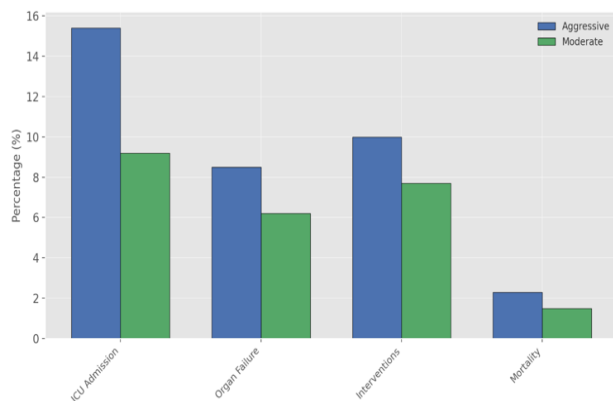
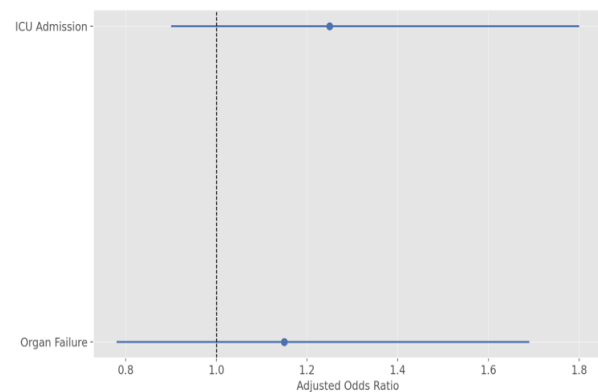
**Figure 1:** Frequency of key clinical outcomes between aggressive and moderate fluid protocols

Table 2 differentiate between the patients on aggressive LR with moderate LR protocols with regards to primary and secondary outcome and laboratory markers specifically change in hematocrit and blood urea nitrogen (BUN) after 24 hours of admission.

Figure 1 shows the differences in key clinical events between the two fluid regimens. It shows percentage differences in the number of ICU admissions, organ failures, interventions and mortality.

**Figure 2:** Adjusted odds ratios for key clinical outcomes

Multivariate logistic regression adjusting for age, AP etiology, and admission BISAP score, body mass index, comorbidities, and baseline laboratory values, fluid strategy was not independently associated with persistent organ failure (adjusted OR 1.15, 95% CI 0.78–1.69) or ICU admission (adjusted OR 1.25, 95% CI 0.90–1.80). These adjusted effect estimates are depicted in Figure 2.

Subgroup analyses showed no interaction between fluid strategy and etiology (gallstone vs. hypertriglyceridemic vs. alcohol-related AP), nor between fluid strategy and admission severity

(BISAP ≥ 3 vs. < 3). Outcomes within these subgroups remained consistent with the overall cohort, with no significant differences in persistent organ failure, ICU admission, or mortality.

DISCUSSION

In this study, moderate lactated Ringer's resuscitation produced outcomes comparable to aggressive regimens in terms of hospital stay, persistent organ failure, and mortality, while reducing markers of hemodilution such as hematocrit and BUN decline. These results bolster the increasing agreement that fluid therapy in acute pancreatitis need to be goal-oriented and often reevaluated, rather than administered via rigid aggressive guidelines.

The mean age of patients in this study was 46 years, with men comprising a slightly higher proportion (53%) than women. This is very similar to statistics from Pakistan, where AP affects individuals usually in the fourth or fifth decades, and gallstones are the most common cause (~60%).¹¹ In contrast, European research show that alcohol and idiopathic reasons are more common.² Admission BISAP > 3 was noted in 17–19% of patients, slightly lower than Western cohorts (25–30%),^{1,3} indicating an earlier presentation or a milder phenotype.

The median length of stay was 6 days for aggressive resuscitation and 5 days for moderate resuscitation, which is well within the 5–7day range that has been described in international studies.^{8,9} ICU hospitalization occurred in 15.4% (Aggressive protocol) versus 9.2% (Moderate protocol), which is in line with the 10–20% observed worldwide.^{13–15} Persistent organ failure occurred in 5.4% compared to 3.8%, which is lower than the formerly reported rate of 15–20%⁴ but aligns with more recent Asian data,¹⁶ suggesting that early detection and supportive care may have mitigated the rates. The mortality rates in both groups (2.3% vs. 1.5%) fell within the anticipated 1–5% range for first-episode acute pancreatitis,^{3,5} indicating that moderate resuscitation does not correlate with increased risk.

The rates of pancreatic necrosis (10–13%) were more or less similar to the global mean (10–20%). Invasive operations were necessary in 10% compared to 7.7%, indicating a cautious, incremental strategy aligned with contemporary standards.¹³ At 24 and 48 hours, systemic inflammatory response (SIRS ≥ 2) was more likely in actively treated individuals, although the differences were not statistically significant. Hematocrit decreased more significantly with aggressive therapy (–6.1% vs. –1.7%), reflecting the hemodilution signal noted in the Waterfall trial,⁸ and the decline in BUN was also more pronounced, aligning with previous analyses that indicate excessive volume expansion modifies renal indices without enhancing clinical outcomes.^{9,15}

The results of this study are very similar to those of the Waterfall trial, which found that intensive hydration did not lower the risk of organ failure or death but did raise the risk of fluid overload.⁸ Evidence from meta-analyses suggests that maintaining moderate hydration decreases the risk of fluid-related issues without delaying recovery.^{9,15,16} Expert advice and updated evaluations place more emphasis on goal-directed hydration with regular reassessment than on set quantities.^{17–20} Even though early single-

center research in mild AP indicated that forceful fluids could reduce symptoms more quickly.¹³ Buxbaum et al. previously indicated that vigorous hydration may expedite symptom recovery in mild acute pancreatitis; however, this advantage has not been demonstrated in more diverse or severe groups. Historical reviews that previously endorsed intensive hydration⁷ have since been superseded by international consensus. According to the 2019 WSES guidelines, individualized goals should be prioritized over uniform strategies, and current expert consensus advises regular reassessment instead of following strict protocols.^{12,21} Moderate-volume, practical techniques are supported by regional multicenter experiences.^{20,21}

In keeping with the results of the WATERFALL trial and current international guidelines, this study advocates for a pragmatic, goal-oriented approach to fluid management in acute pancreatitis. If there is clinical hypovolemia, the first line of resuscitation should be lactated Ringer's 10–15 mL/kg, followed by maintenance at 1–2 mL/kg/h. Every six to twelve hours, fluid status should be reevaluated utilizing trends in blood urea nitrogen, mean arterial pressure, urine output, and hematocrit. While symptoms of overload (pulmonary crackles, high venous pressure) should prompt rate decrease or the use of diuretics, further boluses may be administered if the hematocrit is $\geq 44\%$ or if the BUN increases. When possible, volume evaluation can be aided by bioimpedance monitoring or bedside ultrasound. This mild, perfusion-guided technique reduces the risk of fluid overload without sacrificing outcomes, reflecting the current consensus that personalized resuscitation is better than rigid, aggressive regimens.^{8,12,17,21} Moderate resuscitation is both safe and feasible in this context, as it does not lead to unnecessary complications. The quasi-experimental allocation approach employed in this study is more prone to bias than randomization. Another limitation is the restriction of follow-up to in-hospital outcomes. Larger, multicenter, randomized studies in low- and middle-income countries (LMIC) are essential to validate these findings and improve fluid management methods.

LIMITATIONS

The single-center study design and small sample size may limit power of the study for rare outcomes. The open-label, pragmatic fluid assignment can cause bias. However, using objective endpoints may reduce this concern. The absence of noninvasive hemodynamic monitoring e.g., ultrasound IVC assessment and inconsistency in the timing of CT imaging may influence the detection of necrosis.

CONCLUSION

In this study, a moderate fluid-resuscitation protocol yielded clinical outcomes equivalent to those of an aggressive protocol. There were no differences in hospital stay, persistent organ failure, ICU admission, need for interventions, SIRS burden, or mortality. Moderate protocols also avoided excess hemodilution caused by high-volume hydration. This real-world data from a South Asian tertiary care center support recent randomized trials and meta-analyses, which similarly report increased fluid-overload complications without outcome benefit in aggressive regimens. The findings of this study endorse a paradigm shift

toward tailored, goal-directed fluid management in acute pancreatitis. Future guidelines should promote moderate, perfusion-directed fluid resuscitation using balanced crystalloids. The goals are to optimize patient safety, conserve resources, and reduce iatrogenic harm.

RECOMMENDATIONS

Further trials should refine phenotype-specific protocols (e.g., biliary vs. hypertriglyceridemic AP), combine real-time hemodynamic tools, and assess long-term outcomes such as quality of life and progression to chronic pancreatitis. Moderate

fluid resuscitation in acute pancreatitis offers protection against organ failure and necrosis, comparable to aggressive fluid management but with fewer volume-related complications. Together with recent trials and meta-analyses, these data support a shift toward phenotype-specific, goal-directed fluid management in acute pancreatitis.

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