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Research Article

Aggressive hydration in early resuscitation phase does not provide mortality benefit in acute pancreatitis

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Abstract

Introduction: Fluid management is the cornerstone of treatment for acute pancreatitis (AP), but the proper rate and volume is still controversial. We aim to evaluate the role of aggressive hydration in AP patients.

Methods: We retrospectively reviewed and analyzed 279 hospitalized patients of AP. Severity was determined by the Revised Atlanta classification; validated clinical scores were also calculated based on clinical information upon presentation. We extracted amount of fluid received by at 6, 12, 24 and 48 hours after presentation. Aggressive hydration was defined as amount higher than 10 ml/kg bolus followed by infusion at 1.5 ml/kg/h. After direct comparison between aggressive versus non-aggressive hydration groups, propensity-score match was performed to control severity, APACHE II and BISAP score. Post-match comparison as well as a subgroup comparison were conducted.

Results: At 24 hours, 125 (44.8%) patients received aggressive hydration averaged at 5.1 L (2-18 L), while 154 (55.2%) patients received non-aggressive hydration averaged at 2.5 L. Post-match comparison showed that aggressive hydration group had longer hospital stay (MAP: 5.3 *vs* 4.5, p = 0.145, MSAP/SAP: 8.3 *vs* 4.8 d, p = 0.007), and higher rate of intensive care unit admission (mild: 12.9% *vs* 4.4%, p = 0.042, moderately severe or severe: 36.8% *vs* 3.1%, p = 0.001), while showed no difference in rate of mortality or re-admission by 1 year. In patients who presented without organ failure, aggressive hydration did not change the rate of development of organ failure (14.1% *vs* 12.5%, p = 0.731), but the aggressive hydration group had a trend towards longer hospital stay (5.5 *vs* 4.6 d, p = 0.083) and higher rate of MICU admission (12.1% *vs* 4.8%, p = 0.051).

Conclusion: Our study did not find mortality or morbidity benefit in patients who received aggressive hydration. The optimal strategy for fluid hydration in AP remains to be elucidated and studies focusing on early non-invasive accurate hemodynamic assessment and fluid resuscitation responsiveness prediction are needed.

More Information

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Introduction

Acute pancreatitis (AP) represents one of the most common gastrointestinal disease in the United States, with increasing frequency of hospitalization and associated costs in the last decade [1,2]. Vigorous fluid resuscitation has been traditionally the corner stone of treatment during the initial phase of management, to prevent pancreatic and extra-pancreatic complications by maintaining adequate splanchnic perfusion and pancreatic microcirculation [2]. However, the type and amount of fluid and target of clinical monitoring remains unclear. Moreover, multiple studies have raised concern with aggressive hydration due to increased mortality and morbidity [3]. A study in Germany found higher mortality in patients who received aggressive hydration. 2 randomized clinical trials (RCTs) in Asia found that

aggressive hydration leading to rapid hemodilution increases mortality and morbidity. Multiple other retrospective and observational studies have provided conflicting results regarding the utility and benefit of aggressive hydration [4]. Factors that complicate the interpretation of these results include: lack of adequate stratification by severity upon initial presentation, lack of adjustment for comorbidities, various definition of aggressive fluid, and composite end-point instead of mortality as primary outcome. The purpose of this retrospective study is to compare aggressive intravenous hydration with standard hydration strategy in strictly matched groups of patients based on clinical severity, to evaluate potential effects on various clinical end-points.

Methods and Materials

Database setup

We retrospectively reviewed the electronic medical records of two hundred and seventy-nine consecutive patients who were diagnosed with AP during hospitalization at John H. Stroger Hospital in Cook County, Chicago, IL, from January 1st, 2014 to July 31st, 2015. We identified potential patients using the discharge diagnoses of AP (i.e., ICD 9 code [577.0] and ICD 10 code [K85.9]). We confirmed the diagnosis of AP based on the American College of Gastroenterology guidelines, which require at least two of the following three criteria to be fulfilled: 1) abdominal pain characteristic of AP, 2) serum lipase equal to or higher than three times the upper normal limit, and 3) characteristic findings of AP on radiologic exams. We excluded patients < 18 years of age, pregnant patients, and those who had missing data as outlined in the variables section. The present study was approved by the Institutional Review Board of the Cook County Health & Hospitals System, Chicago. The database was set up and maintained by the Department of Medicine, Cook County Health & Hospitals System.

Variables

Demographic variables, including age, gender, medical history, and alcohol, tobacco, and illicit substance use were abstracted. We obtained biochemical data at diagnosis and 48 hours after presentation. Severity scores including Acute Physiologic Assessment and Chronic Health Evaluation (APACHE II), Bedside Index of Severity in Acute Pancreatitis (BISAP) and Systemic Inflammatory Response Syndrome (SIRS) were determined based on clinical information upon presentation. We also extracted the total amount of fluid received by each patient at 6, 12, 24 and 48 hours after initial presentation. Clinical course of each case was followed to determine the length of stay (LOS) as the primary end-point, as well as other secondary end-points including duration of nil per os (NPO), medical intensive care unit (MICU) admission, in-house mortality, re-admission for AP within 1 year of discharge.

Definition of severity and clinical outcomes

We assessed three organ systems to define organ failure: respiratory, cardiovascular and renal. Organ failure was defined by modified Marshall scoring system as a score of 2 or more [5]. Transient organ failure was defined as organ failure that resolved within 48 hours. Persistent organ failure was defined as organ failure that persisted beyond 48 hours. Local pancreatic complications were defined as the development of acute peri-pancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection and wall-off necrosis as demonstrated on computed tomography. Systemic complications were defined as the exacerbation of pre-existing co-morbidity, such as coronary artery disease, or chronic lung disease. Mild acute pancreatitis (MAP) was defined by the absence of organ failure and the absence of local or systemic complications. Moderately severe acute pancreatitis (MSAP) was defined by the presence of transient organ failure or local or systemic complications in the absence of persistent organ failure. Severe acute pancreatitis (SAP) was defined by the presence of persistent organ failure according to current guideline [6,7].

Definition of aggressive hydration

We categorized patients into aggressive hydration group and non-aggressive hydration group at 6, 12, 24 and 48 hours after initial presentation. Aggressive hydration was defined as receiving fluid amount higher than standard strategy in utilized in previous studies (10 ml/kg bolus followed by infusion at 1.5 ml/kg/h during each period). This aggressive rate was adopted based on recent randomized trials of goal-directed *vs*. standard fluids [8,9].

Statistical analysis

We performed analyses to describe and summarize the distributions of variables. We use the Student's *t*-test, Wilcoxon rank sum test, or Kruskal–Wallis test to compare continuous nonparametric variables, and the Chi-square test or Fisher's exact test to compare categorical variables. Propensity-score match was performed based on age, gender and severity using APACHE II score, and BISAP score upon presentation to determine the effect of aggressive hydration on various clinical end-points, in the entire cohort and in patients without organ failure upon presentation, respectively. All statistical analyses were performed using STATA (Version 14.0, College station, TX). We considered p values of < 0.05 to be statistically significant.

Results

Cohort characteristics and hydration strategy

We reviewed and included in the analysis two hundred and seventy-nine patients with definitive diagnosis of AP and complete dataset (Table 1). Most patients were male (167, 59.8%); the mean age at diagnosis was 49.2 years. The most

Table 1: Characteristics of patients with acute pancreatitis, John H. Stroger Hospital of Cook County.

Variables	Acute Pancreatitis (*n* = 279)
Age, mean (SD), y†	49.2 (12.4)
Gender, *n* %, male‡	167 (59.8)
Etiology of AP, *n* %‡	
EtOH	113 (40.5)
Cholelithiasis	73 (26.1)
Hypertriglyceridemia	24 (8.6)
Miscellaneous	69 (24.7)
Severity, *n* %‡	
Mild	202 (72.4)
Moderately severe	35 (12.5)
Severe	42 (15.1)
APACHE II, mean (SD) †	4.2 (3.9)
BISAP, mean (SD) †	0.75 (0.78)
CT severity index, mean (SD) †	2.5 (2.2)
Length of stay, mean (SD), d†	5.7 (7.7)
NPO, mean (SD), d†	2.5 (2.6)
MICU admission, *n* %	33 (11.8)
In-hospital mortality, *n* %‡	4 (1.4)
Re-admission, *n* %‡	60 (21.5)

Abbreviations: n: number; SD: Standard Deviation; AP: Acute Pancreatitis; EtOH: Alcohol; APACHE: Acute Physiologic Assessment and Chronic Health Evaluation; BISAP: Bedside Index of Severity in Acute Pancreatitis; CT: Computed Tomography; NPO: Nil Per OS; MICU: Medical Intensive Care Unit
†Continuous variable. Presented as mean value and standard deviation.
‡Categorical variables. Presented as number and percentage of patients.

common etiology of AP was alcohol-induced (40.5%), followed by cholelithiasis-related (26.1%), and hypertriglyceridemia-induced (8.6%). The majority of cases were mild without organ failure or local/systemic complications (72.4%); the average APACHE II score was 4.2, the average BISAP score was 0.75. Thirty-three (11.8%) patients required MICU admission, and sixty (21.5%) patients were re-admitted for acute pancreatitis within 1 year of discharge. At 6 hours after initial presentation, 92 (32.9%) patients received aggressive hydration, averaged at 2.4 L, while 187 (67.1%) patients received non-aggressive hydration, averaged at 0.7 L. In comparison, at 24 hours after initial presentation, 125 (44.8%) patients received aggressive hydration averaged at 5.1 L, while 154 (55.2%) patients received non-aggressive hydration averaged at 2.5 L. The percentage of patients receiving aggressive hydration consistently increased as time elapsed after initial presentation (32.9% at 6 hours, 40.8% at 12 hours, 44.8% at 24 hours, and 49.1% at 48 hours). As expected, patients with MSAP and SAP received higher amount of fluid based on physician judgment as compared to those with MAP, as demonstrated by the absolute amount of fluid as well as percentage of patients received aggressive hydration (Table 2).

Aggressive hydration showed trend of elongating hospital stay

The primary end-point of LOS was higher in patients with higher APACHE II score upon presentation (7.4 *vs* 4.7, $p = 0.003$), in patients with persistent SIRS as compared to transient or no SIRS (9.0 *vs* 5.0, $p < 0.001$), in patients with MSAP/SAP as compared to those with MAP (7.8 *vs* 4.8, $p = 0.002$). Patients who received aggressive hydration showed consistent trend of a longer LOS as compared to those who received non-aggressive hydration (Table 3). Although the difference was only statistically significantly when dichotomized by 48 hours (6.8 *vs* 4.5, $p = 0.007$), it was obvious that at other time points aggressive hydration groups all had a trend of a longer hospital stay (6.2 *vs* 5.4 at 6 hours, 6.4 *vs* 5.2 at 12 hours and 6.2 *vs* 5.3 at 24 hours).

Propensity score match and post-match comparison of various clinical end-points

The direct comparison of clinical end-points between aggressive and non-aggressive hydration groups is easily biased by the difference in the severity of AP upon presentation. Even after subcategorization into MAP and MSAP/MAP, residual differences in severity within each group persisted, as demonstrated by the significant differences in APACHE II score (MAP: 3.8 *vs* 2.9 $p = 0.019$, MSAP/SAP: 7.7 *vs* 5.4, $p = 0.019$) (Table 4). Thus, we performed propensity score match (based on to severity of AP, APACHE II, BISAP) to strictly control the difference in severity of disease (Table 4). The success of match was confirmed as in post-match cohort of 246 patients, the percentage of MSAP/SAP does not differ between aggressive and non-aggressive hydration groups (30.1% *vs* 26.0%, $p = 0.397$), and APACHE II scores showed no statistically significant difference in aggressive and non-aggressive hydration groups in both MAP (3.8 *vs* 3.4 $p = 0.419$) and MSAP/SAP (7.3 *vs* 5.6 $p = 0.135$).

Post-match comparison demonstrated that there was no

Table 2: Correlation between severity of acute pancreatitis and amount of fluid received

Time since initial presentation		MAP	MSAP	SAP	*p**
6 hours	Fluid amount†	1.2 (0.9)	1.0 (0.9)	1.8 (2.0)	0.002
	Aggressive hydration‡	64 (31.7)	9 (25.7)	19 (45.2)	
12 hours	Fluid amount†	2.0 (1.2)	2.2 (1.6)	3.1 (2.7)	< 0.001
	Aggressive hydration‡	79 (39.1)	13 (37.1)	22 (52.4)	
24 hours	Fluid amount†	3.3 (1.6)	3.8 (2.4)	4.9 (3.6)	< 0.001
	Aggressive hydration‡	85 (42.1)	17 (48.6)	23 (54.8)	
48 hours	Fluid amount†	5.2 (2.7)	6.0 (3.2)	7.8 (5.3)	< 0.001
	Aggressive hydration‡	88 (43.5)	18 (51.4)	31 (73.8)	

Abbreviations: MAP: Mild Acute Pancreatitis; MSAP: Moderately Severe Acute Pancreatitis; SAP: Severe Acute Pancreatitis; Fluid amount in Liters.
**p* - value obtained with *Student's t test* for continuous values, *Chi-square test* or *Fisher's exact test* for categorical variables. †Continuous variable. Presented as mean value and standard deviation. ‡Categorical variables. Presented as number and percentage of patients.

Table 3: Length of stay in days by APACHE II, SIRS, severity and hydration strategy.

Variables	Categories		p*
APACHE II†	< = 4	> 4	
	4.7 (0.3)	7.4 (1.1)	0.003
SIRS†	None/transient	Persistent	
	5.0 (0.3)	9.0 (2.1)	< 0.001
Severity†	MAP	MSAP/SAP	
	4.8 (0.3)	7.8 (1.4)	0.002
Hydration†	Non-aggressive	Aggressive	0.238
6 hours	5.4 (0.6)	6.2 (0.7)	
12 hours	5.2 (0.4)	6.4 (0.9)	0.103
24 hours	5.3 (0.7)	6.2 (0.5)	0.158
48 hours	4.5 (0.4)	6.8 (0.8)	0.007

Abbreviations: APACHE: Acute Physiologic Assessment and Chronic Health Evaluation; MAP: Acute Pancreatitis; MSAP: Moderately Severe Acute Pancreatitis; SAP: Severe Acute Pancreatitis; *p - value obtained through *Student's t test* for continuous values; †Continuous variable. Presented as mean value and standard deviation. Length of stay presented in days.

Table 4: Propensity score match and post-match comparison by hydration strategy at 24 hours.

Variables	Non-aggressive	Aggressive	p*
Pre-match			
APACHE II†			
Cohort, mean (SD)	3.5 (3.1)	5.1 (4.6)	< 0.001
MAP, mean (SD)	2.9 (2.6)	3.8 (3.2)	0.019
MSAP/SAP, mean (SD)	5.4 (3.9)	7.7 (5.8)	0.019
Post-match			
Cohort, *n* (%)‡	123 (50)	123 (50)	
MAP			
APACHE II, mean (SD)†	3.4 (2.7)	3.8 (3.2)	0.419
LOS, mean (SD), d†	4.5 (3.9)	5.3 (5.7)	0.145
NPO, mean (SD), d†	2.4 (1.6)	2.3 (1.5)	0.927
MICU admission, *n* (%)‡	4 (4.4)	11 (12.9)	0.042
Re-admission, *n* (%)‡	23 (25.3)	21 (24.7)	0.931
MSAP/SAP			
APACHE II, mean (SD)†	5.6 (3.6)	7.3 (5.3)	0.135
LOS, mean (SD), d†	4.8 (2.8)	8.3 (7.2)	0.007
NPO, mean (SD), d†	2.1 (1.4)	3.6 (3.8)	0.018
MICU admission, *n* (%)‡	1 (3.1)	14 (36.8)	0.001
Re-admission, *n* (%)‡	6 (18.7)	8 (21.1)	0.810

Abbreviations: APACHE: Acute Physiologic Assessment and Chronic Health Evaluation; n: number; SD: Standard Deviation; MAP: Mild Acute Pancreatitis; MSAP: Moderately Severe Acute Pancreatitis; SAP: Severe Acute Pancreatitis; LOS: Length of Stay; NPO: Nil Per OS; *p - value obtained through *Student's t test* for continuous values, *Chi-square test* or *Fisher's exact test* for categorical variables. †Continuous variable. Presented as mean value and standard deviation. ‡Categorical variables. Presented as number and percentage of patients.

differences in re-admission rate (21.1% *vs* 18.7%, $p = 0.810$) or in-hospital mortality (2.6% *vs* 0.0%, $p = 1.000$) (Table 4). In MAP, aggressive hydration within 24 hours exerted no effect in LOS (5.3 *vs* 4.5, $p = 0.145$), length of NPO (2.3 *vs* 2.4, $p = 0.927$), re-admission rate (24.7% *vs* 25.3% $p = 0.931$). However, in MSAP/SAP, aggressive hydration was associated with significantly higher LOS (8.3 *vs* 4.8, $p = 0.007$), longer NPO (3.6 *vs* 2.1, $p = 0.018$), and more MICU admissions (36.8% *vs* 3.1%, $p = 0.001$). This effect was further confirmed with post-match comparison of LOS between aggressive versus non-aggressive hydration groups at different timing (Table 5), which showed that LOS was significantly longer universally in the former group (6 hours: 6.2 *vs* 4.9, $p = 0.043$, 12 hours: 5.6 *vs* 5.3, $p = 0.323$, 24 hours: 6.2 *vs* 4.6, $p = 0.008$, 48 hours: 6.2 *vs* 4.5, $p = 0.005$).

Patients without organ failure upon presentation

In patients who presented without organ failure, aggressive hydration within 24 hours was associated with higher APACHE II score (3.9 *vs* 2.9 $p = 0.019$) (Table 6). However, the rate of development of organ failure or local/systemic complications within the first 48 hours, thus MSAP/SAP showed no differences between groups (14.1% *vs* 12.0%, $p = 0.635$). After successful controlling of initial severity by APACHE II, BISAP scores, the above rate still showed no differences between hydration groups (14.1% *vs* 12.5% $p = 0.731$). However, there were trends towards a longer LOS (5.5 *vs* 4.6 $p = 0.083$) as well as higher rate of MICU admission rate (12.1% *vs* 4.8%, $p = 0.051$).

Discussion

The pancreas is arterially supplied by 2 major arteries; celiac trunk and superior mesenteric artery, both of which bifurcates deeply into the pancreas forming intricate microscopic circulation that supplies the pancreatic acini and islet cells [10]. Regardless of the etiology of AP, disruption of the microcirculation and capillary leak syndrome are associated with the development of severe AP and progression of disease. Several underlying etiologies leads to this phenomenon; hypovolemia, increase capillary permeability and hypercoagulability, which lead to increase secretion of pro-inflammatory cytokines and vasoactive mediators, that further

Table 5: Post-match comparison of length of stay by hydration strategy at different time point since initial presentation.

LOS, mean (SD), d†	Non-aggressive	Aggressive	p*
6 hours	4.9 (4.3)	6.2 (6.6)	0.043
12 hours	5.3 (5.2)	5.6 (5.3)	0.323
24 hours	4.6 (3.7)	6.2 (6.4)	0.008
48 hours	4.5 (4.5)	6.2 (5.7)	0.005

Abbreviations: LOS: Length of Stay; SD: Standard Deviation; *p - value obtained with *Student's t test* for continuous values, †Continuous variable. Presented as mean value and standard deviation.

Table 6: Propensity score match and post-match comparison by hydration stratified at 24 hour in patients without organ failure upon presentation.

Variables	Non-aggressive	Aggressive	p*
Pre-match			
Cohort, *n* (%)‡	133 (57.3)	99 (42.7)	
APACHE II, mean (SD)†	2.9 (2.7)	3.9 (3.3)	0.019
MSAP/SAP, *n* (%)‡	16 (12.0)	14 (14.1)	0.635
Post-match			
Cohort, *n* (%)‡	104 (51.2)	99 (48.7)	
APACHE II, mean (SD)†	3.5 (2.8)	3.9 (3.3)	0.325
MSAP/SAP, *n* (%)‡	13 (12.5)	14 (14.1)	0.731
LOS, mean (SD), d†	4.6 (3.9)	5.5 (5.5)	0.083
NPO, mean (SD), d†	2.3 (1.5)	2.4 (1.6)	0.597
MICU admission, *n* (%)‡	5 (4.8)	12 (12.1)	0.051

Abbreviations: APACHE: Acute Physiologic Assessment and Chronic Health Evaluation; *n*: number; SD: Standard Deviation; MAP: Mild Acute Pancreatitis; MSAP: Moderately Severe Acute Pancreatitis; SAP: Severe Acute Pancreatitis; LOS: Length of Stay; NPO: Bil Per Os

*p - value obtained through *Student's t test* for continuous values, *Chi-square test* or *Fisher's exact test* for categorical variables.

†Continuous variable. Presented as mean value and standard deviation. ‡Categorical variables. Presented as number and percentage of patients.

decrease capillary permeability and tissue destruction leading to further insult and eventual development of necrotizing pancreatitis [10-12]. Administration of intravenous fluids provides hemodynamic support to the patient by expanding the intravascular space and improving perfusion to the pancreas.

In the early treatment of sepsis, which is a clinical condition with physiologic and biologic similarities to acute pancreatitis (i.e. hypovolemia and third-spacing of fluid), goal-directed intravenous fluid therapy has been successfully adopted with the main focus of administering aggressive fluid resuscitation in the first 6 hours, guided by surrogate markers of hemodynamic circulation stability; including central venous pressure, mean arterial pressure, mixed central venous oxygen saturation and inotropic agent use [13]. Similar approach in AP have been assessed in multiple studies, but has not shown convincing benefits [14]. Wu, et al. investigated the utility of BUN as a resuscitation target in a small multicenter randomized clinical trial, and concluded that goal-directed fluid therapy did not decrease SIRS and C-reactive protein [9]. Hematocrit, another biomarker known to be associated with pancreatic necrosis, was put to challenge by a more recent study that used it as a goal for resuscitation. The result suggested that rapid hemodilution was associated with higher incidence of mortality and sepsis [15], which further elucidates that overly aggressive therapy leads to complications without added mortality benefit [16,17]. In summary, 4 RCTs have attempted to answer the question of which fluid strategy improves outcomes by comparing aggressive hydration *vs*. goal-directed hydration. In all 4 trials, there was no difference between groups in terms of mortality, pancreatic necrosis or persistent multi-organ failure rates. A big limitation of these studies is that they had composite end-points and they did not account for persistent multiorgan failure [9-15,18,19].

In the present study, we were able to capture the exact amount of fluid at different time points, and determine the severity of AP according to the Revised Atlanta Classification, as well as to calculate various validated clinical severity scores. As expected, the absolute amount of fluid and proportion of patients received aggressive hydration correlated closely with the severity of disease, re-demonstrating the importance of successful match according to severity when evaluating the effect of aggressive hydration in retrospective cohorts. Furthermore, even within same severity group as defined based on modified Marshall score, APACHE II scores still differ significantly between aggressive versus non-aggressive hydration groups. This demonstrates residual differences which need to be further controlled with strict matching to allow for more effective comparison of clinical endpoints, which is lacking in previous retrospective studies [4,15,17,18,20-24].

Post-match comparison revealed that in patients with MAP, those who received aggressive hydration within 24 hours required more MICU admissions, possibly for frequent monitoring and occasionally intravenous insulin when concurrent diabetic ketoacidosis is present. Furthermore, in patients with MSAP/MAP, despite of same severity of disease upon initial presentation, aggressive hydration was associated with longer hospital stay, longer period of NPO, and higher rates of MICU admissions, without any added benefit in in-hospital mortality or re-admission for AP within one year. This seemingly counterintuitive finding points against the common belief that the more severe the AP, the more fluid would benefit the patient, and echoes the recent study by de Madaria, et al. which showed overly aggressive hydration might be unnecessary or even harmful [17]. Among all patients with AP, those presented without organ failure required special attention as early resuscitation strategy potentially determines the clinical trajectory, namely whether remains mild acute pancreatitis or develop organ failure thus classified as MSAP/SAP. Again, our result demonstrated that after matching with APACHE II score, aggressive hydration group showed trends of longer hospital stay and more MICU admission requirement, while no differences in the rate of mortality or development of organ failure by 48 hours (thus MSAP/SAP), thus doubting the benefit of aggressive hydration in this population as well.

There are several limitations to the present study, similar to prior studies: retrospective nature, low mortality rate, and small sample size. However, our study has severe strengths: we were able to strictly control the initial severity to maximize the comparison yield and capture at different points in time the exact amount of fluid given to each patient which is a unique strength. Despite low mortality rate, we delineated the clear difference of LOS and rate of MICU admission between groups, which supported the above arguments sufficiently.

Conclusion

The present study suggest that aggressive hydration in the early resuscitation phase of AP does not provide mortality or morbidity benefit nor decrease readmissions rate due to AP, but rather lengthens the hospital stay, and increases the rate of MICU admission. This effect is more obvious in moderately severe and severe AP. The optimal strategy for fluid hydration in AP remains to be elucidated and prospective randomized trials focusing on early non-invasive accurate hemodynamic assessment and fluid resuscitation responsiveness prediction are needed.

Compliance with ethical standards

- No potential conflicts of interest to disclose.
- Research does not involve human participants and/or animals.
- Informed consent acquired and IRB approval obtained.

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