Pancreatology 19 (2019) 646–652

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

# Ascites in acute pancreatitis: not a silent bystander

Jayanta Samanta [a], Atul Rana [a], Narendra Dhaka [a], Roshan Agarwala [a], Pankaj Gupta [a], Saroj Kant Sinha [a], Vikas Gupta [b], Thakur Deen Yadav [b], Rakesh Kochhar [a, *]

[a] Department of Gastroenterology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[b] Department of Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India

ARTICLE INFO

*Article history:*
Received 10 March 2019
Received in revised form
3 May 2019
Accepted 8 June 2019
Available online 9 June 2019

*Keywords:*
Ascites
Abdominal paracentesis
Acute pancreatitis
Intra-abdominal pressure
Intra-abdominal hypertension

ABSTRACT

*Background & aim:* Ascites in patients with acute pancreatitis (AP) is understudied although recent literature hints at its evident role in the final outcome. This study was planned to study the characteristics of ascites in patients of AP and its effect on the disease course and outcome.
*Methods:* Consecutive patients of AP were studied and patients with or without ascites were evaluated for the baseline parameters and severity assessment. Ascites was quantified and fluid analyzed for its characteristics. Intraabdominal pressure (IAP) was monitored. The various outcome parameters were compared between the two groups of patients with and without ascites.
*Results:* Of the cohort of 213 patients, 82 (38.5%) developed ascites. Ascites group had significantly higher rates of organ failure ($p = 0.001$), necrosis ($p = <0.001$) and higher severity assessment scores. The ascites group had significantly longer hospital and ICU stay and higher ventilator days compared to the non-ascites group. Mortality was also higher in the ascites group (34.1% vs 8.45; $p = 0.001$). Majority of patients with ascites had moderate to gross ascites (75.6%), low serum ascites albumin gradient (87.8%) with low amylase levels (71.9%). Sub-group analysis in ascites group showed that patients with fatal outcome had higher rates of moderate to gross ascites, higher baseline IAP and lower reduction in IAP after 48 h. Moderate to gross ascites and grades of intra-abdominal hypertension (IAH) were significant predictors of mortality (AUC − 0.76).
*Conclusion:* AP patients with ascites have a more severe disease with poorer outcome. Higher degrees of ascites and IAH grades are significant predictors of mortality.


## Introduction

Acute pancreatitis (AP) can have varied presentations depending on the severity of the attack. Severe AP constitutes around 20% of all cases, and usually requires aggressive early management, intensive care support, referral to tertiary care facilities and timely interventions [1,2]. In spite of the best efforts the mortality is as high as 25% with severe disease [3]. Over the last two decades, there has been a paradigm shift in the management of AP from surgical to more of a "step-up" approach using percutaneous catheter drainage (PCD) or endoscopic drainage followed by minimally invasive necrosectomy [4].

Development of ascites has been extensively studied as a complication in the natural history of chronic pancreatitis [5,6]. However, the free-flowing spontaneous ascites that develops in the setting of AP, its nature, characteristics and its effect on the overall outcome are not well established. The widely used severity assessment tool currently followed is the revised Atlanta Classification [7] wherein AP is classified as mild, moderately severe and severe. The definition of local complications in this classification includes acute peri-pancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection and walled-off necrosis but not ascites. Whether presence or absence of ascites within the same class of severity of AP has an influence on the outcome is unknown.

Recent studies have shown a beneficial effect on the outcome in patients subjected to abdominal paracentesis drainage (APD) for ascites in AP. APD has been shown to decrease the level of cytokines [8]. Moreover, ascites can contribute to the development of intra-abdominal hypertension (IAH) which in itself has been found to be a bad prognostic marker [9] and reduction of IAP has been shown to be protective [10]. Thus, recent literature gives some evidence of the role of ascites on the outcome in patients with AP.

* Corresponding author.
*E-mail address:* dr_kochhar@hotmail.com (R. Kochhar).

https://doi.org/10.1016/j.pan.2019.06.004
1424-3903/

However, very little data exists on the characterization of ascites that develops in patients with AP and its role on the outcome parameters.

The current study was planned to study the characteristics of the ascites that develops in patients of AP and its effect on the disease course and outcome compared to those not developing ascites.

## Material and methods

### *Patients*

Between July 2016 to June 2018, all consecutive patients presenting to the Gastroenterology and Surgical services (TDY, VG) of a tertiary care center in North India with the diagnosis of AP were screened for inclusion in the study. The demographic, radiographic and laboratory data of these patients were collected prospectively and the data were analyzed retrospectively. Patients with history of pre-existing chronic pancreatitis were excluded. The study was approved by the institute ethics committee. Written informed consent was taken from all patients.

### *Definitions*

The diagnosis of AP was made if a patient had two or more of the following three findings: typical abdominal pain, elevation of serum enzymes (amylase and/or lipase) to more than three times the upper limit of the normal and imaging (ultrasonography or computed tomography (CT)) suggestive of AP [7].

Ascites was defined by ultrasonographic findings of free-flowing fluid collection (>50 mL), mostly aimed at abdominal or pelvic cavity.

### *Severity assessment*

Severity assessment of AP was done as per the revised Atlanta Classification [7] into mild, moderately severe and severe. Absence of organ failure (OF) or local or systemic complications was labelled as mild AP. Moderately severe AP was defined by presence of transient OF or local complications such as fluid collection or necrotic collection or exacerbation of co-morbid illness. Severe AP was termed when there was persistent OF for more than 48 h. OF was defined using the modified Marshall scoring system [11]. Severity parameters such as Acute Physiology and Chronic Health evaluation (APACHE)-II [12], Systemic Inflammatory Response Syndrome (SIRS) and Bedside index for severity in AP (BISAP) [13] were calculated. CT severity index (CTSI) was calculated for patients undergoing CT. Necrosis was defined using the CTSI [14]. Pancreatic pseudocyst or walled off necrosis (WON) was defined as well formed collection beyond 4 weeks following an episode of acute edematous or necrotizing pancreatitis respectively [7].

### *Ascites assessment*

The development of ascites was assessed by ultrasound by an experienced sonologist. The assessment for ascites was done at admission for patients referred from other hospital or within 2 weeks of onset of illness or if CT scan done at 5–7 days suggested it. Acute peri-pancreatic fluid collection is usually localised fluid which can be differentiated from the free flowing peritoneal fluid seen in ascites on ultrasound. All patients with sonographically established ascites underwent quantification of ascites by a radiologist by calculating total estimated abdominal ascites (TEAA). The ascites volume was labelled as mild (TEAA <200–600 mL), moderate (TEAA >600–800 mL) and gross (TEAA >800 mL) [15]. The ascitic fluid in all ascites patients was analyzed for cell counts, amylase, protein, albumin and culture sensitivity.

### *Intra-abdominal pressure measurement*

All patients with ascites and 42 of those without ascites underwent measurement of IAP by the standard technique. IAP was expressed as mm of Hg or cm of water (1 mm of Hg = 1.36 cm of $H_2O$). As per the consensus document by the World Society of the Abdominal Compartment Syndrome (WSACS), Intra-abdominal Hypertension (IAH) is defined by a persistent or repeated elevation of IAP over 12 mmHg [16].IAH was graded as: Grade I:IAP 12–15 mmHg (16–20 cm of $H_2O$); Grade II:IAP 16–20 mmHg(21–27 cm of $H_2O$); Grade III:IAP 21–25 mmHg(28–34 cm of $H_2O$); Grade IV:IAP > 25 mmHg(>34 cm of $H_2O$). IAP was measured at baseline and after that every 24 h till normalization of IAP. IAP was also documented prior to APD placement and sequentially after that post procedure every 24 h for drop or normalization.

### *Management*

Patients were managed as per the standard recommendations(17), including adequate fluid resuscitation, organ system support, pain management, and nutritional support (enteralor or parenteral) [18,19]. Extra-pancreatic infections and suspected infected pancreatic necrosis (IPN) were managed with antibiotics.

IPN was suspected on the basis of deteriorating clinical course of the patient and diagnosed by culture positivity of the drain output or CECT showing gas within the necrosis. In cases of persistent OF, suspected IPN and/or pressure symptoms, the fluid collections were drained (USG/CT guided percutaneous catheter (PCD) or endoscopically). A dedicated unit comprising of gastroenterologists and an interventional radiologist decided upon the site and route of drainage based upon the location, type and extent of collection. Patients not showing improvement or worsening on medical management and drainage of collection were subsequently taken up for surgical necrosectomy.

The decision for abdominal paracentesis drainage (APD) for the ascites was taken in cases of moderate to gross ascites with 1) increasing abdominal distension; 2) persistent OF or worsening OF; 3) development of IAH. The placement of APD was simply an ultrasound guided percutaneous drainage of the free-flowing fluid in the flanks as is done for the standard management of seroperitoneum. The initial drain catheter was with a 8–10 Fr catheter which was later upgraded, if necessary. Decision for removal of drain was made whenever the drain output decreased to less than 10 mL/day for 3 days and imaging showed no evidence of residual fluid.

### *Outcome measures*

Severity parameters were compared between the two groups. The parameters studied were SIRS, BISAP, and APACHE II scores and the severity of AP as per revised Atlanta classification. Outcome measures evaluated included the requirement of organ support (mechanical ventilation and dialysis), need for intensive care (ICU) admission, surgical necrosectomy, and drainage of collections, duration of hospital stay and mortality in the index hospital admission. The response to the placement of APD was assessed by measuring the reduction in IAP after 48 h of placement of APD.

### *Statistical analysis*

All data were entered in Microsoft Excel 2010. The data was analyzed using SPSS software (version 22.0, IBM, USA). The data

was checked for normal distribution by Kolmogorov-Smirnov test. For normally distributed data, student *t*-test was used for continuous variables while for skewed data, non-parametric tests were used. Dichotomous variables were compared using Chi square test. Quantitative data was described as mean and standard deviation with 95% confidence intervals.

Logistic regression analysis was performed to identify the characteristics that significantly determined mortality among the selected pool of patients. Simple logistic regression analysis was used to determine unadjusted association of mortality with each characteristic. Multiple logistic regression model was applied using step-wise selection model for the predictors of mortality in the subgroup of ascites patients.

A p value of less than 0.05 was taken as statistically significant.

## Results

A cohort of 256 patients of AP admitted to our tertiary care center in Northern India from the period of July 2016 to June 2018 was screened of which 43 patients were excluded from the study and 213 were included. Of these 82 patients (38.5%) had developed ascites while 131 patients (61.5%) did not, during their course of illness (Fig. 1.). Being a tertiary care center, majority of the patients (n = 137; 64.3%) were secondary transfers from other hospitals.

### *Demographic parameters*

Comparison of the baseline demographic parameters between the two groups showed that the two groups were evenly placed for age, sex or etiology of AP (Table 1).

### *Disease course*

On comparing the disease course between the two groups (Table 1), OF was found to be significantly higher in the ascites group (78.1% vs 29.8%; $p = 0.001$) with all the various organ involvements such as ALI, AKI and shock being significantly higher ($p < 0.0001$). Patients having ascites showed higher rates of pancreatic necrosis (82.9% vs 48.1%; $p < 0.0001$) than those not having.

Various severity assessment parameters such as SIRS, BISAP and APACHE II at admission were significantly higher in the ascites group. CTSI scores were higher ($p = 0.016$) in patients with ascites than those without. However, the Atlanta classification did not show any difference.

### *Outcome parameters*

The outcome measures such as ICU stay, hospital stay and

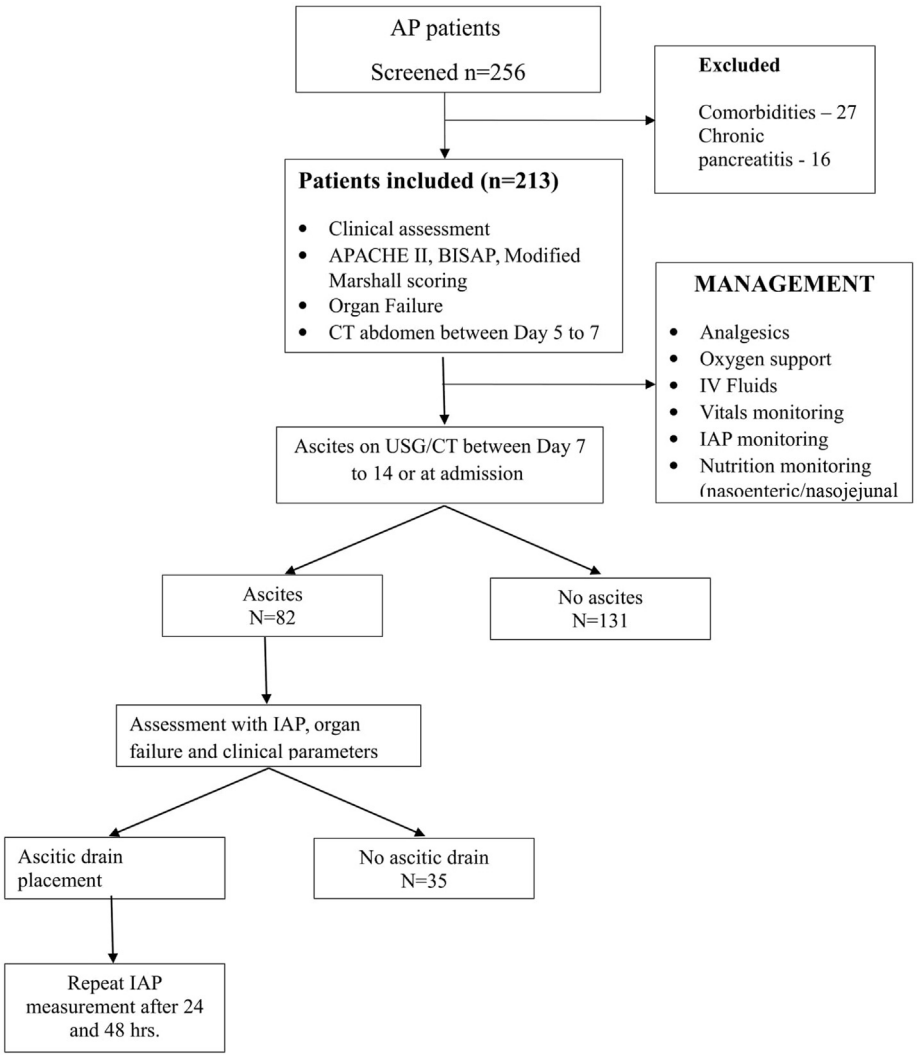


**Fig. 1.** Study design.

**Table 1**
Comparison between patients with and without ascites.

| | Ascites (n = 82) | Non-ascites (n = 131) | P value |
|---|---|---|---|
| Demography | | | |
| Age | 40.33 ± 12.9 | 41.05 ± 13.7 | 0.70 |
| Sex | | | |
| Male | 60 (73.2%) | 95 (72.5%) | |
| Female | 22 (26.8%) | 36 (27.5%) | |
| Etiology Alcohol | 39 (48.1%) | 64 (49.2%) | |
| Gall stone | 26 (32.1%) | 43 (33.1%) | |
| Others | 16 (19.8%) | 23 (17.7%) | |
| **Baseline parameters** | | | |
| Organ failure | 64 (78.1%) | 37 (29.8%) | 0.001 |
| ALI | 62 (75.6%) | 32 (24.4%) | <0.0001 |
| AKI | 30 (36.6%) | 11 (8.4%) | <0.0001 |
| Shock | 22 (26.8%) | 8 (6.1%) | <0.0001 |
| Necrosis | 68 (82.9%) | 63 (48.1%) | <0.0001 |
| SIRS | 71 (86.6%) | 78 (60.9%) | <0.0001 |
| BISAP | 2.07 ± 0.87 | 1.20 ± 1.0 | 0.001 |
| APACHE II admission | 9.18 ± 4.5 | 6.76 ± 3.2 | 0.001 |
| CTSI | 8.09 ± 2.4 | 7.67 ± 2.6 | 0.016 |
| Atlanta classification | | | |
| MAP | 12 (14.6%) | 29 (23.8%) | |
| MSAP | 45 (54.9%) | 57 (46.7%) | |
| SAP | 25 (30.5%) | 36 (29.5%) | 0.26 |

ALI: Acute lung injury; AKI: Acute kidney injury; SIRS: Systemic inflammatory response syndrome; BISAP: Bedside Index of Severity of AP; APACHE: Acute Physiology and Chronic Health Evaluation; CTSI: CT severity index; MAP: Mild AP; MSAP: Moderately severe AP; SAP: Severe AP.

number of ventilator days were significantly higher in the ascites group as compared to those without ascites (Table 2). Mortality was found to be significantly higher (34.1% vs 8.4%; p = 0.001) in the ascites group.

*Characteristics of ascitic fluid*

The characteristics of the ascitic fluid were analyzed (Table 3). Majority (n = 62; 75.6%) had moderate to gross ascites. Majority of the patients had ascitic fluid amylase of less than 1000 IU/mL (n = 59; 71.9%). The mean protein level was 3.04 ± 0.95 g/dL. The serum ascites albumin gradient (SAAG) was less than 1.1 in the majority of patients (n = 72; 87.8%). The fluid was mostly sterile (n = 77; 93.9%). No significant difference in the infection rate of ascitic fluid was seen between the patients who received an abdominal paracentesis drain vs. those who did not (10.6% vs. 0%; p = 0.07).

Out of 82 patients with ascites, 47 (57.3%) needed APD placement. Overall, percutaneous drain (PCD) for infected necrosis was needed in 101 patients (47.4%), 24 (11.3%) underwent endoscopic drainage and 19 (8.9%) underwent surgical drainage.

*Patients with ascites - subgroup analysis*

A sub-group analysis of the patients with ascites was done to look for factors contributing to the final outcome of mortality (Table 4). The ascites group had a higher mortality rate of 34.1%

**Table 2**
Outcome parameters between patients with and without ascites.

| | Ascites (n = 82) | Non-ascites (n = 131) | P value |
|---|---|---|---|
| ICU stay | 9.1 [14] | 1.44 (0) | 0.001 |
| Hospital stay | 27.3 [24] | 12.54 [24] | 0.001 |
| Ventilator days | 3.37 [3] | 0.25 (0) | 0.01 |
| Need for dialysis | 11 (5.9%) | 37 (6.3%) | 0.52 |
| Mortality | 28 (34.1%) | 11 (8.4%) | 0.001 |

ICU: Intensive care unit.

**Table 3**
Characteristics of ascitic fluid in the sub-group of patients with ascites.

| Ascites | Results |
|---|---|
| **Severity** | 82(38.5%) |
| Mild | 20(24.4%) |
| Moderate to Gross | 62(75.6%) |
| Amylase | |
| <1000 | 59(71.9%) |
| >1000 | 23(29.1%) |
| SAAG | |
| Low SAAG | 72(87.8%) |
| High SAAG | 10(22.2%) |
| Culture | |
| Sterile | 77(93.9%) |
| Infected | 5(6.1%) |
| | |
| Need for drainage of ascites (APD) | 47(57.3%) |
| Mean protein concentration (g/dL) | 3.04 ± 0.95 |

SAAG: Serum ascites albumin gradient.

(n = 28). Evidently, overall OF rates and the individual organ involvement such as ALI, AKI and shock were significantly higher in the mortality group as also the severity scores such as APACHE II at admission, CTSI and Marshall scores.

No differences were found in regard to the fluid nature of ascitic fluid such as amylase levels of more than 1000 IU/mL or SAAG. However, patients having a fatal outcome had significantly higher rates of moderate to gross ascites (92.9% vs 66.7%; p = 0.013) and had lower rates of APD placement (44.7% vs 55.3%; p = 0.033). Moreover, the mortality group exhibited significantly higher rates of baseline IAP (p = 0.0003) and lower rates of reduction in IAP after 48 h of APD placement (33.3% vs 42.9%; p = 0.04). Patients with ascites had higher IAP as compared to those who did not have ascites (p = 0.004).

Multiple logistic regression analysis was applied to look for predictors of mortality using independent parameters – ascites grade, ascitic fluid amylase, SAAG, ascitic fluid culture, use of APD and IAH grade. It was found that moderate to severe ascites (p = 0.04) and IAH grading were significant predictors of mortality (Table 5). A ROC curve was plotted using IAH grade and ascites grade as shown in Fig. 2 with AUC of 0.76. Another multivariate model using the severity parameters of SIRS, BISAP, APACHE II, CTSI and Atlanta classification showed that APACHE II was a significant predictor (OR 4.924; p = 0.012) of mortality in the subset of patients with ascites.

## Discussion

This study is a retrospective analysis of a prospectively collected data to compare the outcome of AP patients who developed ascites with those who did not. This is the first study of its kind on a comprehensive overview of the characteristics of ascites that develops in AP – pancreatitis-associated ascitic fluid (PAAF) and its clinical implications on the outcome. Our study had 38.5% patients developing ascites. The patients developing ascites had significantly higher rates of organ failures and severity scores with greater mortality. In the ascites group, moderate to severe ascites and grades of IAH were found to be significant predictors of mortality.

The characteristics of PAAF have been the subject of interest in multiple studies. PAAF has been found to be an exudate rich fluid that accumulates in up to 60% of the severe AP patients [20]. It not only modulates the function of the peritoneal macrophages [21], but also upregulates the pro-inflammatory cytokines such as TNF-α and IL-6 [22]. Thus, PAAF adds on to the perpetuation of the pathogenic cytokine storm in AP and is not a silent bystander. Liu e

**Table 4**
Sub-group analysis of ascites patients for final outcome measures.

| | Discharged; n = 54 (65.9%) | Death; n = 28 (34.1%) | P value |
|---|---|---|---|
| Disease course | | | |
| BISAP | 1.92 ± 0.9 | 2.36 ± 0.75 | 0.3 |
| APACHE II admission | 7.66 ± 3.57 | 12.07 ± 4.7 | 0.001 |
| Marshall score | 1.68 ± 1.6 | 2.85 ± 1.0 | 0.001 |
| Organ failure | 38 (70.4%) | 27 (96.4%) | 0.008 |
| ALI | 35 (64.8%) | 27 (96.4%) | 0.001 |
| AKI | 14 (25.9%) | 16 (57.1%) | 0.008 |
| Shock | 7 (13.0%) | 15 (53.6%) | 0.001 |
| CTSI | 7.62 ± 2.56 | 9.0 ± 1.7 | 0.016 |
| **Ascitic fluid characteristics** | | | |
| Ascites Mild | 18 (33.3%) | 2 (7.1%) | 0.013 |
| Moderate-gross | 36 (66.7%) | 26 (92.9%) | |
| Ascitic fluid amylase >1000 | 15 (27.8%) | 8 (28.6%) | 1.00 |
| SAAG <1.1 | 47 (87%) | 25 (89.3%) | 1.00 |
| ≥1.1 | 7 (13%) | 3 (10.7%) | |
| Need for ascitic drain | 26 (55.3%) | 21 (44.7%) | 0.033 |
| **IAP grade** | | | |
| Normal (<16) | 35 (83.3%) | 7 (16.7%) | 0.003 |
| Grade 1 [16–20] | 10 (41.7%) | 14 (58.3%) | |
| Grade 2 [21–27] | 4 (44.4%) | 5 (55.6%) | |
| Grade 3 [28–33] | 5 (71.4%) | 2 (28.6%) | |
| Percentage reduction in IAP after 48 h | 42.9% (27.6) | 33.3% (34.5) | 0.04 |

BISAP: Bedside Index of severity of AP; APACHE: Acute Physiology and Chronic Health Evaluation; ALI: Acute lung Injury; AKI: Acute Kidney injury; CTSI: CT severity index; SAAG: Serum ascites albumin gradient; IAP: Intra-abdominal pressure.

**Table 5**
Odds ratio estimates for mortality in the ascites group.

| Odds ratio estimates for death among those patients who had ascites | | | | |
|---|---|---|---|---|
| Parameters | Odds Ratio | 95% Wald Confidence Limits | | p value |
| IAH grade I vs 0 | 5.326 | 1.63 | 17.41 | 0.0056 |
| IAH grade II vs 0 | 7.506 | 1.39 | 40.64 | 0.0193 |
| IAH grade III vs 0 | 1.654 | 0.25 | 11.1 | 0.6042 |
| Ascites grade: moderate-gross vs mild | 5.874 | 1.08 | 32.01 | 0.0407 |

IAH: Intra-abdominal hypertension.

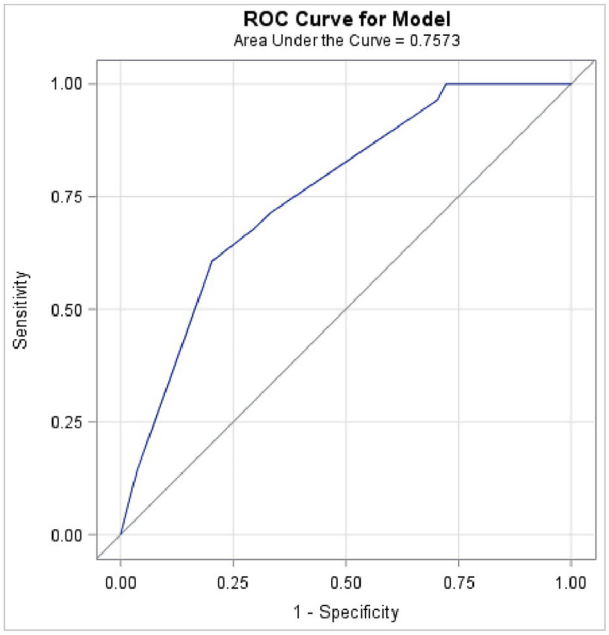


**Fig. 2.** ROC curve for overall predictive model for death among ascites cases (Predictors = IAH grade and ascites grade).

al [8] described reduction of cytokines by almost half after placement of APD. The mechanism of ascites development can be postulated to be either a duct disruption causing a high amylase ascites or a capillary leak phenomenon with maintained ductal anatomy leading to a low amylase ascites [23]. In the current study, low amylase (<1000 IU/mL) was found in 71.9% of the patients. Interestingly, Haas et al. [23] showed that lower ascitic amylase and lower ascites to serum amylase ratio portends a higher risk for mortality. However, in our study, ascitic fluid amylase did not have any influence on mortality. PAAF is usually a high protein ascites as seen in the present study (mean = 3.04 g/dL) similar to previous studies [23–25]. The serum ascites albumin gradient (SAAG) was low (<1.1) in majority of the cases (87.8%).

Severity assessment in AP has undergone a sea change after the advent of the revised Atlanta Classification [7]. However, PAAF has not been dealt with in this classification system as a part of collections or local complications. Emerging data have suggested a significant role of ascites in the final outcome. In our study, although revised Atlanta Classification did not show any difference, all the other severity scores such as SIRS, BISAP and APACHE II at admission were found to be significantly higher in the ascites group as also the necrosis and the CTSI scores. OF was also significantly higher in the ascites group implicating an overall severe disease course. Haas et al. [23] had pointed out that clinically apparent ascites was a significant predictor of mortality. In their study, patients with ascites had overall mortality of 39%. Maringhini et al.

[26], in their study of 100 patients with AP, found 18% to have ascites with the odds ratio for severe disease being 5.9. Thus, ascites has been consistently shown to be associated with poor outcome.

A modification of the conventional Balthazar CTSI index [14] was proposed by Mortele et al. [27], the modified CTSI (mCTSI), wherein extra pancreatic complications which included ascites were granted an additional 2 points in the final scoring. They found that mCTSI was more closely related to outcome measures as compared to the original CTSI. A few subsequent studies found mCTSI to have better accuracy [28] with a stronger correlation with outcome [29]. However, others found that the two scoring systems were comparable [30] and had predictive accuracies akin to the clinical scoring systems [31].

Outcome parameters such as length of hospital stay, ICU stay and number of ventilator days required were significantly higher in the ascites group. Mortality was significantly higher ($p = 0.001$) in the ascites group, similar to previous studies [23,32]. The mortality in the ascites group was 34.1%, similar to 39% mortality found by Haas et al. [23].

On analysis of mortality predictors, the various factors like OF and the severity scores such as APACHE II at admission, CTSI and Marshall scoring evidently contributed to mortality prediction. Interestingly, it was observed that placement of APD had better survival ($p = 0.033$) than those in whom it was not placed. This corroborates with recent studies highlighting the beneficial effect of APD by a multitude of pathways. Liu et al. [8] highlighted that patients who underwent APD ahead of PCD had lower inflammatory markers, less OF and a lower mortality than the PCD-only group. In another study, Liu et al. [33] had defined the various predictors of need for PCD after APD placement. Placement of APD has not been shown to be associated with increased infections [34]. Hongyin et al. [35] demonstrated that APD can help improve tolerance of enteral nutrition.

A cardinal predictor of poor outcome in AP is development of IAH and abdominal compartment syndrome (ACS). IAH develops in 60–80% of patients with severe AP and 30–40% develop ACS [9]. Development of IAH in patients with AP is multi-factorial and ascites is one of these factors [16,36]. In our study, on multivariate logistic regression analysis, it was found that the grade of ascites and the grades of IAH were significant predictors of mortality. This evidently underlies the role of ascites in the modulation of severity of AP. Multiple studies have shown the beneficial effect of reduction of IAP [37,38] with reduced infection and improvement in OF [10]. In fact, in the present study, higher percentage of APD had better survival and a lower percentage reduction in the IAP was associated with a higher mortality ($p = 0.04$).

## Limitations and future perspectives

The study has been conducted in a tertiary care center wherein a large number of patients were referred with more severe disease and it might have led to referral bias. We have not looked at the impact of ascites on cytokine levels. Another limitation of the study is that the effect of different sites of necrosis and sites of collection between the two groups (with or without ascites) was not studied. Whether temporal correlation exists between development of ascites and worsening of clinical picture is an area that needs to be addressed. A more systematic study of the timing of APD needs to be carried out to better fine tune the “step-up” approach and whether it should be placed before PCD placement for collections or independent of it. Development of ascites in the disease course of AP should be considered a bad prognostic marker and may be needed to be included in future severity assessment measures.

## Conclusion

In summary, the results of our study comprehensively establish that AP patients with ascites have a more severe disease course with poorer outcome as compared to those who do not. Higher degree of ascites and IAH grades are significant predictors of mortality. Drainage of ascites and effective IAP reduction improves survival.

## Grant support

Nil.

## Disclosures

The authors declare no potential conflicts of interest.

## References

[1] Lerch MM. Classifying an unpredictable disease: the revised Atlanta classification of acute pancreatitis. Gut 2013;62(1):2–3.
[2] van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. NEJM 2010;362(16):1491–502.
[3] Yeung YP, Lam BY, Yip AW. Apache system is better than Ranson system in the prediction of severity of acute pancreatitis. Hepatobiliary Pancreat Dis Int : HBPD INT. 2006;5(2):294–9.
[4] Besselink MG, van Santvoort HC, Nieuwenhuijs VB, Boermeester MA, Bollen TL, Buskens E, et al. Minimally invasive 'step-up approach' versus maximal necrosectomy in patients with acute necrotising pancreatitis (PANTER trial): design and rationale of a randomised controlled multicenter trial [ISRCTN13975868]. BMC Surg 2006;6:6.
[5] Sankaran S, Walt AJ. Pancreatic ascites: recognition and management. Arch Surg 1976;111(4):430–4.
[6] Cameron JL. Chronic pancreatic ascites and pancreatic pleural effusions. Gastroenterology 1978;74(1):134–40.
[7] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62(1):102–11.
[8] Liu WH, Ren LN, Chen T, Liu LY, Jiang JH, Wang T, et al. Abdominal paracentesis drainage ahead of percutaneous catheter drainage benefits patients attacked by acute pancreatitis with fluid collections: a retrospective clinical cohort study. Crit Care Med 2015;43(1):109–19.
[9] Mifkovic A, Skultety J, Sykora P, Prochotsky A, Okolicany R. Intra-abdominal hypertension and acute pancreatitis. Bratisl Lek Listy 2013;114(3):166–71.
[10] Wang T, Liu LY, Luo H, Dai RW, Liang HY, Chen T, et al. Intra-abdominal pressure reduction after percutaneous catheter drainage is a protective factor for severe pancreatitis patients with sterile fluid collections. Pancreas 2016;45(1):127–33.
[11] Marshall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. Crit Care Med 1995;23(10):1638–52.
[12] Larvin M, McMahon MJ. Apache-II score for assessment and monitoring of acute pancreatitis. Lancet 1989;2(8656):201–5.
[13] Wu BU, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA. The early prediction of mortality in acute pancreatitis: a large population-based study. Gut 2008;57(12):1698–703.
[14] Balthazar EJ, Robinson DL, Megibow AJ, Ranson JH. Acute pancreatitis: value of CT in establishing prognosis. Radiology 1990;174(2):331–6.
[15] Alnumieiri MSAC, Ahmed BH, Abdalla EA. Evaluation of ascites and its etiology using ultrasonography. J Res Development 2015;3.
[16] Kirkpatrick AW, Roberts DJ, De Waele J, Jaeschke R, Malbrain ML, De Keulenaer B, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. Intensive Care Med 2013;39(7):1190–206.
[17] Mallick B, Dhaka N, Gupta P, Gulati A, Malik S, Sinha SK, et al. An audit of percutaneous drainage for acute necrotic collections and walled off necrosis in patients with acute pancreatitis. Pancreatology 2018;18(7):727–33.
[18] Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013;41(2):580–637.
[19] Hasibeder WR, Torgersen C, Rieger M, Dunser M. Critical care of the patient with acute pancreatitis. Anaesth Intensive Care 2009;37(2):190–206.
[20] Dugernier T, Laterre PF, Reynaert MS. Ascites fluid in severe acute pancreatitis: from pathophysiology to therapy. Acta gastro-enterologica Belgica 2000;63(3):264–8.
[21] Satoh A, Shimosegawa T, Masamune A, Fujita M, Koizumi M, Toyota T. Ascitic fluid of experimental severe acute pancreatitis modulates the function of

peritoneal macrophages. Pancreas 1999;19(3):268–75.
[22] Wang J, Xu P, Hou YQ, Xu K, Li QH, Huang L. Pancreatitis-associated ascitic fluid induces proinflammatory cytokine expression in THP-1 cells by inhibiting anti-inflammatory signaling. Pancreas 2013;42(5):855–60.
[23] Haas LS, Gates JrJr. The ascites to serum amylase ratio identifies two distinct populations in acute pancreatitis with ascites. Pancreatology 2002;2(2):100–3.
[24] Dubick MA, Mayer AD, Majumdar AP, Mar G, McMahon MJ, Geokas MC. Biochemical studies in peritoneal fluid from patients with acute pancreatitis. Relationship to etiology. Dig Dis Sci 1987;32(3):305–12.
[25] Mann SK, Mann NS. Pancreatic ascites. Am J Gastroenterol 1979;71(2):186–92.
[26] Maringhini A, Ciambra M, Patti R, Randazzo MA, Dardanoni G, Mancuso L, et al. Ascites, pleural, and pericardial effusions in acute pancreatitis. A prospective study of incidence, natural history, and prognostic role. Dig Dis Sci 1996;41(5):848–52.
[27] Mortele KJ, Wiesner W, Intriere L, Shankar S, Zou KH, Kalantari BN, et al. A modified CT severity index for evaluating acute pancreatitis: improved correlation with patient outcome. AJR Am J Roentgenol 2004;183(5):1261–5.
[28] Banday IA, Gattoo I, Khan AM, Javeed J, Gupta G, Latief M. Modified computed tomography severity index for evaluation of acute pancreatitis and its correlation with clinical outcome: a tertiary care hospital based observational study. J Clin Diagn Res 2015;9(8):TC01–5.
[29] Raghuwanshi S, Gupta R, Vyas MM, Sharma R. CT evaluation of acute pancreatitis and its prognostic correlation with CT severity index. J Clin Diagn Res 2016;10(6):TC06–11.
[30] Bollen TL, Singh VK, Maurer R, Repas K, van Es HW, Banks PA, et al. Comparative evaluation of the modified CT severity index and CT severity index in assessing severity of acute pancreatitis. AJR Am J Roentgenol 2011;197(2):386–92.
[31] Bollen TL, Singh VK, Maurer R, Repas K, van Es HW, Banks PA, et al. A comparative evaluation of radiologic and clinical scoring systems in the early prediction of severity in acute pancreatitis. Am J Gastroenterol 2012;107(4):612–9.
[32] Geokas MC, Rinderknecht H, Brodrick JW, Largman C. Studies on the ascites fluid of acute pancreatitis in man. Am J Dig Dis 1978;23(2):182–8.
[33] Liu WH, Wang T, Yan HT, Chen T, Xu C, Ye P, et al. Predictors of percutaneous catheter drainage (PCD) after abdominal paracentesis drainage (APD) in patients with moderately severe or severe acute pancreatitis along with fluid collections. PLoS One 2015;10(2):e0115348.
[34] Liu L, Yan H, Liu W, Cui J, Wang T, Dai R, et al. Abdominal paracentesis drainage does not increase infection in severe acute pancreatitis: a prospective study. J Clin Gastroenterol 2015;49(9):757–63.
[35] Hongyin L, Zhu H, Tao W, Ning L, Weihui L, Jianfeng C, et al. Abdominal paracentesis drainage improves tolerance of enteral nutrition in acute pancreatitis: a randomized controlled trial. Scand J Gastroenterol 2017;52(4):389–95.
[36] Jaipuria J, Bhandari V, Chawla AS, Singh M. Intra-abdominal pressure: time ripe to revise management guidelines of acute pancreatitis? World J Gastrointest Pathophysiol 2016;7(1):186–98.
[37] Kochhar R, Dhaka N, Sinha S, Samanta J, Prasad R, Berry N, et al. Reduction in intra-abdominal pressure after percutaneous catheter drainage predicts outcome in patients of severe acute pancreatitis. Gastroenterology 2017;152(5):S292.
[38] Yadav SK, Reddy YR, Dhaliwal HS, Jaysawal M, Samanta J, Sinha SK, et al. 591e Significance of Intra-Abdominal Pressure in the Course and Outcomes of Acute Pancreatitis. Gastroenterology 2015;148(4):S-114.