

# Intra-abdominal pressure at ICU admission: Evaluation as a predictor of severity and mortality in severe acute pancreatitis

**Ratender Kumar Singh, Parnandi Bhaskar Rao, Arvind Kumar Baronia, Banani Poddar, Afzal Azim, Mohan Gurjar, Neha Singh, Vasudevan Senthilvel, Kamlesh Singh**

*Department of Critical Care Medicine, Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow, India*  
**Ratender Kumar Singh**, MD

*Department of Anaesthesiology and Critical Care, Pondicherry Institute of Medical Sciences (PIMS), Pondicherry, India*  
**Parnandi Bhaskar Rao**, MD

*Department of Critical Care Medicine, SGPGIMS, Lucknow, India*  
**Arvind Kumar Baronia**, MD  
**Banani Poddar**, MD  
**Afzal Azim**, MD  
**Mohan Gurjar**, MD

*Department of Anaesthesiology and Critical Care, PIMS, Pondicherry, India*  
**Neha Singh**, MD

*Department of Community Medicine, PIMS, Pondicherry, India*  
**Vasudevan Senthilvel**, BSc (Statistics)

*Department of Clinical Epidemiology, Chhatrapati Sahuji Maharaj Medical University, Lucknow, India*  
**Kamlesh Singh**, BSc (Statistics)

**Corresponding author:** R K Singh (ratenderrks70@gmail.com)

**Background and aims.** Approximately 20% of acute pancreatitis progresses to a severe form characterised by multiple extrapancreatic organ dysfunction. Elevated intra-abdominal pressure (IAP), a frequent finding in these patients, further adds to the mortality. Currently used prognostication indices have their own set of limitations. We evaluated IAP at intensive care unit (ICU) admission as a predictor of mortality in severe acute pancreatitis (SAP).

**Methods.** A retrospective analysis of 50 patients with SAP admitted to the ICU of a tertiary-care Indian institute over a period of 3 years was done. Data relating to demographic profile, cause of pancreatitis, ICU admission, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, IAP, interventions instituted and mortality were analysed.

**Results.** Biliary stones (38%) were the most common cause of acute pancreatitis. Survivors differed from non-survivors with respect to organ failure, APACHE II and SOFA scores and IAP on admission. There was a significant correlation between IAP on ICU admission and admission SOFA ( $r=0.56$ ,  $p<0.001$ ) and APACHE II ( $r=0.54$ ,  $p<0.001$ ) in predicting mortality. Patients with elective admission had a mortality rate of 53% (20/38) compared to 83% (10/12) for those admitted as emergencies. Analysis of receiver operating characteristic curves for detecting mortality revealed an area under the curve of 0.915 (95% confidence interval (CI) 0.83 - 0.99) for IAP, 0.826 (95% CI 0.71 - 0.93) for SOFA, and 0.831 (95% CI 0.71 - 0.94) for APACHE II.

**Conclusion.** IAP at ICU admission is a useful predictor of severity of illness and mortality in SAP.

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Acute pancreatitis (AP) is an inflammatory disease of the pancreas with a mild and self-limiting course in 80% of patients. However, the remainder may develop a severe form of the disease known as

severe acute pancreatitis (SAP), characterised by multiple organ dysfunction and higher mortality.<sup>1</sup> High Acute Physiology and Chronic Health Evaluation II (APACHE II) and/or Sequential Organ

Failure Assessment (SOFA) scores, presence of intra-abdominal hypertension (IAH) and extent of infected pancreatic necrosis are some of the factors known to adversely affect prognosis in SAP.<sup>2</sup> Early identification of patients at risk of IAH and implementation of steps to halt its progression to abdominal compartment syndrome (ACS) may reduce mortality.<sup>3</sup>

In this study, we attempted to analyse whether intra-abdominal pressure (IAP) on admission to the intensive care unit (ICU) is useful in predicting severity and mortality in patients with SAP.

## Material and methods

### Setting

The study was conducted in a 12-bed medical-surgical general ICU in a tertiary-care teaching hospital in India with a 900-bed capacity. The ICU manages 300 - 400 critically ill patients annually.

### Study population

After approval from the ethics committee of the institute, we retrospectively analysed records of patients with SAP admitted to the ICU over a period of 3 years (2007 - 2010).

### Exclusion criteria

Postoperative patients with an open abdomen, with bladder pathology or for whom IAP data on admission to ICU were not available were excluded from the study.

### Definitions

Patients with AP associated with evidence of extrapancreatic organ failure (particularly a systolic blood pressure of <90 mmHg, arterial partial pressure of oxygen (PaO<sub>2</sub>) ≤60 mmHg, serum creatinine >176.8 μmol/l after rehydration, gastrointestinal bleeding (>500 ml in 24 hours), platelets <100×10<sup>9</sup>/l, serum fibrinogen <3 μmol/l, fibrin split products >80 mg/l, serum calcium ≤1.9 mmol/l) and/or local complications (pancreatic necrosis, abscess or pseudocyst) were considered to have SAP.<sup>4</sup>

At ICU admission, severity of illness was assessed using the APACHE II score<sup>5</sup> and SOFA score.<sup>6</sup>

Organ dysfunction was defined according to the recommendations of the 1991 consensus conference of the American College of Chest Physicians/Society of Critical Care Medicine.<sup>7</sup> Organ failure was defined as a SOFA score ≥3 for each organ described.<sup>6</sup>

As per the World Society of the Abdominal Compartment Syndrome, a sustained intra-abdominal pressure (IAP) exceeding 12 mmHg was considered to be intra-abdominal hypertension (IAH). When a sustained IAP ≥20 mmHg was associated with new organ dysfunction or failure, it was classified as ACS.<sup>8</sup>

### IAP measurement

Intra-bladder pressure was measured as a proxy of IAP using the revised closed-system repeated-measurement technique.<sup>9</sup> In this technique, a ramp with three stopcocks was inserted in the drainage tubing connected to a Foley catheter. A standard infusion set was connected to a bag of saline and attached to the first stopcock. A 50 ml syringe was connected to the second stopcock, and the third stopcock was connected to a pressure transducer via rigid tubing. The system was flushed with saline to remove air, and the

pressure transducer was zeroed at the level of the iliac crest in the mid-axillary line with the sedated patient in a supine position.<sup>8</sup> The bladder was then completely emptied and the urinary drainage tubing clamped distal to the ramp device. Twenty-five millilitres of saline at room temperature was aspirated from the bag into the syringe and then instilled into the bladder.<sup>10</sup> After opening the stopcocks in line with the pressure transducer, measurement was recorded at end-expiration after 30 - 60 seconds.<sup>8</sup> Values at admission were collected for all patients after achieving a Richmond Agitation Sedation Scale of -2 to -3.<sup>11</sup>

### Data collection

Computerised database and patient records were used for data collection. We recorded demographic profile, cause of pancreatitis, APACHE II score, SOFA score and IAP value at admission to the ICU, any interventions (non-surgical v. surgical) done, and in-hospital mortality. The data for survivors and non-survivors were then compared.

### Statistics

The data were described as proportions/mean (standard deviation (SD)), as appropriate. The mean values in the two groups (survivors v. non-survivors) were compared using a two-sample *t*-test, or the Mann-Whitney test if the data did not satisfy assumption of normalcy. The significance of the difference in the proportion between two categorical variables was tested by using the chi-square test or Fisher's exact test, and a *p*-value ≤0.05 was considered significant.

Logistic regression analysis was used to estimate the best cut-off point of IAP for prediction of mortality at ICU admission. A curve showing the sensitivity/specificity against probability cut-off was drawn from the model. Detailed sensitivity and specificity were calculated taking each observed value as cut-off point for the prediction of mortality, and a value with the minimum difference between sensitivity and specificity was taken as the best cut-off.

Detailed sensitivity and specificity were calculated for the prediction of mortality. Predictive accuracy of all three parameters studied was compared by measuring the area under the receiver operating curve (AUC), and Pearson's correlation coefficient was used to determine the correlation between the three parameters. All calculations were done using statistical software Stata 10.1 (Stata Corp Inc., College Station, TX, USA).

## Results

During the study period, a total of 406 patients were admitted to our ICU, of whom 53 (13%) had SAP. Three patients were excluded; one was a postoperative patient with an open abdomen, and in 2 cases we could not find the admission IAP values. We were therefore only able to analyse data for 50 patients, all of whom fulfilled the Atlanta criteria for SAP.

Twenty of these 50 patients (40%) survived. The most common cause of AP observed in this study was biliary stones (38%), followed by alcohol abuse (36%); 2 patients had both. In the remaining 22% of cases we were unable to find any cause for the pancreatitis (Table 1).

Of the study population, 38 (76%) were intra-hospital transfers who had received consultations from our outreach team at least

**Table 1. Demographic variables, aetiology, organ failure (SOFA  $\geq 3$ ) and scores at ICU admission**

Demographic variables	Survivors (n=20)	Non-survivors (n=30)	p-value
Median age (years) (range)	34 (18 - 65)	44 (23 - 64)	0.22
Male:female ratio	3:1	5:1	0.47
Aetiology (alcoholic:gallstone)	7:5	11:14	0.24
Days of pancreatitis before ICU admission (median)	10	6	0.68
Type of admission (elective/emergency)	18:2	20:10	0.09
Comorbidities, n			
Diabetes	6	7	0.37
Hypertension	4	11	0.47
Organ failure, n			
Respiratory	13	30	0.001*
Cardiovascular	6	27	0.001*
Central nervous system	0	2	NS
Liver	0	7	0.05*
Renal	2	17	0.01*
Coagulation	1	11	0.05*
Scores at ICU admission, mean (SD)			
APACHE II	12.7 (4.7)	19.3 (5.7)	$\leq 0.001^*$
SOFA	4.9 (2.5)	9.7 (4.3)	$\leq 0.001^*$
IAP (mmHg)	13.1 (2.2)	17.9 (2.8)	$\leq 0.001^*$

\* $p < 0.05$  = significant.

once before being transferred to our ICU. Twelve patients (24%) were referred to us as emergencies (pulseless and/or gasping) from either inter- or intra-hospital units with no previous referrals. The former category of patients was termed elective admissions and the latter emergency ICU admissions. Occasionally even elective cases could not be transferred timeously to the ICU because of non-availability of beds. Mortality was 53% (20/38) among elective admissions as opposed to 83% (10/12) among emergency admissions.

In decreasing order, rates of organ failure (either alone or in combination) at ICU admission were respiratory (86%), cardiovascular (66%), renal (38%), coagulation (24%), hepatic (14%) and neurological (4%). Significant differences were observed between the survivors and the non-survivors with regard to the prevalence of respiratory ( $p=0.001$ ), cardiovascular ( $p=0.001$ ), renal ( $p=0.01$ ), coagulation ( $p=0.05$ ) and hepatic ( $p=0.05$ ) failure (Table 1).

The overall prevalence of failure of one or more extrapancreatic organs on admission (SOFA score  $\geq 3$ ) was 75% (15/20) in the patients who survived but 100% (30/30) in non-survivors.

The APACHE II score, SOFA score and IAP on ICU admission were significantly higher in the non-survivors than in the survivors (Table 1).

All non-survivors had IAH, while among the survivors it was present in 80%. Ten of the 30 non-survivors (33.3%) had ACS at ICU admission.

There was a statistically significant correlation ( $r$ ) between admission IAP and admission SOFA ( $r=0.56$ ,  $p < 0.001$ ) and APACHE II scores ( $r=0.54$ ,  $p < 0.001$ ) in predicting mortality.

Analysis of the receiver operating characteristic (ROC) curves for detecting mortality revealed an AUC of 0.91 (95% confidence interval (CI) 0.83 - 0.99) for IAP, 0.82 (CI 0.71 - 0.93) for SOFA, and 0.83 (95% CI 0.71 - 0.94) for APACHE II (Fig. 1). In addition, pairwise comparative significance between the three parameters

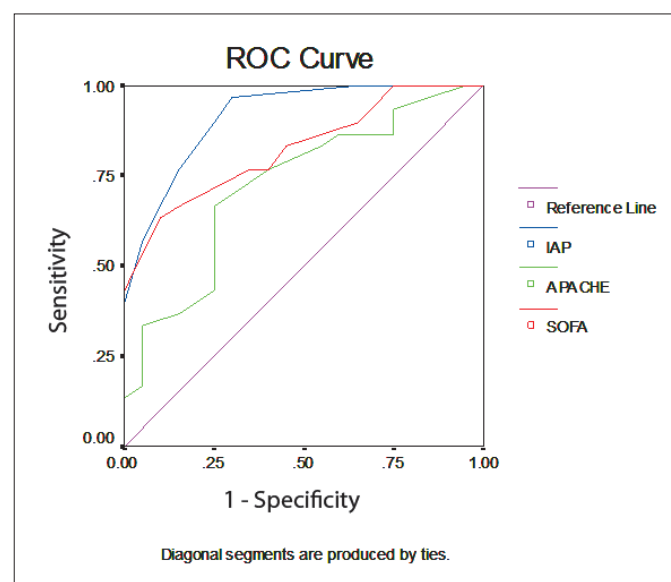


Fig. 1. ROC curves for detecting mortality taking IAP and APACHE II and SOFA scores on admission.

**Table 2. Area under the receiver operating characteristic curve for IAP, APACHE II and SOFA at ICU admission for detecting mortality and pairwise significance level for AUROC**

Studied parameters	AUROC (95% CI)
IAP	0.91 (0.83 - 0.99)
APACHE II	0.72 (0.58 - 0.87)
SOFA	0.82 (0.71 - 0.93)
Parameter pairs	p-value
SOFA-APACHE II	0.24
SOFA- IAP	0.15
IAP-APACHE II	0.03*

$p \leq 0.05$  = significant.

AUROC = area under the receiver operating characteristic curve.

revealed IAP at ICU admission to be statistically better than APACHE II in predicting mortality, but equivalent to the SOFA score (Table 2).

The cut-off value of admission IAP in predicting mortality was found to be 16 mmHg, with a sensitivity of 77% (95% CI 57.72 - 90.07), a specificity of 85% (95% CI 62.11 - 96.79), a positive predictive value (PPV) of 88% (95% CI 69.85 - 97.55), a negative predictive value (NPV) of 71% (95% CI 48.91 - 87.38) and an accuracy index of 80%.

## Discussion

We evaluated admission IAP in comparison with admission APACHE II and SOFA scores as a predictor of severity and mortality in SAP.

The incidence of SAP in our ICU was 13%, and cholelithiasis was the most common cause.<sup>12-14</sup> Neither gender nor cause of pancreatitis were found to be of prognostic significance, as was also found by Doley *et al.*<sup>13</sup>

The degree of organ dysfunction is higher in patients with higher IAPs, and as IAP rises it adversely affects every organ system in the body, directly or indirectly.<sup>15</sup> Pulmonary dysfunction secondary to rising IAP is a major component of multi-organ failure, contributing to higher mortality in SAP.<sup>16</sup> Respiratory dysfunction was the most frequent systemic complication in our study, followed by the cardiovascular system (66%).<sup>17</sup> We noted a comparatively high rate of cardiovascular dysfunction, which may indicate inadequate and/or delayed efforts at resuscitation before the patient was admitted to our ICU, and contributed to mortality.<sup>16</sup> The reported incidence of renal involvement in SAP varies widely.<sup>17</sup> Of our patients, 38% had renal failure, and its contribution to mortality was in agreement with other studies.<sup>16</sup>

Several scoring systems have been developed to predict outcome in patients with pancreatitis, of which the APACHE II and SOFA scores have stood the test of time and been found to be reasonably accurate.<sup>12</sup> The APACHE II score provides numerous advantages, such as freedom of calculation at admission and during ICU stay. It is therefore a useful tool not only for monitoring disease progression but also for guiding therapy. However, it is very complex,<sup>18</sup> in addition to being less accurate on admission than after 48 hours

of ICU stay.<sup>19</sup> SOFA, on the other hand, is a simple, reliable and recommended scoring system for assessing disease progression and prognosis in the ICU, but rates of inaccurate recordings tend to be high (52%).<sup>20</sup> Like many other researchers,<sup>21,22</sup> we observed higher mean APACHE II and SOFA scores at ICU admission in non-survivors compared with survivors. It is well known that IAH adversely affects prognosis both directly and indirectly by promoting bacterial translocation, infected pancreatic necrosis and extrapancreatic organ failure in SAP.<sup>21,23</sup> In contrast to the study by Rosas *et al.*,<sup>24</sup> who found maximal IAP to be an easy and useful prognostic marker in pancreatitis, we focused on the first IAP measurement on admission to the ICU, as IAP may reach its maximum at a later stage when the patient's condition has deteriorated to the extent that intervention is futile.<sup>24</sup> For any variable to be a useful predictor of mortality, its timely detection is vitally important, as interventions can then be targeted early to reduce morbidity and mortality. The combination of IAH and multiple organ dysfunction results in excessive mortality. We found significantly higher IAP at ICU admission among non-survivors than survivors.<sup>21</sup>

Depending on the threshold value (IAP  $\geq 12$  or  $\geq 15$  mmHg), reported prevalences of IAH vary between 40% and 84% in SAP.<sup>21,25</sup> In our study, IAH (IAP  $\geq 12$  mmHg) and ACS were present in 72% and 20%, respectively, which are lower figures than those reported by Keskinen *et al.*<sup>21</sup> Although 80% of our survivors had IAH at ICU admission, none of them presented with ACS. In contrast, all non-survivors had IAH at admission and 33.3% (10/30) had ACS. A strong correlation was observed between IAP and APACHE II and SOFA scores as mortality predictors at ICU admission in our study. This finding was supported by ROC curve analysis, which showed the AUC for IAP to be equivalent to that for SOFA and better than that for APACHE II, both of which are well-established predictors. Furthermore, the best cut-off value for admission IAP in predicting mortality was 16 mmHg, with sensitivity, specificity, PPV, NPV and accuracy comparable to those for APACHE II (cut-off  $\geq 9$ ),<sup>26</sup> SOFA (cut-off  $>4$ )<sup>27</sup> and IAP (cut-off 18 mmHg).<sup>28</sup>

Both operative and non-operative IAP reduction strategies have been shown to improve survival in IAH/ACS.<sup>3</sup> Ultrasound-/computed tomography-guided interventions such as percutaneous catheter drainage (PCD) of pancreatic and peripancreatic collections in IAH/ACS, and laparotomy with or



without laparostomy when the IAP is  $\geq 20$  mmHg despite PCD, are advocated.<sup>29</sup> Postponing pancreatic necrosectomy, the gold-standard therapy, beyond the 4th week of disease is advised in order to allow the immune system to better demarcate the necrotic area.<sup>30</sup> Non-operative strategies such as PCD and conservative medical therapies such as sedation, analgesia, neuromuscular blockade, nasogastric and rectal decompression and prokinetics were utilised in more than 70% of our patients,<sup>31</sup> but the majority (>50%) nevertheless required surgical intervention later on.<sup>32</sup> All the non-survivors required PCD and/or surgical intervention. One patient with ACS, who underwent surgical intervention within 2 weeks of SAP, died of his illness.

Reported mortality rates in ICU patients with SAP are high and variable. In our series the overall mortality was 60%, which although high is comparable to rates reported by other researchers.<sup>17,33</sup> Emergency admissions had higher mortality (83%) compared with the 53% for elective admissions. High APACHE II and SOFA scores indicate significantly established extrapancreatic organ involvement in all our patients, even before ICU admission.<sup>12</sup> In addition, absence of even basic intensive care support in the peripheral hospitals, delayed ICU transfers and lack of optimally trained teams to transport the critically ill could all have contributed to the higher mortality rate.

Our study limitations include small sample size from a single centre, retrospective study design, and missing data on the studied parameters prior to ICU admission. In addition, most of our patients were referred to us in a late stage of the disease, and results may be different for patients with pancreatitis admitted to the ICU earlier. Despite these limitations, we still evaluated IAP at ICU admission, since APACHE II and SOFA scores are also computed at this time, irrespective of the stage of the disease, and are considered of paramount importance for prognostication in the ICU.

## Conclusions

In conclusion, evaluation of IAP is rapid, reproducible, inexpensive and minimally invasive, and continues to be useful as an ideal predictor of mortality.<sup>34</sup> Irrespective of the duration of SAP, IAP at ICU admission appears to be a useful tool to predict severity of illness and mortality. An IAP cut-off value of 16 mmHg may help in distinguishing between patients who are and are not likely to survive. Further, we recommend a large, multicentric study to conclusively establish the predictive power of IAP in SAP, and whether interventions known to reduce IAP, especially below 16 mmHg, can alter the ultimate outcome.

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